The Chemistry of Dienes and Polyenes. Volume 1
Edited by Zvi Rappoport

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The chemistry of
dienes and polyenes

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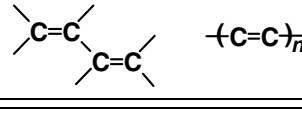

The chemistry of **dienes and polyenes**

Volume 1

Edited by

ZVI RAPPOPORT

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To

Judith and Zeev

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Foreword

In recent years *The Chemistry of Functional Groups* series has included three volumes on composite functional groups in which a C=C double bond was attached to another group. *The chemistry of enones* (edited by S. Patai and Z. Rappoport) appeared in 1989; *The chemistry of enols* (edited by Z. Rappoport) appeared in 1990 and *The chemistry of enamines* (edited by Z. Rappoport) appeared in 1994. We believe that the time has arrived for a book dealing with the combination of C=C double bonds, namely dienes and polyenes. The two double bonds can be conjugated, and conjugated dienes have a chemistry of their own, but even non-conjugated dienes show certain reactions that involve both double bonds. Allenes and cumulenes, which represent a different combination of the double bonds were treated in *The chemistry of ketenes, allenes and related compounds*, edited by S. Patai in 1980.

The present volume contains 21 chapters written by experts from 11 countries and is the first volume of a set of two. We hope that the missing topics will be covered in the second volume which is planned to appear in 2–3 years' time.

The present volume deals with the properties of dienes, described in chapters on theory, structural chemistry, conformations, thermochemistry and acidity and in chapters dealing with UV and Raman spectra, with electronic effects and the chemistry of radical cations and cations derived from them. The synthesis of dienes and polyenes, and various reactions that they undergo with radicals, with oxidants, under electrochemical conditions, and their use in synthetic photochemistry are among the topics discussed. Systems such as radialenes, or the reactions of dienes under pressure, comprise special topics of these functional groups.

The literature coverage is up to 1995 or 1996.

I would be grateful to readers who call my attention to mistakes in the present volume.

Jerusalem
August, 1996

ZVI RAPPOPORT

The Chemistry of Functional Groups
Preface to the series

The series 'The Chemistry of Functional Groups' was originally planned to cover in each volume all aspects of the chemistry of one of the important functional groups in organic chemistry. The emphasis is laid on the preparation, properties and reactions of the functional group treated and on the effects which it exerts both in the immediate vicinity of the group in question and in the whole molecule.

A voluntary restriction on the treatment of the various functional groups in these volumes is that material included in easily and generally available secondary or tertiary sources, such as Chemical Reviews, Quarterly Reviews, Organic Reactions, various 'Advances' and 'Progress' series and in textbooks (i.e. in books which are usually found in the chemical libraries of most universities and research institutes), should not, as a rule, be repeated in detail, unless it is necessary for the balanced treatment of the topic. Therefore each of the authors is asked not to give an encyclopaedic coverage of his subject, but to concentrate on the most important recent developments and mainly on material that has not been adequately covered by reviews or other secondary sources by the time of writing of the chapter, and to address himself to a reader who is assumed to be at a fairly advanced postgraduate level.

It is realized that no plan can be devised for a volume that would give a complete coverage of the field with no overlap between chapters, while at the same time preserving the readability of the text. The Editors set themselves the goal of attaining reasonable coverage with moderate overlap, with a minimum of cross-references between the chapters. In this manner, sufficient freedom is given to the authors to produce readable quasi-monographic chapters.

The general plan of each volume includes the following main sections:

(a) An introductory chapter deals with the general and theoretical aspects of the group.

(b) Chapters discuss the characterization and characteristics of the functional groups, i.e. qualitative and quantitative methods of determination including chemical and physical methods, MS, UV, IR, NMR, ESR and PES — as well as activating and directive effects exerted by the group, and its basicity, acidity and complex-forming ability.

(c) One or more chapters deal with the formation of the functional group in question, either from other groups already present in the molecule or by introducing the new group directly or indirectly. This is usually followed by a description of the synthetic uses of the group, including its reactions, transformations and rearrangements.

(d) Additional chapters deal with special topics such as electrochemistry, photochemistry, radiation chemistry, thermochemistry, syntheses and uses of isotopically labelled compounds, as well as with biochemistry, pharmacology and toxicology. Whenever applicable, unique chapters relevant only to single functional groups are also included (e.g. 'Polyethers', 'Tetraaminoethylenes' or 'Siloxanes').

This plan entails that the breadth, depth and thought-provoking nature of each chapter will differ with the views and inclinations of the authors and the presentation will necessarily be somewhat uneven. Moreover, a serious problem is caused by authors who deliver their manuscript late or not at all. In order to overcome this problem at least to some extent, some volumes may be published without giving consideration to the originally planned logical order of the chapters.

Since the beginning of the Series in 1964, two main developments have occurred. The first of these is the publication of supplementary volumes which contain material relating to several kindred functional groups (Supplements A, B, C, D, E, F and S). The second ramification is the publication of a series of 'Updates', which contain in each volume selected and related chapters, reprinted in the original form in which they were published, together with an extensive updating of the subjects, if possible, by the authors of the original chapters. A complete list of all above mentioned volumes published to date will be found on the page opposite the inner title page of this book. Unfortunately, the publication of the 'Updates' has been discontinued for economic reasons.

Advice or criticism regarding the plan and execution of this series will be welcomed by the Editors.

The publication of this series would never have been started, let alone continued, without the support of many persons in Israel and overseas, including colleagues, friends and family. The efficient and patient co-operation of staff-members of the publisher also rendered us invaluable aid. Our sincere thanks are due to all of them.

The Hebrew University
Jerusalem, Israel

SAUL PATAI
ZVI RAPPOPORT

Contents

List of abbreviations used

Ac	acetyl (MeCO)
acac	acetylacetone
Ad	adamantyl
AIBN	azoisobutyronitrile
Alk	alkyl
All	allyl
An	anisyl
Ar	aryl
Bz	benzoyl (C_6H_5CO)
Bu	butyl (also *t*-Bu or Bu^t)
CD	circular dichroism
CI	chemical ionization
CIDNP	chemically induced dynamic nuclear polarization
CNDO	complete neglect of differential overlap
Cp	η^5-cyclopentadienyl
Cp*	η^5-pentamethylcyclopentadienyl
DABCO	1,4-diazabicyclo[2.2.2]octane
DBN	1,5-diazabicyclo[4.3.0]non-5-ene
DBU	1,8-diazabicyclo[5.4.0]undec-7-ene
DIBAH	diisobutylaluminium hydride
DME	1,2-dimethoxyethane
DMF	*N*,*N*-dimethylformamide
DMSO	dimethyl sulphoxide
ee	enantiomeric excess
EI	electron impact
ESCA	electron spectroscopy for chemical analysis
ESR	electron spin resonance
Et	ethyl
eV	electron volt

Fc	ferrocenyl
FD	field desorption
FI	field ionization
FT	Fourier transform
Fu	furyl(OC_4H_3)
GLC	gas liquid chromatography
Hex	hexyl(C_6H_{13})
c-Hex	cyclohexyl(C_6H_{11})
HMPA	hexamethylphosphortriamide
HOMO	highest occupied molecular orbital
HPLC	high performance liquid chromatography
i-	iso
Ip	ionization potential
IR	infrared
ICR	ion cyclotron resonance
LAH	lithium aluminium hydride
LCAO	linear combination of atomic orbitals
LDA	lithium diisopropylamide
LUMO	lowest unoccupied molecular orbital
M	metal
M	parent molecule
MCPBA	*m*-chloroperbenzoic acid
Me	methyl
MNDO	modified neglect of diatomic overlap
MS	mass spectrum
n	normal
Naph	naphthyl
NBS	*N*-bromosuccinimide
NCS	*N*-chlorosuccinimide
NMR	nuclear magnetic resonance
Pc	phthalocyanine
Pen	pentyl(C_5H_{11})
Pip	piperidyl($C_5H_{10}N$)
Ph	phenyl
ppm	parts per million
Pr	propyl (also *i*-Pr or Pr^i)
PTC	phase transfer catalysis or phase transfer conditions
Pyr	pyridyl (C_5H_4N)

R	any radical
RT	room temperature
s-	secondary
SET	single electron transfer
SOMO	singly occupied molecular orbital
t-	tertiary
TCNE	tetracyanoethylene
TFA	trifluoroacetic acid
THF	tetrahydrofuran
Thi	thienyl(SC_4H_3)
TLC	thin layer chromatography
TMEDA	tetramethylethylene diamine
TMS	trimethylsilyl or tetramethylsilane
Tol	tolyl(MeC_6H_4)
Tos or Ts	tosyl(*p*-toluenesulphonyl)
Trityl	triphenylmethyl(Ph_3C)
Xyl	xylyl($Me_2C_6H_3$)

In addition, entries in the 'List of Radical Names' in *IUPAC Nomenclature of Organic Chemistry*, 1979 Edition. Pergamon Press, Oxford, 1979, p. 305–322, will also be used in their unabbreviated forms, both in the text and in formulae instead of explicitly drawn structures.

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CHAPTER **1**

Contribution of quantum chemistry to the study of dienes and polyenes

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I. INTRODUCTION

Dienes and polyenes have been a subject of great interest due to their important role in biology, materials science and organic synthesis. The mechanism of vision involves *cis–trans* photoisomerization of 11-*cis*-retinal, an aldehyde formed from a linear polyene. Moreover, this kind of molecule exhibits high linear and non-linear electrical and optical properties. Short polyenes are also involved in pericyclic reactions, one of the most important classes of organic reactions.

A knowledge of the structure and properties of dienes and polyenes is necessary to understand the mechanisms of these processes. Quantum chemical calculations can be very helpful to achieve this goal. Several reviews have discussed the theoretical contributions to different aspects of dienes and polyenes[1–5]. Orlandi and coworkers[1] have reviewed the studies devoted to the ground state structure and spectra of linear polyenes. The molecular electrical properties of several organic molecules, including polyenes, have been considered by André and Delhalle[2]. Finally, the mechanism of pericyclic reactions has been discussed by Houk and coworkers[3,4] and Dewar and Jie[5].

The aim of this chapter is to present the most recent theoretical contributions to the study of structure, properties and reactivity of dienes and polyenes. Earlier stages in these areas are covered in the above-mentioned reports[1–5].

In this chapter we do not intend to carry out an exhaustive review of all the theoretical studies related to dienes and polyenes. Instead, we have selected those studies which we think may illustrate the present status of quantum chemical calculations in the study of these compounds. We will emphasize the significance and validity of the results rather than the methodological aspects. We will focus our attention on *ab initio* calculations, although some references to semiempirical results will also be included. In order to make the reading more comprehensive to the nontheoretician, we will briefly present in the next section a survey of the most common theoretical methods. In Section III we will present the studies dealing with the ground state structures and vibrations of linear polyenes. The excited states structures and electronic spectra will be considered in Section IV. Section V will be devoted to electrical and optical properties. Finally, the Diels–Alder reaction will be covered in Section VI, as a significant example of chemical reaction involving dienes.

II. SURVEY OF THEORETICAL METHODS

The purpose of most quantum chemical methods is to solve the time-independent Schrödinger equation. Given that the nuclei are much more heavier than the electrons, the nuclear and electronic motions can generally be treated separately (Born–Oppenheimer approximation). Within this approximation, one has to solve the electronic Schrödinger equation. Because of the presence of electron repulsion terms, this equation cannot be solved exactly for molecules with more than one electron.

The most simple approach is the Hartree–Fock (HF) self-consistent field (SCF) approximation, in which the electronic wave function is expressed as an antisymmetrized product of one-electron functions. In this way, each electron is assumed to move in the average field of all other electrons. The one-electron functions, or spin orbitals, are taken as a product of a spatial function (molecular orbital) and a spin function. Molecular orbitals are constructed as a linear combination of atomic basis functions. The coefficients of this linear combination are obtained by solving iteratively the Roothaan equations.

The number and type of basis functions strongly influence the quality of the results. The use of a single basis function for each atomic orbital leads to the minimal basis set. In order to improve the results, extended basis sets should be used. These basis sets are named double-ζ, triple-ζ, etc. depending on whether each atomic orbital is described by two, three, etc. basis functions. Higher angular momentum functions, called polarization functions, are also necessary to describe the distortion of the electronic distribution due

to the bonding. Although increasing the size of the basis set is expected to improve the description of the system, the exact result will never be achieved with such a monoconfigurational wave function. This is due to the lack of electron correlation in the Hartree–Fock approximation.

Two different correlation effects can be distinguished. The first one, called dynamical electron correlation, comes from the fact that in the Hartree–Fock approximation the instantaneous electron repulsion is not taken into account. The nondynamical electron correlation arises when several electron configurations are nearly degenerate and are strongly mixed in the wave function.

Several approaches have been developed to treat electron correlation. Most of these methods start from a single-reference Hartree–Fock wave function. In the configuration interaction (CI) method, the wave function is expanded over a large number of configurations obtained by exciting electrons from occupied to unoccupied orbitals. The coefficients of such an expansion are determined variationally. Given that considering all possible excitations (Full CI) is not computationally feasible for most of the molecules, the expansion is truncated. The most common approach is CISD, where only single and double excitations are considered. The Møller–Plesset (MP) perturbation theory is based on a perturbation expansion of the energy of the system. The nth-order treatment is denoted MPn. MP2 is the computationally cheapest treatment and MP4 is the highest order normally used. Finally, other methods for including dynamical electron correlation are those based on the coupled cluster (CC) approach.

When the HF wave function gives a very poor description of the system, i.e. when nondynamical electron correlation is important, the multiconfigurational SCF (MCSCF) method is used. This method is based on a CI expansion of the wave function in which both the coefficients of the CI and those of the molecular orbitals are variationally determined. The most common approach is the Complete Active Space SCF (CASSCF) scheme, where the user selects the chemically important molecular orbitals (active space), within which a full CI is done.

An alternative approach to conventional methods is the density functional theory (DFT). This theory is based on the fact that the ground state energy of a system can be expressed as a functional of the electron density of that system. This theory can be applied to chemical systems through the Kohn–Sham approximation, which is based, as the Hartree–Fock approximation, on an independent electron model. However, the electron correlation is included as a functional of the density. The exact form of this functional is not known, so that several functionals have been developed.

The inclusion of electron correlation is generally necessary to get reliable results. However, the use of methods that extensively include electron correlation is limited by the computational cost associated with the size of the systems.

Even *ab initio* Hartree–Fock methods can become very expensive for large systems. In these cases, the semiempirical methods are the ones generally applied. In these methods, some of the integrals are neglected and others are replaced using empirical data.

Up to now, we have only considered the computation of the electronic energy of the system. To get a thorough description of the structure of a molecule, it is necessary to know the potential energy surface of the system, i.e. how the energy depends on the geometry parameters. Optimization techniques allow one to locate stationary points, both minima and saddle points on the potential energy surface. These methods require the derivatives of the energy with respect to the geometry parameters. Second derivatives are necessary to obtain the harmonic frequencies. Higher-order derivatives are much more difficult to obtain.

In this section we have surveyed the most common methods of quantum chemistry on which are based the studies presented in the next sections. A more extensive description of these methods can be found in several excellent textbooks and reports[6–11].

III. GROUND STATE STRUCTURE AND VIBRATIONAL SPECTRA

The structure of the ground state of linear polyenes has been the subject of several theoretical studies[12–37]. Molecular geometries and vibrational frequencies for polyenes up to $C_{18}H_{20}$ have been reported. Much emphasis has been placed on the calculation of force constants that can be used in the construction of force fields.

We will first discuss results corresponding to 1,3-butadiene. This molecule is the simplest of the series, so that several levels of calculation have been used, thus permitting one to establish the minimum requirements of the theoretical treatment. The extension to trienes, tetraenes and longer polyenes will be discussed in further subsections.

A. Butadiene

The ground state structure of butadiene has been extensively studied using different kinds of theoretical methods[19,21,23,31,34,36]. For this molecule, several conformations associated with rotation around the single C−C bond are possible. Experimental evidence shows that the most stable one is the planar *s-trans* conformation. All theoretical calculations agree with this fact.

1. Geometry

Figure 1 shows schematically the structure of *s-trans*-1,3-butadiene. Several studies show that proper geometry parameters are only obtained with a basis set of at least double-ζ quality, including polarization functions for carbon atoms. Table 1 presents a selection of the results obtained at several levels of calculation, using a basis set of this kind.

At the HF level, the value of the C=C bond length is clearly underestimated. The inclusion of electron correlation at different levels of calculation leads to values in closer agreement with experiment. The value of the C−C bond length is less sensitive to the inclusion of electron correlation. As a consequence of this fact, the CC bond alternation (the difference between CC single and double bond lengths) is overestimated at the HF level. The inclusion of dynamical electron correlation through MP*n* calculations corrects this error. A very similar result is obtained at the CASSCF level of calculation[31].

The values of the C−H bond lengths also change with the inclusion of electron correlation, leading to a better agreement with the experimental values. On the other hand, the values of the CCC and CCH bond angles are less sensitive to the level of calculation. These results show that the inclusion of electron correlation is necessary to obtain geometry parameters within the range of the experimental results. However, some of the geometry parameters are already well reproduced at lower levels of calculation.

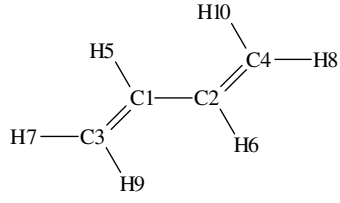


FIGURE 1. Schematic representation of the structure of *s-trans*-1,3-butadiene

TABLE 1. Geometry[a] (in Å and degrees) of *s-trans*-1,3-butadiene at several levels of calculation[b]

	HF[c]	MP2[c]	MP3[c]	MP4[d]	exp[e]
C1C3	1.323	1.342	1.338	1.349	1.337–1.349
C1C2	1.468	1.456	1.463	1.464	1.463–1.467
C1H5	1.078	1.090	1.090	1.094	1.093–1.108
C3H7	1.075	1.084	1.085	1.089	1.093–1.108
C3H9	1.077	1.086	1.087	1.091	1.093–1.108
C1C2C4	124.1	123.7	123.7	123.8	122.8–124.4
C1C2H6	116.6	116.7	116.5	116.5	114.7–117.7
C2C4H10	121.7	121.4	121.6	121.5	119.5–120.9
C2C4H8	121.1	121.7	121.8	121.8	119.5–102.5

[a] See Figure 1 for numeration.
[b] A basis set of double-ζ+polarization quality is used in all cases.
[c] Reference 23.
[d] Reference 35.
[e] Reference 38.

TABLE 2. Selected vibrational frequencies (cm^{-1}) of *s-trans*-1,3-butadiene computed at several levels of calculation[a]

Symmetry	Description	HF[b]	MP2[b]	MP4[c]	exp[d]
a_g	CH str	3242	3200	3165	3025
	CH_2 str	3325	3217	3149	3014
	C=C str	1898	1745	1721	1644
	C−C str	1326	1265	1250	1206
	CCC bend	550	522	515	513
b_u	CH str	3343	3207	3165	3062
	CH_2 str	3331	3216	3156	2986
	C=C str	1818	1678	1657	1579
	CCC bend	319	298	295	301
a_u	CCCC tors	167	160	160	163[e]

[a] A basis set of double-ζ+polarization quality is used in all cases.
[b] Reference 23.
[c] Reference 35.
[d] Reference 39.
[e] Reference 40.

2. Vibrational frequencies and force field

Harmonic vibrational frequencies for *s-trans* butadiene have also been calculated at several levels of calculation[19,21,23,24,31,35]. Table 2 presents the computed values of some of the vibrational frequencies.

HF frequencies are generally larger than the corresponding experimental data. The inclusion of electron correlation improves the results, but the theoretical frequencies are still higher than the experimental ones. Both the introduction of electron correlation and the size of the basis set seem to be important in order to obtain reliable results.

In order to obtain better agreement between theory and experiment, computed frequencies are usually scaled. Scale factors can be obtained through multiparameter fitting towards experimental frequencies. In addition to limitations on the level of calculation, the discrepancy between computed and experimental frequencies is also due to the fact that experimental frequencies include anharmonicity effects, while theoretical frequencies are computed within the harmonic approximation. These anharmonicity effects are implicitly considered through the scaling procedure.

TABLE 3. Selected force constants (mdyn $Å^{-1}$) computed for *s-trans* butadiene at several levels of calculation[a]

	HF[a]	MP2[b]	MP4[c]	exp[d]
C=C	11.259	9.591	9.263	8.886
C−C	5.859	5.687	5.491	5.428
C=C/C−C	0.398	0.414	0.409	
C=C/C=C	−0.093	−0.110	−0.116	

[a]A basis set of double-ζ+polarization quality is used in all cases.
[b]Reference 23.
[c]Reference 35.
[d]Reference 39.

A knowledge of the force field for the ground state of a molecule is essential for understanding its static and dynamical properties. The characterization of the potential surfaces from vibrational data alone is not possible for most molecules, even when the harmonic approximation is assumed. The large number of adjustable parameters in the force constants matrix requires information from different isotopic species which are very difficult to obtain in a highly purified form for many molecules. The number of parameters can be reduced by truncation of the off-diagonal interaction constants. However, this approximation introduces great uncertainty in the derivation of accurate force fields. Force constants can be computed from theoretical calculations without any assumption regarding the off-diagonal coupling terms. Scaled force constants can be generally transferred from one molecule to another and allow the construction of accurate force fields. These force fields are necessary to interpret the vibrational spectra of more complex molecules.

Table 3 presents the values of the force constants corresponding to the C skeleton vibrations of *s-trans*-1,3-butadiene obtained at several levels of calculation. The computed values are very sensitive to the inclusion of electron correlation. Stretching C=C and C−C force constants decrease when electron correlation is taken into account. This effect is generally larger for basis sets without polarization functions than for those with polarization functions[23]. On the contrary, the values of the C=C/C−C and C=C/C=C coupling constants do not vary much upon increasing the level of calculation of electron correlation.

3. Conformational equilibrium

The potential energy function corresponding to the rotation around the C−C bond of butadiene has been studied in detail by Guo and Karplus[23]. The second stable isomer corresponds to a *gauche* conformation, with a CCCC torsion angle between 35 and 40 degrees. At the MP3/6-31G* level of calculation, this conformation is 2.6 kcal mol^{-1} higher than the most stable *s-trans* conformation, in excellent agreement with the experimental value of 2.7 kcal mol^{-1}[41], and 0.9 kcal mol^{-1} lower in energy than the planar *s-cis* conformation, which would correspond to the transition state linking two different *gauche* structures.

The form of the torsional potential in the region between CCCC = 0–120 degrees is not sensitive to the addition of polarization functions or inclusion of electron correlation. The effects are somewhat larger in the region between 120 and 180 degrees. The C−C and C=C bond lengths are very sensitive to a change in the torsional angle. This behavior can be related to the change in the degree of π bond delocalization[22,23]. Finally, the C=C−C bond angle remains almost constant when the torsional angle varies from 0 to 135 degrees, but dramatically increases in going from 135 to 180 degrees, due to the repulsion between two methylene groups.

A density functional calculation reported by Oie and coworkers[34] shows that the potential energy surface between the *s-cis* and *gauche* regions is extremely flat, so that the potential energy surface should be considered of a *cis–trans* type rather than of a *gauche–trans* type.

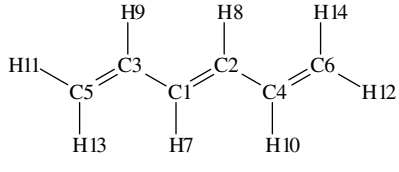
Several studies have considered the role of substituents on the conformational equilibrium in butadiene[19,27,28,32,33]. Guo and Karplus[27] have studied the structures of stable conformations and potential energy functions about the central C−C bond for 18 different methylated butadienes. They showed that methyl substitution at the (*E*)-4-position has little effect on the potential function, while the methyl substitution at the (*Z*)-4-position has a larger effect on the shape of the potential function. All the three trimethylated derivatives of butadiene have a global potential energy minimum at the *gauche* conformation, while for 2,4-dimethylpentadiene there is a second stable structure corresponding to the *s-trans* conformation. The stable conformations of 1,3-dienes and the shapes of potential functions can be determined from two basic interactions: conjugation and steric repulsion. Conjugation tends to stabilize the planar conformations (*s-cis* or *s-trans*), while steric repulsion is normally strongest in the planar conformations and weakest in the nonplanar ones. The changes in the shape of the potential function produced by methyl substitution are mainly due to the increase of steric interactions.

B. Trienes and Tetraenes

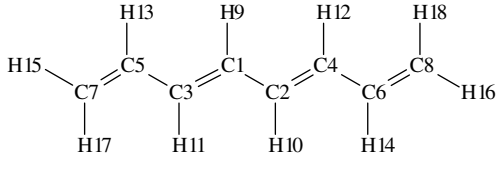
We will now consider the studies devoted to the next two linear polyenes: 1,3,5-hexatriene and 1,3,5,7-octatetraene. First, we will present the results corresponding to geometries and conformational energies computed for these compounds. We will then discuss the computed frequencies and force fields.

1. Geometries and conformations

The most stable conformation of both hexatriene and octatetraene is the all-*s-trans* one. Figure 2 represents these structures schematically.



(a)



(b)

FIGURE 2. Schematic representation of the structure of: (a) all-*trans*-1,3,5-hexatriene and (b) all-*trans*-1,3,5,7-octatetraene

TABLE 4. Selected geometrical parameters[a] (Å) of all-*trans*-hexatriene computed at several levels of calculation[b]

Bond	HF[c]	ACPF[d]	CASSCF[d]	exp[e]
C1=C2	1.325	1.350	1.353	1.368
C3=C5	1.319	1.341	1.347	1.337
C1−C3	1.460	1.451	1.459	1.458

[a] see Figure 2 for numeration.
[b] A basis set of double-ζ+polarization quality is used in all cases.
[c] Reference 21.
[d] Reference 31.
[e] Reference 38a.

TABLE 5. Selected geometrical parameters[a] (Å) of all-*trans*-octatetraene computed at several levels of calculation[b]

Bond	HF[c]	CASSCF[c]	MP2[d]	exp[e]
C1−C2	1.461	1.457	1.442	1.451
C1=C3	1.335	1.355	1.355	1.327
C3−C5	1.465	1.461	1.448	1.451
C5=C7	1.330	1.350	1.345	1.336

[a] See Figure 2 for numeration.
[b] A basis set of double-ζ+polarization quality is used in all cases.
[c] Reference 30.
[d] Reference 36.
[e] Reference 42.

Several theoretical studies have been devoted to the ground state structure of all-*trans*-1,3,5-hexatriene[21,25,31] and all-*trans*-1,3,5,7-octatetraene[18,21,26,30,31,36]. Tables 4 and 5 present the values of the CC bond lengths obtained in some selected theoretical calculations.

The introduction of electron correlation produces the same kind of effects on the CC bond lengths as those observed for butadiene. For hexatriene and octatetraene the inner C=C bonds are predicted to be longer than the outer C=C bonds. This result is in excellent agreement with experimental data corresponding to hexatriene, but differs from the experimental result in the case of octatetraene. This discrepancy has been suggested to be due to an important experimental error in the reported values[42].

When these results are compared with those corresponding to butadiene (Table 1), one can observe that bond alternation decreases upon increasing the chain length at all levels of calculation, in excellent agreement with experimental results.

High energy stable rotamers of hexatriene have also been theoretically studied[25,29]. Two possible *Cis/Trans* isomers are possible with respect to the C1=C2 bond (see Figure 2). For each of them, the rotation around the C1−C3 and C2−C4 bonds can lead to *s-trans* and *gauche* conformations. The *gauche-Trans-trans*, *trans-Cis-trans* and *gauche-Cis-trans* conformers have been found to be 3.0, 2.0 and 5.1 kcal mol^{-1} above the most stable all-*trans* conformation, respectively[25].

For *trans-Cis-trans*-hexatriene Liu and Zhou[29] have found a planar C_{2v} structure at the HF, MP2 and CASSCF levels of calculation, while the experimental data[43] suggest a nonplanar structure with a dihedral angle of 10 degrees around the central C1=C2 double bond. The calculated torsional potential curves around both the central C1=C2 double bond and the C1−C3 single bond are very flat in the range between −10 and 10 degrees.

This fact allows the effective relaxation of steric repulsion. The potential barrier for the motion around the C−C single bonds is smaller than that corresponding to the motion around the central C=C bond. Using the potential functions computed for these motions, and assuming a Boltzmann distribution, average torsional angles of 7.7 and 7.1, at 300 K, are obtained for rotations around C1−C3 and C1=C2, respectively. This torsional motion seems to be due to the nonplanar structure observed experimentally.

Panchenko and Bock[26] have studied three high energy rotamers of octatetraene: *g,T,t,T,t-*, *t,T,t,C,t-* and *g,T,t,C,t-* where *C* and *T* refer to *Cis/Trans* isomerism around the C1=C3 and C2=C4 double bonds, while *g* and *t* refer to *gauche* and *s-trans* conformations around C5−C3, C1−C2 and C4−C6 single bonds (see Figure 2). The most stable structure is *t,T,t,C,t-*, which lies 1.9 kcal mol^{-1} above the all-*trans* conformer. The *g,T,t,T,t-* and *g,T,t,C,t-* conformations are 3.0 and 5.0 kcal mol^{-1} higher in energy than the all-*trans* structure, respectively. These conformational energies are very similar to those computed for hexatriene and butadiene.

2. Vibrational frequencies and force constants

Vibrational frequencies of hexatriene and octatetraene have been reported by several authors[21,24−26,36]. The increase in the size of these molecules with respect to butadiene limits the use of highly accurate levels of calculation, so that a good choice of scaling factors is necessary to obtain useful results. Kofraneck and coworkers[21] have shown that employing scale factors determined from vibrational data for *trans* structures alone does not give a balanced description of *cis* and *trans* structures.

The experimental vibrational spectra of hexatrienes are complicated by the overlapping of the vibronic coupling, which manifests itself in a decrease of the experimental value of the total symmetric vibration of the C=C double bonds. This is the result of an interaction between the ground and the lowest excited state frequencies of the dominant double bond stretching modes. In order to take into account this effect, Panchenko and coworkers[25] have used a special scale factor for the central C=C double bond stretching coordinate. For the rest of the modes, the scale factors transferred from butadiene are used. This treatment has been extended to all-*trans*-octatetraene[26] and a complete assignment of its experimental spectra has been achieved.

Liu and Zhou[29] have computed the quadratic force field of *cis*-hexatriene by a systematic scaling of *ab initio* force constants calculated at the planar C_{2v} structure. Their results reproduce satisfactorily the observed spectral features of this molecule.

Lee and colleagues[36] have computed the vibrational frequencies of all-*trans*-octatetraene. They have found that the mean absolute percentage deviation for frequencies is 12% at the HF level, while it decreases to 4% at the MP2 level. Among the low-frequency modes, the frequencies of the in- and out-of-plane CCC skeletal bends are lower than the experimental values by 16%. When d basis functions on each carbon atom are added, the frequencies of some of the low-frequency modes approach the observed frequencies.

When the electron correlation level improves from HF to MP4, the C=C/C=C coupling constant remains basically unchanged in the DZ and 6-31G basis sets. The coupling constants of MP4/DZ, MP4/6-31G* and MP2/6-311G(2d,p) increase no more than 23% from the HF/DZ value. The C−C/C=C coupling constant does not vary appreciably upon increasing the correlation level.

C. Longer Polyenes

The possibility that the results obtained for short polyenes can be extrapolated to longer polyenes and to polyacetylene has been discussed by several authors[21,24,31,37].

It is generally assumed that increasing the degree of polymerization of any polymer leads to a number of very regular and systematic trends, provided that the backbone conformation does not change in the course of this process. The latter condition is fulfilled for all-*trans*-polyenes. However, how fast the convergence to bulk and convergence to edge effects is reached for a particular mode depends very much on the system under consideration. In the case of the all-*trans*-polyenes, the most prominent feature that has been observed in the vibrational spectra is the decrease of the lowest totally symmetric C=C double bond stretching frequency. A correct description of the C=C stretching region of the vibrational spectra requires good estimates of the off-diagonal force constants, that can only be achieved when electron correlation is taken into account in the computation of the force field. For this reason, the use of calculations at the Hartree–Fock level and conventional scaling techniques is insufficient to obtain a good description of the vibrational spectra of long polyenes.

Kofraneck and coworkers[24] have used the geometries and harmonic force constants calculated for *trans*- and *gauche*-butadiene and for *trans*-hexatriene, using the ACPF (Average Coupled Pair Functional) method to include electron correlation, to compute scaled force fields and vibrational frequencies for *trans*-polyenes up to 18 carbon atoms and for the infinite chain.

Complete harmonic force fields have been computed up to $C_{10}H_{12}$. For $C_{14}H_{16}$ only the in-plane force field has been calculated while for $C_{18}H_{20}$ calculations have been restricted to that part of the force field directly related to the carbon backbone. The results obtained show that diagonal force constants for C=C decrease as the length of the chain increases, whereas the opposite occurs for C−C. For a polyene of a specified chain length, the force constant corresponding to a C=C is lower in the center of the chain than it is at the edge of the molecule. C−C force constants behave oppositely. An almost linear correlation is observed between equilibrium distances and diagonal force constants. Faster convergence is observed for force constants corresponding to bonds at the edge of a polyene than for force constants of central bonds.

Structural features of the methylene end group converge very fast upon chain length extension. A similar fast convergence is obtained for the methine C−H bond lengths and all bond angles. On the other hand, a slower convergence is obtained for the central CC single and double bonds[24,31,37]. The reduction of the bond alternation is the most important geometry change accompanying the increase in the chain length.

For most of the force constants, extrapolation to the infinite length polyene is unnecessary because convergence is practically already achieved for $C_{14}H_{16}$. The only slowly converging part of the force field is connected with carbon–carbon single and double bond stretches and the coupling between them. According to these results, we could expect that the knowledge of an accurate force field for butadiene and hexatriene will allow a rather safe extrapolation to longer polyenes and to polyacetylene for very large portions of their force fields. However, the pending problem is the determination of the CC stretching diagonal and off-diagonal force constants and, eventually, a few further coupling constants between CC stretching and other internal coordinates.

IV. EXCITED STATES

Understanding the nature of the low-lying excited states of short polyenes has presented a formidable challenge for both experimentalists and theoreticians[1]. Most of the discussion has been focused on the relative ordering of the two lowest $2\,^1A_g$ and $1\,^1B_u$ singlet states. The excited $1\,^1B_u$ state can be described as a single excitation from the highest occupied orbital (HOMO) to the lowest unoccupied orbital (LUMO). The $2\,^1A_g$ state is characterized by a large component of the HOMO,HOMO → LUMO,LUMO double excitation.

It is currently accepted that for long polyenes starting with octatetraene, the lowest excited singlet state corresponds to the $2\,^1A_g$ state[44]. Because the $X\,^1A_g \rightarrow 2\,^1A_g$ electronic transition is dipole forbidden, the $2\,^1A_g$ state is difficult to characterize experimentally. The $X\,^1A_g \rightarrow 1\,^1B_u$ electronic transition is dipole-allowed and it appears in the spectra as a very intense band. This $1\,^1B_u$ state undergoes very rapid internal conversion to the $2\,^1A_g$ state, which then decays to the $X\,^1A_g$ state by fluorescence[1]. For the shorter polyenes, butadiene and hexatriene, the lack of fluorescence suggested that the above mechanism does not hold[45]. Because of that, the ordering of these two states in the shorter polyenes has been a subject of great controversy for a long time. Recently, experimental results have suggested that the $2\,^1A_g$ state lies below the $1\,^1B_u$ state[46–48].

The two lowest triplet states are the $1\,^3B_u$ and $1\,^3A_g$ states. The former is mainly described by the HOMO $\rightarrow$ LUMO single excitation while the latter is a mixture of single excitations of proper symmetry, i.e. HOMO$-1 \rightarrow$ LUMO and HOMO $\rightarrow$ LUMO $+ 1$.

The determination of accurate relative excitation energies by *ab initio* methods has been shown to present great difficulties and to require extensive calculations[49,50]. First, extended basis sets are needed to account for the diffuse character of some of the excited states. Second, electron correlation effects have to be treated in a balanced way. Moreover, while the most important correlation effects (nondynamic) are described by configurations within the π space, inclusion of dynamic correlation effects is important to obtain quantitative results for the excitation energies. Especially important is the dynamic polarization of the σ orbitals in the excited states which are dominated by ionic valence structures. Finally, low-lying Rydberg states can interact with nearby valence excited states. Because of the different correlation effects, the extent of this mixing is highly sensitive to the theoretical method used.

Recent calculations using the multiconfiguration second-order perturbation (CASPT2) method have been shown to yield accurate excitation energies for a number of organic molecules[49,50]. This method is based on the Complete Active Space Self-Consistent-Field (CASSCF) procedure, which is used to calculate the molecular orbitals and the reference wave function. This step accounts for the most important interactions such as the mixing of nearly degenerate configurations, which is commonly found in excited states. In a second step, the dynamical correlation effects are added using the second-order perturbation theory. This method represents a very efficient alternative to the multireference configuration interaction (MRCI) method which becomes impracticable for large molecules due to the size of bottleneck inherent in this approach. The CASPT2 vertical excitation energies to the low-lying valence excited states of butadiene, hexatriene and octatetraene are given in Table 6. These values will be discussed in the next subsections.

A. Butadiene

Because butadiene is the smallest polyene, its low-lying electronic states have been extensively studied theoretically[49,51–62]. Most of the studies have been performed for the most stable *trans* isomer.

It is now generally agreed that the first allowed transition in *s-trans* butadiene corresponds to the $X\,^1A_g \rightarrow {}^1B_u$ excitation, the experimental vertical excitation energy being determined to be 5.92 eV[63,64]. There has been, however, some disagreement on the location of the $2\,^1A_g$ state. That is, while Doering and McDiarmid suggested the vertical energy to be 7.3 eV[65], the results of Chadwick and coworkers[47,48], based on resonance Raman spectroscopy, placed the $2\,^1A_g$ state 0.25 eV below the $1\,^1B_u$ state. For the two lowest triplet states, $1\,^3B_u$ and $1\,^3A_g$, the experimental vertical excitation energies are found to be 3.2 and 4.91 eV, respectively[63].

TABLE 6. CASPT2 vertical excitation energies (eV) for the low-lying excited states of butadiene, hexatriene and octatetraene[a]

State	*trans*-Butadiene[b]	*trans*-Hexatriene[b]	*trans*-Octatetraene[c]
$1\,^1B_u$	6.23(5.92)	5.01(4.95)	4.42(4.41)
$2\,^1A_g$	6.27	5.19(5.21)	4.38
$1\,^3B_u$	3.20(3.22)	2.55(2.61)	2.17(2.10)
$1\,^3A_g$	4.89(4.91)	4.12(4.11)	3.39(3.55)
	cis-Butadiene[d]	*cis*-Hexatriene[d]	
$1\,^1B_2$	5.58(5.49)	5.00(4.92)	
$2\,^1A_1$	6.04	5.04	
$1\,^3B_2$	2.81	2.57	
$1\,^3A_1$	4.74	3.94	

[a]Experimental values in parentheses.
[b]Reference 49.
[c]Reference 30.
[d]Reference 62.

Theoretical calculations have also shown discrepancies in the relative vertical excitation energies of the two $2\,^1A_g$ and $1\,^1B_u$ singlet states. Early calculations[51] placed the $2\,^1A_g$ state below the $1\,^1B_u$ state, while more recent theoretical studies show the reversed order when the ground state $X\,^1A_g$ geometry is used[49].

It can be observed in Table 6 that the CASPT2 method gives accurate vertical excitation energies. In particular, it can be observed that the vertical transitions to the two lowest triplet states are in excellent agreement with the experimental results. For the singlet states of *s-trans* butadiene the CASPT2 method shows the largest errors for the states of B_u symmetry, due to valence–Rydberg mixing[49]. However, these errors are still smaller than 0.4 eV, which demonstrates the adequacy of the method. Other accurate calculations have been performed for the vertical excitation energies of butadiene. In particular, Graham and Freed[60] have reported results for the excited states of *trans*-butadiene using an effective valence Hamiltonian (EVSH) method, obtaining similar accuracy to that of the CASPT2 method.

Particularly interesting is the relative ordering of the $2\,^1A_g$ and $1\,^1B_u$ states. CASPT2 results indicate that both states are very close in energy with the $1\,^1B_u$ state lying below the $2\,^1A_g$ state. The CASPT2 energy difference between the two states is computed to be 0.04 eV, in good agreement with the EVSH results[60] which place the $1\,^1B_u$ state 0.05 eV below the $2\,^1A_g$ state. Because of valence–Rydberg mixing in the $1\,^1B_u$ state, the error in the computed excitation energy is expected to be larger for this state than for the $2\,^1A_g$ state, which is clearly of valence character. Based on earlier experience, Serrano-Andrés and coworkers estimate the vertical transition to the $2\,^1A_g$ state to be above the $1\,^1B_u$ state by around 0.3 eV[49].

The computed vertical excitation energies of *cis*-butadiene are shifted down compared to those of *s-trans*-butadiene. The ordering of the lowest singlet states ($1\,^1B_2$ and $2\,^1A_1$) is equivalent to the one found in the *trans* isomer. That is, the $1\,^1B_2$ state ($1\,^1B_u$ for *trans*) lies below the $2\,^1A_1$ state ($2\,^1A_g$ for *trans*). However, the computed energy difference (0.46 eV) in the *cis* isomer is larger than that of the *trans* structure (0.04 eV). It is interesting to note that valence–Rydberg mixing in *cis*-butadiene is smaller than in *trans*-butadiene, and

so the error in the excitation energy to the $1\,^1B_2$ state is expected to be smaller than the one corresponding to the equivalent $1\,^1B_u$ state.

The relative ordering of the two lowest singlet states is in contrast to the resonance Raman scattering experiments[47,48], which seem to indicate that the $2\,^1A_g$ state is 0.25 eV below the $1\,^1B_u$ state. However, it is not clear that the reported ordering corresponds to the vertical excitation energies. Thus, this discrepancy might be attributed to the fact that the $2\,^1A_g$ state is more sensitive to geometry relaxation than the $1\,^1B_u$ state[52,54,55]. As a consequence, the adiabatic excitation energies show the reversed order, the $2\,^1A_g$ state being now more stable than the $1\,^1B_u$ state.

Ab initio calculations on the geometry optimization of the $2\,^1A_g$ state of *s-trans*-butadiene have shown that the C_{2h} planar structure is not stable since it presents several imaginary frequencies associated to out-of-plane vibrations. Three nonplanar structures are found to be stable minima on the potential energy surface. The nonplanarity of this state makes the out-of-plane vibrations effective accepting modes. This fact strongly increases the rate of $2\,^1A_g \rightarrow 1\,^1A_g$ internal conversion, which would explain the lack of fluorescence in butadiene[56].

B. Hexatriene

Ab initio calculations for hexatriene are less numerous than for butadiene due to its larger size[49,52,62,66–71]. However, CASPT2 results for hexatriene[49] have shown that the study of this molecule present less difficulties than that of butadiene or ethene. This is due to the fact that in hexatriene there is no significant mixing between valence and Rydberg states. Thus, correlation effects are treated in a more balanced way and consequently the vertical excitation energies are more accurate (Table 6).

Similarly to *s-trans*-butadiene, the $1\,^1B_u$ state lies below the $2\,^1A_g$ state in *trans*-hexatriene. The CASPT2 vertical excitation energies of these two states are in excellent agreement with the experimental results. The computed energy difference (0.2 eV) between the $1\,^1B_u$ and $2\,^1A_g$ states is slightly smaller than the estimated value (0.3 eV) for *s-trans*-butadiene[49,30]. In *cis*-hexatriene the lowest singlet state is also the $1\,^1B_2$ state, although for this isomer the two singlet states are very close in energy[62].

The effect of geometrical relaxation on the relative excitation energies has been studied by Cave and Davidson, who performed *ab initio* CI calculations using semiempirical optimized geometries of the ground and excited states[52]. Their results showed that the $2\,^1A_g$ state is again more affected by the geometrical changes than the $1\,^1B_u$ state. As a consequence, the adiabatic excitation energies show the reversed order, in agreement with recent experimental results for *cis*-hexatriene which indicate that the $2\,^1A_g$ state lies 5270 cm^{-1} below the $1\,^1B_u$ state[46].

CASSCF calculations for *cis*-[68] and *trans*-hexatriene[67] have also shown that the planar structure in the $2\,^1A_g$ state is not stable, since it presents two imaginary frequencies. For *cis*-hexatriene[68], the release of symmetry constraints leads to two stable minima, one of C_2 symmetry and one of C_s symmetry, corresponding to out-of-plane deformations of the terminal hydrogen atoms. These results are in agreement with the experimental spectrum which could only be interpreted as arising from two non-planar configurations in the $2\,^1A_g$ state. However, the stabilization energy associated with the distortion from planarity is small, thus indicating that this molecule is extremely flexible with respect to the out-of-plane distortions. As in the case of butadiene, the non-planarity of hexatriene

in the $2\,^1A_g$ state could account for the absence of fluorescence due to a strong increase of radiationless decay to the ground state.

C. Octatetraene

Octatetraene is the shortest unsubstituted polyene that exhibits fluorescence. The $X\,^1A_g \rightarrow 2\,^1A_g$ transition is clearly seen in one- and two-photon absorption spectra and the $2\,^1A_g$ is unambiguously identified to be the lowest singlet state[1].

Few *ab initio* studies have been performed for *trans*-octatetraene[30,67,72]. All these studies, except the more recent calculations at the CASPT2 level[30], locate the $2\,^1A_g$ state above the $1\,^1B_u$ state. The CASPT2 vertical energies corresponding to both states are very close and show the reverse ordering (Table 6). The computed vertical energy to the $2\,^1A_g$ state (4.38 eV) is somewhat larger than the value estimated from vertical absorption (3.97 eV)[44] which confirms previous indications that this estimated value is too low[67,72]. The computed vertical energy to the dipole allowed $1\,^1B_u$ state (4.42 eV) is in excellent agreement with the experimental result (4.41 eV)[30].

In addition to the CASPT2 vertical excitation energies, Serrano-Andrés and coworkers also reported the adiabatic excitation energies and the fluorescence maxima at the same level of calculation[30]. The geometries of the ground and low-lying $2\,^1A_g$ and $1\,^1B_u$ states have been obtained at the CASSCF level using a large basis set. Since both experiments and theoretical calculations have indicated that the structure of octatetraene in these states is planar, calculations were performed assuming a C_{2h} symmetry. Similarly to shorter polyenes, the lengths of the double bonds in the excited states increase while those of the single bonds decrease. The effect of geometry changes on the excitation energies appears to be also more important for the $2\,^1A_g$ state than for the $1\,^1B_u$ one. That is, the difference between the vertical (4.38 eV) and adiabatic energy (3.61 eV) for the $2\,^1A_g$ state is 0.77 eV, while for the $1\,^1B_u$ state the adiabatic excitation energy (4.35 eV) is only 0.07 eV less than the vertical (4.42 eV) one. These results are in good agreement with experimental observations, which estimate an energy difference of 0.79 eV[73] between the 0–0 transitions of the $2\,^1A_g$ and $1\,^1B_u$ states. Also, the computed value of 2.95 eV for the fluorescence maximum agrees very well with the experimental one, 3.1 eV[74].

D. Longer Polyenes

Because highly accurate, correlated *ab initio* methods are still computationally very expensive for large molecules, most of the theoretical studies on longer polyenes have been performed using the Parriser–Parr–Pople (PPP) method or other semiempirical methods[4,75–78]. These studies have provided an important insight on the dependence of vibrational, geometrical and excitation energy features with increasing length of the polyene.

Similarly to shorter polyenes, calculations of the excited states of longer polyenes have shown that the lengths of the double bonds increase upon excitation while those of the single bonds decrease[75–78]. However, these changes are not equally distributed along the chain. Instead, they tend to localize in the central region of the molecule and are more pronounced in the $2\,^1A_g$ state, for which calculations indicate a reversal of the bond alternation pattern.

Calculations have also given a better understanding of the anomalous frequency increase of the C=C stretch mode upon excitation to the $2\,^1A_g$ state in polyenes[1,67,78]. By comparing the calculated adiabatic and diabatic frequencies, this increase is explained in terms of

the vibronic coupling between the $1\,^1A_g$ and $2\,^1A_g$ states. As the polyenes get longer, the frequency of the C=C stretch mode decreases in the ground state and increases slightly in the $2\,^1A_g$ state, due to the decrease of the $X\,^1A_g - 2\,^1A_g$ energy gap which leads to a more effective vibronic coupling.

As has already been mentioned, the lowest singlet state has been unambiguously identified to be the $2\,^1A_g$ state for long polyenes, the energy difference between the $2\,^1A_g$ and $1\,^1B_u$ states increasing with the length of the polyene. It has also been shown that the longer the polyene, the smaller the excitation energy for the $X\,^1A_g \rightarrow 2\,^1A_g$ transition[1], thus explaining the observed decrease in the fluorescence quantum yield, due to the increase in the rate of internal conversion. Therefore, the lack of fluorescence in the shorter polyenes, butadiene and hexatriene, and in *trans*-polyacetylene, arise from different sources. That is, while in the shorter polyenes the increase in the rate of radiationless decay is due to the nonplanarity of the $2\,^1A_g$ state, in very long polyenes it is due to the small energy gap between the $X\,^1A_g$ and $2\,^1A_g$ states[1,56].

V. MOLECULAR ELECTRIC PROPERTIES

Conjugated polyenes exhibit large linear and nonlinear optical properties due to the mobility of electrons in extended π-orbital systems. Hence, this is another reason for the growing interest shown in these molecules in recent years[2,79–89].

Molecular electric properties give the response of a molecule to the presence of an applied field E. Dynamic properties are defined for time-oscillating fields, whereas static properties are obtained if the electric field is time-independent. The electronic contribution to the response properties can be calculated using finite field calculations[90], which are based upon the expansion of the energy in a Taylor series in powers of the field strength. If the molecular properties are defined from Taylor series of the dipole moment μ, the linear response is given by the polarizability α, and the nonlinear terms of the series are given by the nth-order hyperpolarizabilities (β and γ).

The various response tensors are identified as terms in these series and are calculated using numerical derivatives of the energy. This method is easily implemented at any level of theory. Analytic derivative methods have been implemented using self-consistent-field (SCF) methods for α, β and γ, using multiconfiguration SCF (MCSCF) methods for β and using second-order perturbation theory (MP2) for γ[90]. The response properties can also be determined in terms of 'sum-over-states' formulation, which is derived from a perturbation theory treatment of the field operator $-\mu E$, which in the static limit is equivalent to the results obtained by SCF finite field or analytic derivative methods.

The static electronic dipole polarizability and second hyperpolarizability tensors have been computed for a series of conjugated polyenes using the *ab initio* SCF method[79,88]. Results for polyenes from C_4H_6 to $C_{22}H_{24}$ were reported by Hurst and coworkers[79] while longer polyenes up to $C_{44}H_{46}$ have recently been reported by Kirtman and coworkers[88]. The basis set dependence was analyzed in the study of Hurst and coworkers, who showed that for the shorter polyenes, such as C_4H_6, extra diffuse functions and diffuse polarization functions are important for describing the second hyperpolarizability. However, it was also shown that as the length of the polyene increases, the size of the basis set becomes less important. Therefore, the calculations up to $C_{44}H_{46}$ have been performed using the split-valence 6-31G basis set[88].

The computed 6-31G values for the longitudinal polarizability and longitudinal hyperpolarizability per unit cell are given in Table 7. It can be observed that the longitudinal polarizability and longitudinal hyperpolarizability increase with the chain length. However, the rate of variation of these magnitudes decreases with N, in such a way that α_L/N

TABLE 7. Static longitudinal polarizabilities α_L (in a.u.) and longitudinal hyperpolarizabilities γ_L (in 10^4 a.u.) per unit for linear $C_{2n}H_{2n+2}$ polyenes[a]

	α_L/N	γ_L/N		α_L/N	γ_L/N
C_4H_6	37.4	0.3	$C_{26}H_{28}$	112.3	151.5
C_6H_8	47.3	1.8	$C_{28}H_{30}$	115.6	171.4
C_8H_{10}	57.2	5.4	$C_{30}H_{32}$	118.5	190.7
$C_{10}H_{12}$	66.4	12.0	$C_{32}H_{34}$	121.1	209.7
$C_{12}H_{14}$	74.7	21.9	$C_{34}H_{36}$	123.3	226.5
$C_{14}H_{16}$	82.2	35.2	$C_{36}H_{38}$	125.5	243.4
$C_{16}H_{18}$	88.9	51.3	$C_{38}H_{40}$	127.4	260.1
$C_{18}H_{20}$	94.8	69.7	$C_{40}H_{42}$	129.2	273.5
$C_{20}H_{22}$	100.0	89.4	$C_{42}H_{44}$	130.8	287.9
$C_{22}H_{24}$	104.6	110.0	$C_{44}H_{46}$	132.3	301.1
$C_{24}H_{26}$	108.7	130.9			

[a]Reference 88.

and γ_L/N approach an asymptotic limit. The results for the finite polyenes are extrapolated to predict the unit-cell longitudinal polarizability and longitudinal hyperpolarizability of infinite polyacetylene. Kirtman and coworkers[88] using an improved extrapolation procedure have predicted the asymptotic polyacetylene limit of α_L/N to be 166 a.u. $\pm$ 3% and of γ_L/N to be 691×10^4 a.u. $\pm$5.6%.

The results reported in Table 7 correspond to the static electronic contribution to the response properties. However, when a molecule is placed under the effect of an electric field, not only the electronic cloud is modified but also the nuclei positions are changed and the vibrational motion is perturbed[91–93]. Thus, aside from the electronic response to the applied field there is a vibrational contribution which arises from the relaxation (deformation) of the nuclear frame upon the application of an external electric field, and also from the change in the vibrational energy. Recently, Champagne and coworkers have reported *ab initio* calculations on the vibrational polarizability of polyacetylene chains[87]. The results obtained show that the vibrational contribution to the polarizability is about 10% of the electronic contribution. The vibrational longitudinal polarizability per unit cell increases with the chain length as does the corresponding electronic contribution until saturation is reached, the extrapolated value being approximately one order of magnitude smaller than the electronic one.

The experimental measures of these molecular electric properties involve oscillating fields. Thus, the frequency-dependence effects should be considered when comparing the experimental results[90]. Currently, there are fewer calculations of the frequency-dependent polarizabilities and hyperpolarizabilities than those of the static properties. Recent advances have enabled one to study the frequency dispersion effects of polyatomic molecules by *ab initio* methods[90,94]. In particular, the frequency-dependent polarizability α and hyperpolarizability γ of short polyenes have been computed by using the time-dependent coupled perturbed Hartree–Fock method. The results obtained show that the dispersion of α increases with the increase in the optical frequency[81,94]. At a given frequency, α and its relative dispersion increase with the chain length. Also, like α, the hyperpolarizability γ values increase with the chain length[81]. While the electronic static polarizability is smaller than the dynamic one, the vibrational contribution is smaller at optical frequencies[87].

Further work on long polyenes, including vibrational distortion, frequency dispersion effects and electron correlation, would be important for evaluating more accurate asymptotic longitudinal polarizabilities and hyperpolarizabilities.

VI. CHEMICAL REACTIVITY

The dienes and polyenes are compounds which intervene in a large number of organic reactions, as will be seen in different chapters of this book. Several excellent reviews have been devoted to theoretical studies about their reactivity, with special emphasis on the mechanism of pericyclic reactions[3–5]. As was mentioned in the introduction, this section will only treat, as an example, the Diels–Alder reaction, since it has been the most studied one by theoreticians. Our goal is not to cover all aspects, but instead to show the high potential and usefulness of theoretical methods in order to interpret and rationalize the experimental results. In the rest of the chapter we will concentrate on the last *ab initio* calculations.

A. The Diels–Alder Reaction

The Diels–Alder reaction is among the most useful tools in organic chemistry. It has been the object of a great number of theoretical studies[95–131] dealing with almost every one of the experimental aspects: reactivity, mechanism, selectivity, solvent effects, catalysis and so on.

1. Reaction mechanism

The most simple Diels–Alder reaction, that between butadiene and ethylene, represented schematically in Figure 3, has been extensively studied employing several methods of calculation. The results obtained have initiated some controversy regarding the nature of the reaction mechanism[3–5,95].

High-level *ab initio* calculations reported by Li and Houk[96] show that two different mechanisms can coexist: a one-step concerted mechanism and a two-step mechanism. In the one-step mechanism the reaction takes place through a symmetrical transition state, while in the two-step mechanism the reaction takes place through a biradical intermediate, the rate-determining step being the formation of this intermediate. The proper description of biradical or biradicaloid structures requires the use of a MCSCF method. With this kind of calculation the nondynamic electron correlation is taken into account. At the CASSCF/6-31G* level of calculation the concerted mechanism is more favorable than the two-step mechanism by only 1.9 kcal mol^{-1}. However, the lack of dynamic correlation leads to an overestimation of the stability of biradicaloid structures. When the energies of the concerted transition state and of the transition state leading to the formation of the biradical are recomputed at the QCISD(T) level (Quadratic CI with single and double excitations with the perturbational inclusion of triple excitations), which is

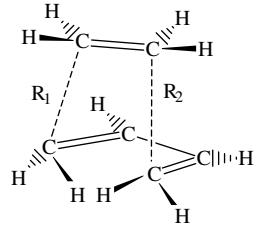


FIGURE 3. Schematic representation of the transition state of the Diels–Alder reaction between butadiene and ethylene

supposed to describe properly all correlation effects, the difference between both mechanisms rises to 10.2 kcal mol^{-1}, in favor of the concerted mechanism. At this point, it seems clear that the reaction between butadiene and ethylene takes place through a concerted mechanism.

In addition to conventional *ab initio* methods, techniques based on the density functional theory (DFT) have also been used to study the Diels–Alder reaction between butadiene and ethylene[97–99]. With these kinds of methods, a concerted mechanism through a symmetric transition state is also predicted. Several kinds of density functionals have been used. The simplest one is based on the Local Density Approach (LDA), in which all the potentials depend only on the density. More sophisticated functionals include a dependence on the gradient of the density, such as that of Becke, Lee, Yang and Parr (BLYP).

Table 8 presents the values of the length of the forming C–C bonds (R) at the concerted transition state, and of the potential energy barrier computed at several levels of calculation, for the reaction between butadiene and ethylene. MP4, QCISD(T) and BLYP yield reasonable energy barriers. LDA greatly underestimates the barrier, while CASSCF overestimates it. This is due probably to an overestimation of the correlation energy at the LDA level and to the lack of dynamic correlation at the CASSCF level. The value of the bond length of the forming C–C bonds does not change very much with the level of calculation. These results show that reliable energy barriers are only obtained with a proper inclusion of dynamic electron correlation.

Reactions of unsymmetrical dienes and/or dienophiles have also been studied[101,103,104]. For these reactions *ab initio* calculations predict concerted non-synchronous mechanisms. The values of the potential energy barriers are very sensitive to the level of calculation and reasonable values are only obtained when electron correlation is included up to the MP3 level[103].

The possibility of a biradical mechanism was suggested using the MNDO and AM1 semiempirical methods, for the addition of protoanemonin (5-methylene-2(5*H*)-furanone) to butadiene[105] and to several substituted dienes[106]. Experimental evidence for this kind of mechanism has recently been published[133]. A biradical mechanism has also been considered for the dimerization of butadiene[96]. For this reaction, CASSCF calculations

TABLE 8. Values of the length (Å) of the forming C–C bonds (R) and of the energy barrier (ΔE) (in kcal mol^{-1}) for the concerted transition state of the butadiene + ethylene reaction computed at several levels of calculation[a]

	R	ΔE
MP2[b]	2.285	17.6
MP4[b]		22.1
CASSCF[c]	2.223	43.8
QCISD(T)[c]		25.5
LDA[d]	2.298	4.5
B-LYP[e]	2.294	21.3
exp[f]		24.2–27.5

[a] A basis set of double-ζ+polarization quality is used in all cases.
[b] Reference 131.
[c] Reference 96.
[d] Reference 97.
[e] Reference 98.
[f] Reference 132.

predict the two-step mechanism as the most favorable by 1.3 kcal mol^{-1}. The stability of biradicaloid structures is probably overestimated at this level of calculation, but the size of the system makes difficult the use of higher-level *ab initio* methods.

2. Selectivity

Diels–Alder reactions with unsymmetrical dienes and/or dienophiles can lead to the formation of different isomers. One of the most interesting aspects in these systems is stereoselectivity, observed in reactions involving cyclic dienes. In these cases, two different stereoisomers can be formed: *endo* and *exo*.

Experimental observations show that in most of the cases the *endo* product is predominant over the *exo* one. Theoretical calculations devoted to this topic[103,107–110] do not always agree with the experimentally observed *endo/exo* selectivity. The discrepancy has been attributed to effects of the medium in which real reactions take place, that are not included in most theoretical calculations. Jorgensen and coworkers[103] have shown that the computed *endo/exo* selectivity is dependent on the level of calculation. In this way, for the reaction of methyl vinyl ketone with cyclopentadiene, calculations using small basis sets predict the preferential formation of the *exo* product, while the *endo* one is shown to be kinetically favored when larger basis sets are used. A similar dependence has been observed by Ruiz-López and coworkers[109] for the reaction between methyl acrylate and cyclopentadiene, and by Sbai and coworkers[110] for the additions of chiral butenolides to cyclopentadiene.

Very recent work[111] has shown that the predominant formation of the *endo* adduct in the reaction between cyclopropene and isotopically substituted butadiene could be attributed to an attractive interaction between a C–H bond of cyclopropene and the π bond being formed in the diene moiety.

Other theoretical studies on the selectivity of Diels–Alder reaction refer to regioselectivity[108,112,113], site-selectivity[105,112,114] and diastereofacial selectivity[110,117]. The latter is presently the subject of much interest in recent years, since this kind of selectivity is very important in the synthesis leading to manifold families of carbocyclic amino acids and nucleosides. Earlier proposals by Cherest and Felkin[115] and Anh and Eisenstein[116] suggested that the controlling factor might be the interaction between the bonding orbital being formed and the antibonding orbitals of adjacent bonds. These suggestions have been criticized by Frenking and coworkers[118], Wong and Paddon-Row[119] and Wu, Houk and coworkers[120,121]. Dannenberg and colleagues[123] have shown, using an extension of FMO theory, that diastereofacial selectivity is influenced by both steric and electronic factors in a complex way. Recent *ab initio* calculations[110], using the 3-21G and 6-31G* basis sets, of the Diels–Alder reaction between crotonolactone and β-angelica lactone have correctly reproduced the experimental *anti* preference, the steric hindrance produced by the methyl group of β-angelica lactone being in this case the controlling factor. The inclusion of zero-point vibrational energies, thermal contributions to the energy and the entropy term do not appreciably change the difference between *syn* and *anti* energy barriers.

3. Solvent effect and catalysis

Another aspect that has been theoretically studied[109,124,129] is experimental evidence that Diels–Alder reactions are quite sensitive to solvent effects in aqueous media. Several models have been developed to account for the solvent in quantum chemical calculations. They may be divided into two large classes: discrete models, where solvent molecules are explicitly considered; and continuum models, where the solvent is represented by its macroscopic magnitudes. Within the first group noteworthy is the Monte Carlo study

of Jorgensen and coworkers[124–126] of the reaction of cyclopentadiene with methyl vinyl ketone. They find that the main factor which intervenes in the acceleration of this reaction by the solvent is not the hydrophobic effect, but the influence of hydrogen bonding. Although the number of hydrogen bonds to the carbonyl oxygen remains constant during the process, the strength of each bond is 1–2 kcal mol^{-1} greater at the transition state. This interpretation through enhanced hydrogen bonding has been recently confirmed using the supermolecule approach. On the other hand, Ruiz-López and coworkers[109], using a continuum model, have shown two other important aspects. First, the solvent increases the asynchronicity of the process. Second, the *endo/exo* selectivity and the facial selectivity increase with the polarity of the solvent.

Theoretical calculations have also permitted one to understand the simultaneous increase of reactivity and selectivity in Lewis acid catalyzed Diels–Alder reactions[101–130]. This has been traditionally interpreted by frontier orbital considerations through the destabilization of the dienophile's LUMO and the increase in the asymmetry of molecular orbital coefficients produced by the catalyst. Birney and Houk[101] have correctly reproduced, at the RHF/3-21G level, the lowering of the energy barrier and the increase in the *endo* selectivity for the reaction between acrolein and butadiene catalyzed by BH_3. They have shown that the catalytic effect leads to a more asynchronous mechanism, in which the transition state structure presents a large zwitterionic character. Similar results have been recently obtained, at several *ab initio* levels, for the reaction between sulfur dioxide and isoprene[130].

As a final remark in this section, we expect that the results presented herein have shown how theoretical methods allow us to obtain some insight into a great variety of experimental facts, even in the complex case of chemical reactivity.

VII. CONCLUDING REMARKS

All along this chapter, we have covered some of the most significant and recent contributions of Quantum Chemistry to the study of dienes and polyenes.

We have shown that theoretical calculations are a complementary tool to experiment in the comprehension of the behavior of such systems. In certain aspects, specially for the smaller systems, quantum chemical calculations already provide sufficiently accurate results. However, for larger molecules and time-dependent phenomena the results have not yet achieved the same level of accuracy.

The enormous development of powerful computers and the implementation of new theoretical methods continuously extends the field in which theory can provide results with chemical accuracy. This fact allows us to foresee that in the near future the structure and properties of dienes and polyenes will be more thoroughly understood.

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CHAPTER **2**

Structural chemistry of dienes and polyenes

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I. INTRODUCTION

The structural chemistry of dienes and polyenes is extremely diverse and intricate since about 12% of all determined structures of organic compounds contain two or more double

bonds. This topic must therefore be restricted to generalized systems which have common features. The structural features of some polyene groups, for example that of metal complexes or of polyenes with heteroatoms directly linked to the double bonds, are so divergent that it is difficult to present a unified view of the structures within such classes of compounds. They are therefore not included in the present discussion.

Consequently, we had to confine ourselves to the groups outlined in the following, also excluding neighboring double bonds (allenes) as well as those systems containing triple bonds and aromatic systems even if there is a significant bond localization which converts, for example, benzene to cyclohexatriene. Because in most cases the large molecules, such as macrocycles, have the same structural characteristics in detail as the comparable smaller molecules, these are also omitted in the following sections. Some of the small molecules, however, display a variety of mutual influences in terms of different electronic and steric effects, so these will be discussed in more detail as representatives of others which have similar characteristics. For a series of molecules also the *ab initio* calculated geometries are presented for comparison without claiming to be comprehensive. They demonstrate the strength of present day computational methods even with basis sets and methods which can be no longer considered as 'high level' calculations. In a few cases these comparisons also display the deficiencies of the methods, calling for either more sophisticated techniques or extended considerations of the models. Restrictions also do not allow one to discuss the discrepancies in detail, as well as the methodological differences of the methods of structure determinations.

II. DIENES AND POLYENES

A. Linear and Branched Dienes and Polyenes

The linear polyenes are divided into the following three groups:

1. Nonconjugated acyclic dienes and polyenes.
2. Conjugated acyclic dienes and polyenes.
3. Sterically strained conjugated acyclic dienes and polyenes.

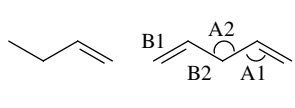
1. Nonconjugated acyclic dienes and polyenes

Rotational isomerism normally complicates the study of gaseous nonconjugated dienes and polyenes because many conformers appear simultaneously, and hence only few structures of free molecules in this category have been studied.

1,4-Pentadiene **(1,4-PD)** is the smallest diene with isolated double bonds. It is also the simplest hydrocarbon molecule capable of '*homoconjugation*', a condition that may occur when two π-systems are separated by a single methylene group. The idea is that there may exist considerable overlap of the π-orbitals across this group (for certain torsion angles), and that this circumstance should facilitate some interesting chemistry, as for example the di-π-methane photorearrangement[1]. The structure and conformations of **1,4-PD** has been studied by gas electron diffraction[2] (GED) as well as by microwave spectroscopy[3] (MW) (see Table 1), and in both studies a mixture of conformers with C_1, C_2 and C_S symmetry was observed. The most recent single-crystal diffraction X-ray data show **1,4-PD** very close to ideal C_2 symmetry[4] (see Figure 1). The C=C−C−C torsion angle is 117.1° (T, mean value) and the central bond angle 112.2°, in good agreement with the calculated *ab initio* values (see Table 1).

The fragment of **1,4-PD** is also present in 1,1-divinylcyclopropane **(DVC)**, where the central methylene group is replaced by a three-membered ring. For this strained molecule a strong interaction between cyclopropane *Walsh* and vinyl π-orbitals was expected. The photoelectron spectra of **DVC**[5] could be best understood with the assumption of optimal

TABLE 1. Structural parameters for 1-butene **(1-BU)** and nonconjugated acyclic dienes and polyenes (distances in Å, angles in degrees)



(1-BU) **(1,4-PD)** **(DVC)** **(1,5-HD)** **(TVM)**

	Symmetry	B1	B2	A1	A2	T1[a]	Method[b]
1-BU	C_1	1.336	1.499	125.6	111.65	119.9	GED(S2)[7]
		1.336	1.507	126.7	114.8	(0.0)	MW(S3)[8]
1,4-PD	C_S	1.339	1.511	125.5	113.1	4.3	GED(S1)[2]
	C_2	1.339	1.511	125.5	108.9	122.2	GED(S1)[2]
		1.324	1.502	125.2	112.2	117.1	XR(S1)[4]
		1.318	1.509	125.1	112.0	118.5	HF[4]
		1.339	1.504	124.4	111.1	116.4	MP2[4]
	C_S	1.318	1.509	125.1	112.4	122.6	HF[4]
DVC	C_1	1.319	1.489	126.3	116.5	127.4	XR(S1)[9]
		1.331[d]	1.483[d]	125.6[d]		−10.3[d]	
	C_1	1.339	1.487	125.2	116.2	116.3	MP2[9]
		1.340[d]	1.484[d]	125.2[d]		−10.4[d]	
1,5-HD	*c*	1.340	1.508	124.6	111.5	—	GED(S3)[6]
TVM	C_1	1.326 to 1.328	1.515 to 1.526	125.9 to 126.7	105.5 to 111.8	—	XR(S1)[4]
	C_1	1.318	1.518 to 1.530	127.2	106.0 to 111.1	—	HF[4]
	S_4	1.319	1.523	127.1	105.5 to 111.5	—	HF[4]
	D_{2d}	1.317	1.538	126.0	108.7 to 109.9	90/180	HF[4]

[a] Torsion angle T1 is C=C−C−C.
[b] HF = RHF/6-31G(d), MP2 = MP2/6-31G(d). GED = gas electron diffraction, MW = microwave, XR = single-crystal X-ray diffraction, esd's for bond lengths and angles in the last digit S1: 1–3, S2: 3–10, S3: >10.
[c] Averaged values for the conformers.
[d] Vinyl group with *anti* conformation.

orbital interactions, which result from bisected *syn* conformations of both vinyl groups in highest molecular symmetry C_{2v}. In the crystal the molecule has asymmetric C_1 form, where only one vinyl group interacts in terms of cyclopropyl conjugation (see Figure 2). The cyclopropane bonds are affected by this interaction, where the *vicinal* bonds (C1−C2, C1−C3) are significantly elongated by 0.02 Å (mean value) 1.515(1)/1.524(1) Å compared to the *distal* bond C2−C3 [1.499(1) Å]. This observation is in agreement with the electron donor properties of cyclopropane (see also Section II.C.1).

Ab initio calculations at the MP2/6-31G(d) level provide the same asymmetric conformation found in the crystal as the global minimum structure, whereas one vinyl group is nearly in *anti* bisected orientation to the ring and the other vinyl group is strongly twisted into *gauche* conformation. The higher symmetric form in C_2, where both vinyl groups

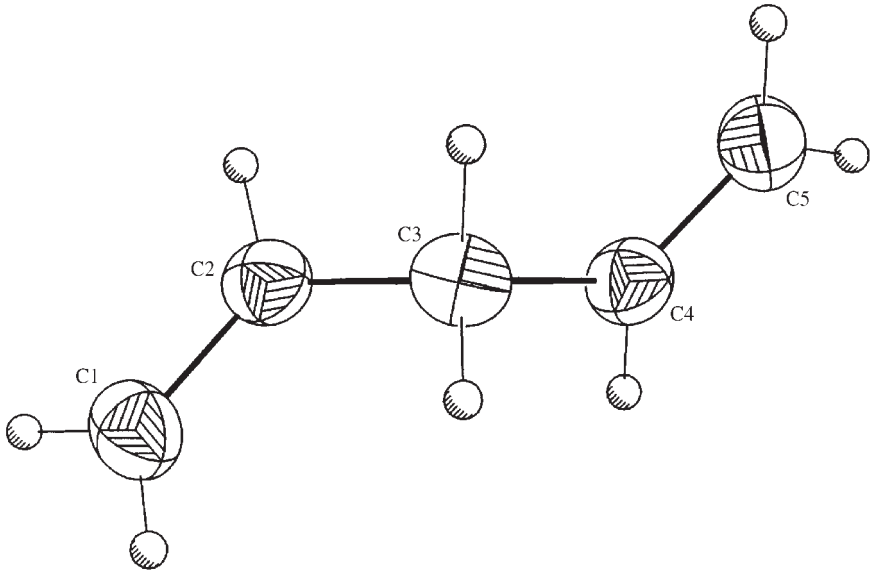


FIGURE 1. Molecular structure of 1,4-pentadiene (**1,4-PD**); presentation with thermal probability plots of 50%

are *gauche* orientated (see C_2 form of **1,4-PD**) is 3.3 kJ mol^{-1} [MP2/6-31G(d)//MP2/6-31G(d)] higher in energy than the C_1 form. The symmetric form of **DVC** in C_{2v} is destabilized by 10.0 kJ mol^{-1}, mainly due to steric reasons with intramolecular H---H repulsions involved, which occur between vinyl and ring H-atoms.

The next homolog, 1,5-hexadiene (**1,5-HD**), is of special chemical interest because the molecule is capable of undergoing the so-called Cope rearrangement. A GED study of **1,5-HD** was also recently reported[6]. Because of the increased conformational complexity of this molecule compared to that of **1,4-PD**, the structural details of the various conformers could not be resolved and only averaged structure parameters were determined from the gas phase. Molecules in the solid state are frozen, mostly in only one conformation, which may but must not represent the conformational ground state. Therefore, conformational isomerization is usually not discussed with X-ray structures presented in the literature.

In Table 1 the structure parameters obtained for the unconjugated dienes/polyenes are compared with data for 1-butene (**1-BU**)[7]. There is nothing in the ground-state molecular structure of either **1,4-PD** or **1,5-HD** that indicates the presence of interaction between the two π-systems of the molecules. The structure parameters are very similar to those observed for **1-BU** by GED[7] and by MW[8]. The bond lengths are approximately the same in all three molecules, and the small differences between the C−C−C angles may be attributed to differences in steric strain between an ethylenic group on one side and a methylene, methyl group or a second ethylenic group, respectively, on the other. In all conformers of the **1,4-PD**, **1,5-HD** and **1-BU** molecules the C=C bonds approximately eclipse a methylene C−H (all molecules) or a C−C (**1,4-PD; 1-BU**) bond. Two recent high-resolution X-ray crystal structures[9], of 1,1-divinylcyclopropane (**DVC**) and tetravinylmethane (**TVM**), both included in Table 1, show slight but significant differences in distances and angles of the respective vinyl groups and are discussed below.

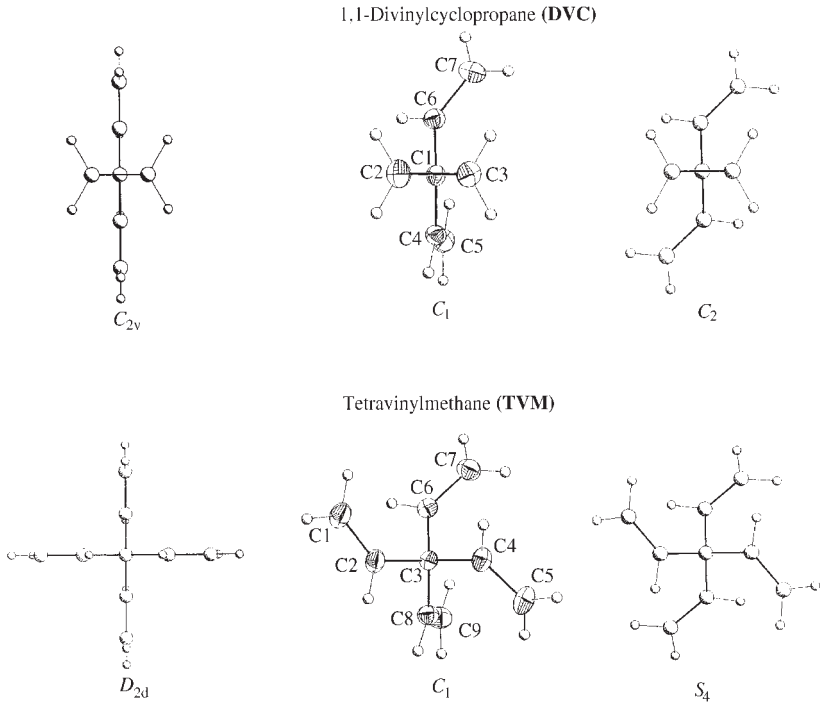


FIGURE 2. Calculated high symmetry conformations (C_{2v}, C_2 and D_{2d}, S_4, respectively) and experimentally determined molecular structures of 1,1-divinylcyclopropane **(DVC)** and tetravinylmethane **(TVM)** in C_1; presentation with thermal probability plots of 50%

Tetravinylmethane **(TVM)** is a very interesting compound with respect to its conformational and structural parameters. All the assumptions on the symmetry of **TVM** are based on D_{2d} and S_4 conformations[10,11]. Surprisingly, none of these conformations is observed in the crystalline state; instead, C_1 symmetry was found in an orthorhombic crystal lattice (space group Pbca). If one of the vinyl groups (C3-C8-C9) is rotated by *ca* 150°, the C_1 symmetry can be transferred to S_4 symmetry (or vice versa). This is evident from Figure 2 where **DVC** is also shown in the same projection which demonstrates that the C_1 symmetry is no coincidence of packing effects.

The calculation of the three conformations of **TVM** on *ab initio* level 6-31G(d)//6-31G(d) (Hartree–Fock) showed that the S_4 symmetric form represents an energetical minimum but the C_1 form is only 1.51 kJ mol^{-1} higher in energy (local minimum, established by frequency calculations). The D_{2d} symmetric form is 56.4 kJ mol^{-1} higher in energy than the S_4 conformation and represents a transition state.

The small difference in energy between S_4 and C_1 forms caused speculations as to whether a second crystalline form might exist which has S_4 symmetry. These assumptions were fed by the fact that an X-ray powder diffractogram revealed another orthorhombic lattice with half of the volume. This polymorphic form emerged when cooling below the

melting point at *ca* 170 K and crystallizing with slower speeds in a capillary by means of a miniature zone melting procedure. Further extensive experiments with the aim of growing a single crystal of the second polymorph finally resulted in another surprise: the same C_1 symmetry was found for the molecules but now existing in an acentric crystal lattice ($P2_12_12_1$). This means that in the first lattice two racemic molecules with C_1 and C_1' symmetry crystallize together; in the second lattice all molecules are identical. During the nucleation process only C_1 forms started to crystallize together, either for the whole bulk and the other material converted to this form, or racemic twins, probably in domains, remained undetected. It seems that the interconversion from C_1 to C_1' is energetically rather likely. The change from S_4 symmetry to C_1 can be carried out by rotation of each of the four vinyl groups. Therefore, statistically more of the C_1 symmetric molecules exist in the melt than those with S_4 symmetry and, although the latter represents the energetic minimum, it more probably crystallizes in the less stable C_1 conformation for entropic reasons. However, a more favorable crystal packing of the C_1 form may overcome the small energy difference between C_1 and S_4. A transformation from S_4 to S_4' is expected via C_1 and C_1' but not via D_{2d}. Figure 3 gives a rough survey of the energy relations of the discussed conformations in C_1, S_4 and D_{2d}.

The structural features of **TVM** in C_1 are a result of complex interplay between through-bond (hyperconjugation) and through-space interaction (homoconjugation). While all four independent double-bond lengths are nearly equivalent [1.332(1)–1.335(1) Å], the single bonds show significant differences [1.515(1)–1.526(1) Å]. This observation is correlated with the degree of hyperconjugation of the σ(C−C) single bond and the surrounding π-systems. For all single bonds the orientation of the π-orbital axis of the remaining three vinyl groups are different relative to the σ(C−C) bonding orbital of the considered bond.

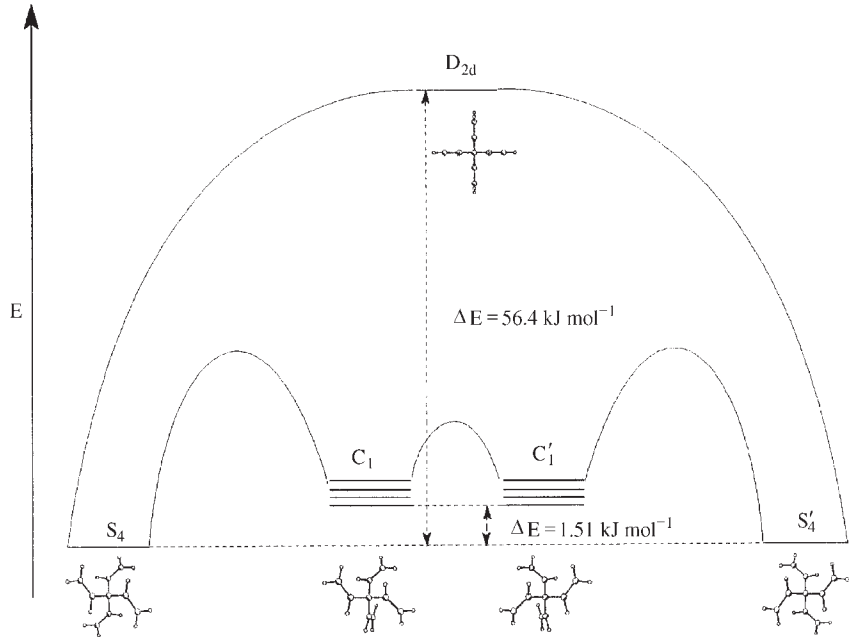


FIGURE 3. Conformational transformations of **TVM** and relative energies of calculated geometries in D_{2d}, S_4 and C_1

Homoconjugational interactions and nonbonding intramolecular contacts of the four π-systems are responsible for the observed distribution of bond angles at the central atom, which are also significantly inequivalent [105.1(1)° to 111.8(1)°].

2. Conjugated acyclic dienes and polyenes

When the π-systems of two or more double bonds overlap, as in conjugated dienes and polyenes, the π-electrons will be delocalized. This has chemical consequences, which implies that the range of possible chemical reactions is vastly extended over that of the alkenes. Examples are various pericyclic reactions or charge transport in doped polyacetylenes. A detailed understanding of the electronic structure of polyenes is therefore of utmost importance for development within this field. We will first discuss the structure of dienes and polyenes based on theoretical studies. Thereafter the results from experimental studies are presented and discussed.

The electron distribution in dienes and polyenes has been the subject of numerous studies that encompass a wide range of experimental[12–14] and theoretical methods[15–19], and the CC bond alternation between double bonds of *ca* 1.34 Å and single bonds of *ca* 1.46 Å in these molecules has been clearly established. The extent of bond alternation in long polyenes is central to the understanding of electronic interactions in π-systems. It has been suggested[20] that a chain-length increase will systematically increase the length of the double bond and decrease the length of the single bond in such a way that the distinction between single and double bonds vanishes for infinitely long polyenes. This would have dramatic effects on the chemical properties, as polyacetylenes with equal carbon–carbon bonds would have metallic properties[17].

A multiconfigurational self-consistent field (MCSCF) study by Villar and Dupuis[17], including the conjugated polyenes C_4H_6, C_6H_8, C_8H_{10} and $C_{10}H_{12}$, showed, however, that a correct description of bond alternacy in polyenes requires the inclusion of electron correlation, and that even large polyene molecules will retain a structure with alternating short (double) and long (single) CC bonds, when electron correlation is properly accounted for. Table 2 gives the optimized parameters for the four smallest conjugated polyenes, as calculated by Villar and Dupuis, using the π-CAS-MCSCF approach. The RHF (Restricted Hartree–Fock) results for $C_{10}H_{12}$ are also shown in order to compare the single bond/double bond alternacy obtained with and without the inclusion of electron correlation. The results obtained using the CAS-MCSCF wave function show a decrease in the single bond/double bond alternacy compared to the RHF results. The difference in bond length between a double and a single bond from the π-CAS-MCSCF calculations is close to the experimental values for polyacetylene[21], where the observed difference is 0.08 Å, in good agreement with the computed values at the MCSCF level for the central unit of $C_{10}H_{12}$.

TABLE 2. Geometrical parameters for 1,3-butadiene (C_4H_6), 1,3,5-hexatriene (C_6H_8), 1,3,5,7-octatetraene (C_8H_{10}) and 1,3,5,7,9-decapentaene ($C_{10}H_{12}$) from π-CAS-MCSCF calculations with 6-31G basis set[17]

Distance (Å)	C_4H_6	C_6H_8	C_8H_{10}	$C_{10}H_{12}$	$C_{10}H_{12}$[a]
$C^1=C^2$	1.349	1.350	1.351	1.350	(1.329)
C^2-C^3	1.463	1.459	1.457	1.458	(1.459)
$C^3=C^4$		1.356	1.357	1.357	(1.336)
C^4-C^5			1.454	1.452	(1.453)
$C^5=C^6$				1.359	(1.337)

[a] RHF/6-31G(d).

Villar and Dupuis explain the decrease in bond alternacy, when electron correlation is included, in terms of occupation numbers of the highest occupied (HOMO) and lowest unoccupied (LUMO) orbitals. The calculated HOMO occupation numbers decrease with polyene chain length; for C_4H_6, C_6H_8, C_8C_{10} and $C_{10}H_{12}$ these are 1.869, 1.846, 1.828 and 1.815, while the corresponding LUMO occupation numbers increase: 0.135, 0.160, 0.179 and 0.193, respectively. For all these conjugated alternate hydrocarbons, the HOMO and LUMO orbitals have opposite bonding properties for any two adjacent C atoms. An increase in the occupation of the LUMOs will therefore result in an elongation of the double bonds and a shortening of the single bonds.

The relationship between π-electron delocalization and the length of CC bonds was originally described in 1939 by Schomaker and Pauling[22], and for a period of 20 years this description was generally accepted. In 1959 Dewar and Schmeising discussed this theory and claimed that the length of any C−C bond is determined by the state of hybridization of the carbon atoms involved in the bonding[23]. Together with *ab initio* calculations it is now possible to carry out natural bond orbital (NBO) analyses[24], which produce — among other quantities — the state of hybridization of all bonding orbitals.

In order to elucidate the possible effect from differences in hybridization states, we have — for the purpose of writing this chapter — carried out NBO analyses for MP2/6-31G(d,p) optimized structures[25] of some relevant molecules, using a CRAY Y-MP supercomputer (Table 3). The orbitals of the $C^3{=}C^4$ σ-bond of the hexatrienes are calculated to have higher % p-character than those of the $C^1{=}C^2$ bond. Hybridization differences appear therefore to offer an alternative explanation for the bonding pattern in conjugated hydrocarbons. The hybridization of the orbitals constituting the single bonds remain, however, practically the same for all carbons in the unsaturated compounds presented in Table 2, while the C−C single bond lengths, according to the MCSCF calculation, show variations of the same order of magnitude as the double bonds. An explanation based on hybridization differences is therefore dubious.

The calculated hybridization of the carbon atom orbitals in the terminal C−H bonds of the conjugated dienes/polyenes is generally equal to those calculated for ethylene ($sp^{2.27}$), corresponding to 69.3% p-character. The angle between two such bonds (∠H−C−H) should accordingly be somewhat smaller than 120°, which is the optimum angle between two sp^2 hybridized carbon orbitals. This is in agreement with experimentally determined terminal H−C−H angles in dienes/polyenes. The p-character of carbon orbitals of nonterminal C−H bonds is generally calculated to be larger than those of the terminal C−H bonds, in agreement with the general observation that the C=C(H)−C angle (in 1,3-butadiene $\geqslant$124°) is normally larger than the terminal C=C−H angles. This implies

TABLE 3. Hybridizations of bonding orbitals for σ-bonds from NBO (Natural Bond Orbital) analyses based on MP2/6-31G(d,p) optimized structures

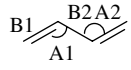
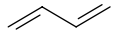
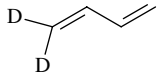
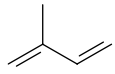
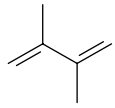
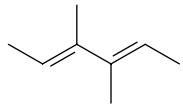
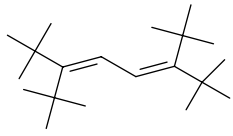
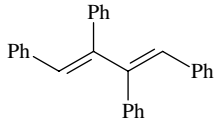
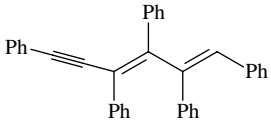
Molecule	$C^1{=}C^2$	C−C	$C^3{=}C^4$	$C^2{-}H^a$
Ethane		$sp^{2.57}$-$sp^{2.57}$		$sp^{3.16}$-s
Ethylene	$sp^{1.57}$-$sp^{1.57}$			$sp^{2.27}$-s
1,3-Butadiene[b]	$sp^{1.55}$-$sp^{1.61}$	$sp^{2.02}$-$sp^{2.02}$		$sp^{2.49}$-s
trans-1,3,5-Hexatriene[c]	$sp^{1.55}$-$sp^{1.61}$	$sp^{2.00}$-$sp^{1.96}$	$sp^{1.63}$-$sp^{1.63}$	$sp^{2.51}$-s
cis-1,3,5-Hexatriene[d]	$sp^{1.55}$-$sp^{1.63}$	$sp^{2.01}$-$sp^{1.99}$	$sp^{1.61}$-$sp^{1.61}$	$sp^{2.48}$-s

[a] For hybridization of the C−H orbitals in the other C−H bonds, see footnotes *b*, *c* and *d*,
[b] C^1(*cis*):$sp^{2.26}$; C^1(*trans*):$sp^{2.31}$,
[c] C^1(*cis*):$sp^{2.25}$; C^1(*trans*):$sp^{2.31}$; C^3: $sp^{2.53}$,
[d] C^1(*cis*):$sp^{2.25}$; C^1(*trans*):$sp^{2.32}$; C^3: $sp^{2.54}$

smaller CCH angles, in agreement with the relatively large p-character of the C−H carbon orbital.

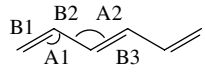
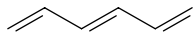
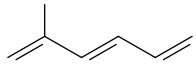
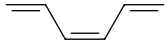
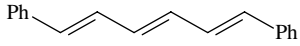
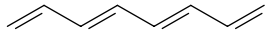
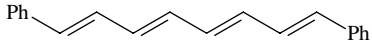
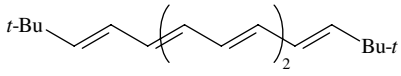
We will now consider the experimental structure data available for acyclic conjugated dienes and polyenes. Tables 4 and 5 list the most relevant structural data for 1,3-dienes and for larger conjugated polyenes. The experimental data shown in Table 4 are generally in agreement with the theoretical description of the bonding properties of 1,3-butadiene, as described above; see Table 2. The X-ray data of 1,3-butadiene could give very accurate geometry parameters[4] in good agreement with the GED investigation[26]. The C=C−C angles in 2-methyl-1,3-butadiene deviate considerably from those in the parent compound. This is, however, reasonable when the need for space of the methyl group is taken into consideration. The enlarged C=C−C angles in *cis*,*cis*-1,2,3,4-tetramethyl-1,3-butadiene may be attributed to the same cause. In the similarly substituted molecule

TABLE 4. Structural parameters determined for acyclic 1,3-dienes (distances in Å, angles in degrees)

	B1	B2	A1	A2	Method[a]
	1.349	1.467	124.4	124.4	GED[26]
	1.335	1.456	123.9	123.9	XR(S1)[4]
	1.337	(1.467)	123.5	123.5	MW[30]
	1.340	1.463	121.4	127.3	GED[31]
	1.349	1.491	122.0	122.0	GED[32]
	1.350	1.473	126.6	126.6	GED[33]
	1.346	1.353	142.3	142.3	XR(S2)[27]
	1.349	1.458	131.1	131.1	XR(S1)[28]
	1.357	1.493	121.3	121.3	XR[34]
	1.363	1.405	129.4	126.3	XR[35]

[a] In parentheses, esd's for bond lengths and angles in the last digit S1: 1–3, S2: 3–10.

TABLE 5. Structural parameters determined for acyclic conjugated polyenes (distances in Å, angles in degrees)

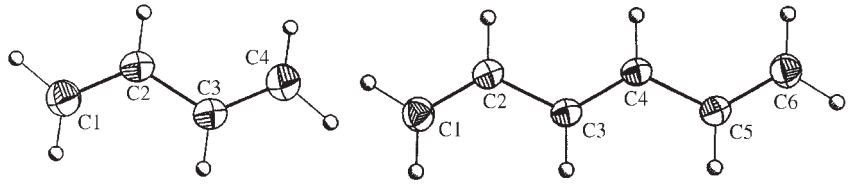
	B1	B2	B3	A1	A2	Method[a]
	1.338	1.451	1.348	124.0	123.8	XR[(S1)4]
	1.337	1.458	1.368	121.7	124.4	GED[36]
	1.348	1.456	(1.348)	119.1	124.8	GED[37]
	1.336	1.462	1.326	122.1	125.9	GED[38]
	1.328	1.433	1.328	124.7	125.5	XR[39]
	1.327	1.451/ 1.451	1.336	125.3	125.1/ 124.7	XR[40]
	1.334	1.442/ 1.445	1.336	122.9	123.8/ 123.5	XR[41]
	1.337	1.433/ 1.437	1.341	125.3	125.2/ 125.5	XR[42]

[a] In parentheses esd's for bond lengths and angles in the last digit S1: 1–3.

cis,*cis*-1,2,3,4-tetraphenyl-1,3-butadiene the C=C−C angles are unusually small. This might be explained by the spacial needs of the *cis*-substituted phenyl groups at each of the C=C bonds. Totally unexpected was the result of an X-ray structure of 1,1,4,4-tetra-*tert*-butyl-1,3-butadiene from 1994 which had amazingly large C=C−C angles and a too short central single bond distance of 1.353 Å[27]. A redetermination by the same authors[28] reconciliated this unusual structure and a value of 1.458 Å is quite in the range of the other 1,3-butadienes. The substance taken for the structure determination was apparently contaminated with a [3]cumulene and cocrystallized with the 1,3-butadiene; the overlap and merge of the electron densities of both molecules lead to the wrong structure which should be seen as a warning of the care needed if totally unexpected and contradictory results are obtained.

The bonding pattern of the last molecule in Table 4 is rather different from that of 1,3-butadiene, a fact which is probably connected to the ethynyl substituent that allows a further delocalization of the π-electrons in this molecule.

The amount of high precision experimental structural data on conjugated polyenes is limited. Some structure results are presented in Table 5. In gas electron diffraction studies it is difficult to determine closely spaced bond distances accurately, because these parameters are highly correlated with the corresponding vibrational amplitudes. Today it is possible to calculate the vibrational amplitudes accurately, if the vibrational frequencies are known. This was, however, not the case when the GED studies presented in Table 5 were carried out. The observed differences between the terminal and central C=C bonds in the GED studies of *trans*-1,3,5-hexatriene and *cis*-1,3,5-hexatriene are probably too large[29]. A very accurate X-ray study of *trans*-1,3,5-hexatriene has, however, been carried out also in connection with the preparation of this chapter[4]. Figure 4 shows the molecular structures of *trans*-1,3-butadiene and *trans*-1,3,5-hexatriene as found in the crystal lattice.



1,3-Butadiene 1,3,5-Hexatriene

FIGURE 4. Molecular structures of 1,3-butadiene and *trans*-1,3,5-hexatriene; presentation with thermal probability plots of 50%

In this study a C=C bond length difference of 0.010 Å is determined, compared with the theoretically calculated difference of 0.006 Å; see Table 2[17]. The single-bond double-bond alternation and the C=C−C valence angles are also quite similar in the two studies.

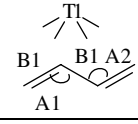
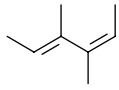
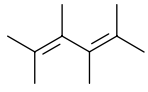
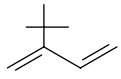
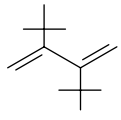
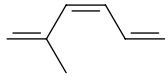
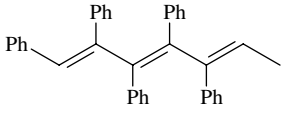
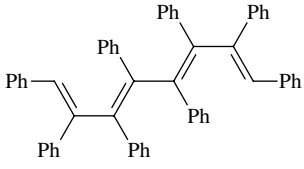
3. Sterically strained linear conjugated dienes and polyenes

Steric strain in conjugated dienes and polyenes generally occurs when the molecules are substituted with spacious groups. Among the di-*tert*-butyl-substituted 1,3-butadienes, the 1,1-substituted isomer is the sterically most heavily strained[43] example. This type of strain is, however, analogous to the strain present in similarly 1,1-disubstituted 1-alkenes and is therefore not connected to the special properties of the diene system. We will limit our discussion on this subject to dienes and polyenes that are sterically strained in a way that influences the delocalized π-system. We have therefore selected dienes/polyenes with conformations deviating by more than 20° from the generally preferred *anti* orientation of adjacent C=C bonds. Table 6 shows relevant structural data observed for such molecules. These data indicate that dienes substituted with moderately large substituents, such as methyl groups, in 1-*cis* and 3- (or 2- and 4-*cis*) positions are destabilized in *anti* conformation because the substituents will be 1,3 parallel oriented, resulting in substantial nonbonded repulsion. For larger substituents, such as *tert*-butyl groups, one substituent in 2- (or 3-) position is sufficient to destabilize an *anti* conformation because of repulsions between the substituent and the C^4 methylene group.

The minimum energy conformation of a conjugated diene will primarily depend on the nonbonded steric interactions and on the interaction between the two π-systems. Both these effects will depend on the dihedral angle at the single bond connecting the two double bonds. For dienes, in which the *anti* conformation becomes unfavorable because of steric strain, the energy contribution of the π-system is analogous to that of the high-energy form of 1,3-butadiene. There has been much discussion about whether the metastable form of 1,3-butadiene has a planar *syn* or a nonplanar *gauche* conformation. Polarized infrared spectra of the matrix isolated metastable isomer provide strong evidence for a planar *syn* structure[44,45]. All recent quantum chemical calculations[46], on the other hand, find the *gauche* structure, characterized by a dihedral angle between 30° and 41°, to be more stable than the planar *syn* form by about 4 kJ mol^{-1}, and the energy variation in the torsional region 0–*ca* 65° is of a similar magnitude. The relation between nonbonded repulsions and the dihedral angle will of course depend on the nature of the substituents.

The molecules in Table 6 may be divided into three groups based on their dihedral angles. For most of these molecules the dihedral angle is close to 60°. In 2,3-di-*tert*-butyl-1,3-butadiene (**2,3-TB**) the dihedral angle is close to 90°, corresponding to an approximately perpendicular conformation, while the dihedral angle in 2-*tert*-butyl-1,3-butadiene (**2-TB**) is determined to be 32.1°.

TABLE 6. Structural parameters observed for sterically strained dienes and polyenes (distances in Å, angles in degrees)

	B1	B2	A1	A2	T1	Method[a]
	1.349	1.479	123.5	123.5	66.7	GED[(S3)47]
	1.359	1.460	120.6	123.3	65.7	GED[(S3)47]
	1.349	(1.487)	125.0	125.0	60.0	GED[(S1)48]
	1.345	1.485	121.7	126.2	32.1	GED[(S2)49]
	1.346 1.326	1.543 1.506	118.3 119.1	118.3 119.1	101.5 96.6	GED[(S3)49] XR[(S1)50]
	1.345	1.463	123–128	—	58.0/180	GED[(S2)51]
	1.347[b]	1.493	122.4–126.0	—	59.3/60.9	XR[52]
	1.347[b]	1.462; 1.487	118.6–120.1	—	62.8/62.3	XR[53]

[a] In parentheses esd's for bond lengths and angles in the last digit S1: 1–3, S2: 3–10, S3: >10.
[b] Average value.

All the molecules with dihedral angles close to 60° will experience some steric strain also in conformations close to planar *syn*. It seems therefore reasonable that the minimum energy conformation to a large extent is determined by the torsional potential connected to the sp^2-sp^2 single bond, as the torsional energy rises sharply for torsional angles larger than *ca* 65° toward a maximum at around 120°[46]. The approximately perpendicular minimum energy conformation of **2,3-TB** must, however, be almost exclusively a result of minimization of the van der Waals steric energy.

When a **2-TB** conformer has a C=C−C=C dihedral angle within the region ±65°, the steric repulsions involving the *tert*-butyl group and the C^4 methylene group will be negligible, and the preferred conformation of the π-system is therefore probably governed by the same factors that are primarily responsible for the preferred conformation of the high-energy conformer of 1,3-butadiene, namely the torsional potential at the C^2-C^3 bond and the nonbonded repulsions between the C^1 and C^4 methylene groups. The concentration of the high-energy form of 1,3-butadiene is very small, and thus it is difficult to study the structure of this conformer experimentally, while the analogous conformer of **2-TB** is present in 100%. The observed conformation for **2-TB** therefore gives strong support to the results obtained by the quantum chemical calculations for metastable 1,3-butadiene.

B. Monocyclic Dienes and Polyenes

In small and medium-sized monocyclic dienes the C=C double bonds are necessarily *cis* connected to the adjacent ring atoms. For rings with at least ten carbon ring atoms *trans* double bonds may be present, without causing high strain energy in the molecule. The existing relevant structural data available for monocyclic dienes/polyenes are therefore presented in two tables. In Table 7 molecular structures for molecules with a maximum of eight ring atoms are shown, while Table 8 gives similar data for larger monocyclic dienes and polyenes. We restrict our discussion to monocyclic dienes and polyenes with no heteroatomic substituents. The available structural data for such molecules are rather limited.

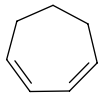
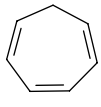
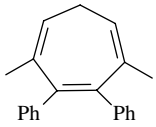
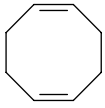
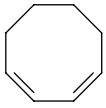
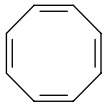
The smallest conceivable conjugated monocyclic diene is 1,3-cyclobutadiene. Several complexes involving cyclobutadiene are known. The compound itself is unstable and has not been studied by structural methods. It will therefore not be included in the present discussion. 1,3-Cyclobutadiene has, however, been isolated in argon matrices, and it has been established that the molecule has D_{2h} symmetry[54]. For the tetra-*tert*-butyl derivative an envelope conformation (twist angle 7°) was found by X-ray methods[55], however the distances in the ring were obviously too similar for an antiaromatic system [1.464(3) and 1.483(3) Å]. A redetermination at even lower temperatures gave more reasonable results (1.441 and 1.527 Å)[56] and a further analysis of the anisotropic parameters revealed that some residual disorder is still responsible for some equilibration and distances of 1.34 and 1.60 Å were assumed to be the correct ones[57].

The next cyclic alkadiene, 1,3-cyclopentadiene, has been experimentally studied by MW, GED and XR methods. The carbon skeleton is planar (C_{2v} symmetry), and the small C=C−C angles compared to those in 1,3-butadiene (124.3°) or *cis*-1-butene (126.4°)[58] do not seem to influence noticeably the lengths of the CC bonds, although other effects, such as π-electron delocalization, might have an opposite effect. The apparently 'normal' structure parameters observed for 1,3-cyclopentadiene might therefore be a result of different forces having opposite effects on the structure parameters.

In Table 7 the *six-membered monocyclic dienes* are represented by the conjugated 1,3-cyclohexadiene and its isomer 1,4-cyclohexadiene. 1,3-Cyclohexadiene has a nonplanar equilibrium conformation that is primarily influenced by three factors: π-electron interaction (optimal for a planar conformation); angle strain and torsion strain (both optimal for a planar conformation). The reduced overlap between the two π-orbital systems is, for the observed C=C−C=C angle of 18°, estimated at *ca* 10% and should therefore not influence the conjugation stabilization drastically, compared to a conformation with coplanar C=C bonds.

It is reasonable to assume that the 1,3-cyclohexadiene molecule is stabilized by its conjugated π-system, relative to the nonconjugated 1,4-isomer. Existing experimental and theoretical information about these two molecules indicate, however, that other forces, in

TABLE 7. Experimentally determined and calculated structure parameters for monocyclic dienes and polyenes; maximum 8 ring atoms (distances in Å, angles in degrees)

	B1	B2 (B3)	A1	A2	T1[b]	Method[a]
	1.340	1.469	109.3	109.4	0.0	GED[59]
	1.342	1.465	109.3	109.3	0.0	MW[60]
	1.344	1.460	109.6	109.1	0.0	XR[(S1)4]
	1.354	1.465	109.2	109.1	0.0	MP2[c4]
	1.347	(1.511)	122.7	122.7	~0	GED[(S2)61]
	1.334	(1.496)	123.4	123.4	~0	GED[(S1)62]
	1.318	(1.468)	123.4	123.5	0.0	XR[(S1)63]
	1.339	1.468	118.2	121.6	17.0	GED[(S2)64]
	1.348	1.464	120.3	120.3	18.0	GED[(S1)65]
	1.350	1.468	120.1	120.1	18.3	GED[(S3)61]
	1.347	1.450	129.1	129.1	0.0	GED[(S2)66]
	1.345	1.470	128.5	125.0	0.0	MP2[d67]
	1.356	1.446	121.8	127.2	α: 40.5[e,f,g] β: 36.5[e]	GED[(S2)68]
	1.337/ 1.357	1.471[h]	121.4[h]	125.1[h]	α: 52.6[e] β: 34.3[e]	XR[69]
	1.340	1.514	130.6	130.6	~0	GED[(S2)70]
	1.347	1.475/ (1.501)	129.0	129.0	38.0	GED[(S2)71]
	1.340 1.333	1.476 1.468	126.1 126.6	126.1 126.6	α: 43.1[g]	GED[(S1)72] XR[(S1)73]

[a] In parentheses, esd's for bond lengths and angles in the last digit S1: 1–3, S2: 3–10, S3: >10.
[b] C=C–C=C torsion angle.
[c] MP2/6-31G(d).
[d] MP2/6-31G(d,p).
[e] α is the angle between the $C^2C^3C^4C^5$ and $C^1C^2C^5C^6$ planes; β is the angle between the $C^1C^6C^7$ and $C^1C^2C^5C^6$ planes.
[f] $C^1{=}C^2{-}C^3{-}C^4$: −86.5°, C–C–C–C: 63.8°, $C^3{-}C^4{-}C^5{=}C^6$: 8.1°, C–C=C–C: 6.2°.
[g] 'Bath tub' angles.
[h] Average value.

addition to the π-electron distribution, contribute to the overall energies of the two isomers. They do, for example, appear to have nearly equal enthalpies of formation[74]. Skancke and coworkers[75] have recently performed *ab initio* calculations at different levels of theory for a number of molecules, including the two cyclohexadienes. Optimized structures of the two isomers at the HF/6-31G(d) level favored the 1,4- over the 1,3-isomer by 1.1 kJ mol^{-1}. Contrary to this, MP2/6-31G(d) and MP2/6-31G(d,p) optimizations found the 1,3-isomer to have the lowest energy of the two, the differences being 1.2 kJ mol^{-1} and 0.1 kJ mol^{-1}, respectively. At a still more advanced level of calculation, MP4dq/6-31G(d,p)//MP2/6-31G(d,p), the 1,4-isomer was again calculated to be the more stable, by 1.1 kJ mol^{-1}. If a conclusion should be drawn from the partly conflicting information presented above, it must be that the energies of the 1,3- and 1,4-cyclohexadiene molecules are nearly the same.

We have already pointed to one effect that should contribute to lowering the relative energy of 1,3-cyclohexadiene, namely the π-electron conjugation. If the energies of the 1,3- and 1,4-cyclohexadiene molecules are approximately equal, this might imply that the 1,3-isomer is destabilized, or the 1,4-isomer stabilized, by other causes. The distribution of torsion angles in the two molecules might give a possible explanation. In a planar 1,4-cyclohexadiene molecule all C−C torsion angles correspond to potential energy minima (although not generally the lowest ones). In the conjugated nonplanar 1,3-isomer none of the torsion angles at the formal single bonds has a value corresponding to the expected potential energy minima. The total effect from the torsions in the two isomers might therefore destabilize the 1,3- relative to the 1,4-isomer by an energy amount comparable to that of the additional π-electron stabilization in the conjugated 1,3-cyclohexadiene molecule.

The next molecules to be discussed are the *seven-membered monocyclic dienes and polyenes*. 1,3-Cycloheptadiene has been studied by GED (Table 7). The molecule has also been studied by MW[76]. This study did not include a complete structure determination, but it was concluded that the carbon skeleton is planar, except for the C^6 carbon, corresponding to C_S symmetry. This is in agreement with the GED results. *Ab initio* calculation at the MP2 level, utilizing the 6-31G(d,p) basis set, has recently been carried out[77]. Both the C_S and C_2 conformers of 1,3-cycloheptadiene were considered, and the MP3/6-31G(d,p)//MP2/6-31G(d,p) calculations predict the C_S conformer to be 3.3 kJ mol^{-1} lower in energy than the C_2 conformer. It was concluded that the calculated C_S conformer at the MP2 level is in excellent agreement with the available MW and GED data. The MP2 and MP3 energetics results allow, however, for the possibility of the presence of a C_2 conformer, as evidenced by NMR data[78]. The experimental results do not rule out the presence of small amounts of a C_2 conformer that is twisted about the diene region.

On the basis of the NMR spectrum of *1,3,5-cycloheptatriene* Doering and Coworkers[79] suggested in 1956 that the molecule has a pseudo-aromatic structure with a planar carbon skeleton. The supposed aromatic structure is reflected in the commonly used name tropylidene for this molecule. There is, however, no doubt that the 1,3,5-cycloheptatriene[68] molecule has a boat-shaped conformation with alternating double and single bonds. A recent MP2/6-31G(d)//MP2/6-31G(d) calculation by Skancke[75] gave almost identical bond lengths and valence angles to those in the GED study; the 'bath tub' angles differed, however, somewhat (α, 27.7°; β, 57.3°). The corresponding angles observed in the X-ray study of 2,5-dimethyl-3,4-diphenyl-1,3,5-cycloheptatriene[69] are, however, similar to those observed by GED for the parent compound.

The final entries in Table 7 concern *eight-membered monocyclic dienes and polyenes*. The unconjugated *1,5-cyclooctadiene* was observed to have twist-boat conformation and C_2 symmetry. In accordance with what is very often the case in GED studies of cyclic

compounds, amounts less than about 10% could not be ruled out. The GED study is in agreement with molecular mechanics calculations[80], which found the twist-boat form to be lower in potential energy than the regular boat by 29 kJ mol^{-1} and the chair lower by 17 kJ mol^{-1}. The twist-boat conformation adopted by the free molecules appears to be a result of minimizing torsional strain and nonbonded repulsions.

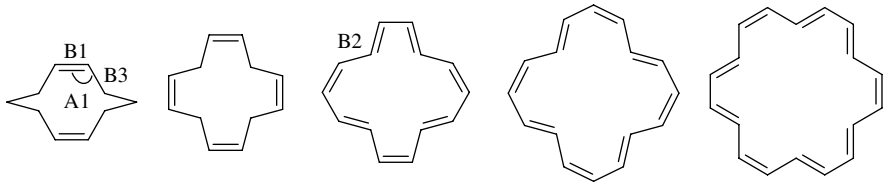
The GED results obtained for *1,3-cyclooctadiene* should be regarded with caution, as the data in Table 7 refer to a 25-year-old study, where it was assumed that only one conformer is present. The structure of 1,3-cyclooctadiene should therefore be reinvestigated.

The observed geometry of *1,3,5,7-cyclooctatetraene* (**COT**) is strikingly similar in the solid state and in the gas phase. The molecule is found to be boat-shaped with D_{2d} symmetry. Single and double bonds are as expected for a nonplanar compound with isolated double bonds and no significant π-orbital overlap. Addition of substituents results in differences in the ring geometry, e.g. repulsion of the methyl groups in octamethyl-**COT** causes significant flattening of the ring[81]. The NMR spectrum of cyclooctatetraenyl dianion is, however, in agreement with a planar aromatic eight-membered ring, with a high degree of resonance stabilization in association with a closed shell of $(4n + 2)$ π-electrons for $n = 2$[82]. As a dianionic ligand the **COT** skeleton is also planar and has aromatic character[83].

Table 8 presents structures observed for monocyclic dienes and polyenes with rings large enough to accommodate *trans* C=C double bonds. In a cyclodecadiene molecule strain-free carbon skeletons can only be derived when two double bonds are diametrically placed and have the same configuration (*cis*, *cis* or *trans*,*trans*). *Cis*,*cis*-Cyclodeca-1,6-diene (**1,6-CDD**) may exist in *twelve* different conformations, and it is therefore noteworthy that it almost exclusively prefers one of these, namely the one indicated in Table 8. This conformer does not have the repulsive transannular HH interactions that destabilize the corresponding saturated molecule in all conceivable conformers.

The *all-cis-1,4,7,10-cyclodecatetraene* (**1,4,7,10-CDT**) molecule is of special interest as a tetrahomo-8π-system, when all four π-bonds are arranged in a way where maximum interaction is guaranteed. This arrangement is realized in the crown conformation, which is also the conformer observed in an X-ray study of the molecule. The mean C=C bond

TABLE 8. Experimentally determined structure parameters for monocyclic dienes and polyenes; minimum 10 ring atoms (distances in Å, angles in degrees)



(1,6-CDD)	(1,4,7,10-CDT)	(14-ANN)	(16-ANN)	(18-ANN)
	B1	B2 (B3)	A1	Method[a]
1,6-CDD	1.326	(1.506)	128.2	GED(S2)[84]
1,4,7,10-CDT	1.324[b]	(1.503)[b]	127.4[b]	XR[85]
14-ANN	1.378[b]	1.378[b]		XR(S3)[86]
16-ANN	1.337[b]	1.454[b]		XR[87]
18-ANN	1.371–1.429	1.371–1.429		XR[88]

[a] In parentheses, esd's for bond lengths and angles in the last digit S2: 3–10, S3: >10.
[b] Average value.

lengths correspond approximately to those in planar 1,4-cyclohexadiene (see Table 7), whereas the single bonds are somewhat longer. The distances between hydrogen atoms pointing toward the center of the ring, *ca* 2.01 Å, are clearly shorter than the sum of the van der Waals radii of 2.4 Å. As the molecule prefers a conformation in which all the double bonds are coplanar, this is interpreted as an absence of homoantiaromatic destabilization.

Results from X-ray studies of three annulenes are presented In Table 8. According to Hückel's rule [14]annulene **(14-ANN)** and [18]annulene **(18-ANN)** should be aromatic and most probably planar molecules, while [16]annulene **(16-ANN)**, as a [4*n*]annulene, should be antiaromatic. The [14]annulene molecule is nonplanar, with a structure that approaches C_{2h} symmetry. The cause of the nonplanarity is the steric overcrowding in the center of the molecule. While the spread of the individual bond lengths implies possible significant differences, there is no significant pattern to the values obtained.

The [16]annulene is nonplanar, with almost complete bond alternation. The single bonds (1.454 Å) are alternately *trans* and *gauche*, and the double bonds (1.337 Å) *cis* and *trans*. The average torsion angle at a *gauche* C−C bond is 41°. The molecule is therefore relatively flat with S_4 noncrystallographic symmetry, and the structure confirms the lack of aromaticity in this [4*n*]annulene.

The investigation of [18]annulene is the oldest of the X-ray annulene studies reported, and it was stated that the hydrogens have not been reliably located. The molecular structure closely resembles that of coronene[89]. This rules out the possibility of a structure with alternate long and short C−C bonds. The observed spread of CC distances in [14]annulene and in [18]annulene is *ca* 0.06 Å, while that in [16]annulene is twice as large, *ca* 0.12 Å. The annulene molecules therefore have structures that are similar to what is expected on the basis of Hückel's rule.

C. Polycyclic Dienes and Polyenes

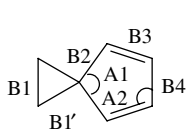
The largest contribution and variety in the family of polyenes is to be found in the group of bicyclic and polycyclic compounds. For this chapter we selected those compounds which represent the most important prototypes of different kinds of interaction, namely cyclopropyl-conjugation, spiroconjugation, hyperconjugation and homoconjugation.

1. Spiropolyenes

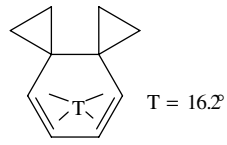
In respect to the similar chemical behavior of alkenes and cyclopropanes but different MO and bonding situations, the determination of exact geometries of cyclopropyl-conjugated hydrocarbons can supply important information. As reported in the literature, the three-membered ring in a substituted cyclopropane derivative is rather sensitive to bond length distortions caused by conjugation effects[90]. The electron-withdrawing effect of a neighboring double bond leads to a lengthening of the *vicinal* bonds and a shortening of the *distal* bond in the three-membered ring if the bisected conformation is fulfilled. In small spirocyclic dienes the conformation is fixed in the bisected form where the best orbital overlap can be achieved.

Table 9 shows the geometrical features of compounds, where strong cyclopropyl conjugation takes place. In spiro[2.4]hepta-4,6-diene **(SHD)** this interaction has an important contribution to the molecular dipole moment, 0.95 Debye measured by microwave analysis[91]. The structural influences are mainly taking place in the three-membered ring, where a strong bond length splitting is observed for most of the experimental and theoretical methods. However, the ED investigation could not distinguish between the cyclopropane bonds. The same problem occurs in the gas-phase structure determination of the dispiro compound **(DSD1)**; unfortunately there are no further

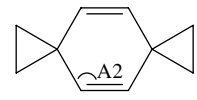
TABLE 9. Experimentally determined and calculated structure parameters for spiro[2.*n*]dienes (distances in Å, angles in degrees)



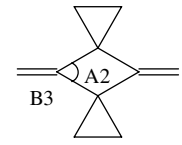
(SHD)



(DSD1)



(DSD2)



(DSOD)

	B1 (B1')	B2	B3	B4	A1	A2	Method[a]
SHD	1.494 (1.546)	1.462	1.361	1.467	107.0	108.9	MW[(S1)91]
	1.486 (1.533)	1.467	1.338	1.448	104.8	109.1	XR[(S1)9]
	1.510[b]	1.509	1.340	1.460	102.6	109.5	GED[(S2)59]
	1.484 (1.528)	1.473	1.360	1.460	105.7	109.0	MP2[9]
DSD1	1.508[b]	1.518	1.345	1.459	117.4	121.6	GED[(S2)92]
DSD2	1.498 (1.526)	1.482	1.335	—	114.6	122.7	XR[(S1)9]
	1.496 (1.521)	1.479	1.354	—	114.6	122.7	MP2[9]
DSOD	1.492 (1.504)	1.518	1.318	—	90.1	89.9	XR[(S1)93]

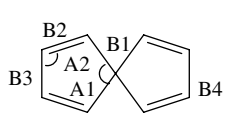
[a]In parentheses, esd's for bond lengths and angles in the last digit S1: 1–3, S2: 3–10. MP2 = MP2/6-31G(d).
[b]Mean values for cyclopropane bonds.

structural data available so far. The dispirodecadiene **(DSD2)** has been analyzed by X-ray and *ab initio* methods; both results are in good agreement with respect to the different models of investigation. The dispiro compound (**DSOD**) can be considered as a derivative of [4]rotane. While the cyclobutane ring is square and planar in **DSOD**, additional strain and rehybridization shortens the vicinal cyclopropane bond and the double bond.

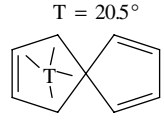
Compounds with two perpendicular π-systems joined by a common spiro-atom exhibit through-space *spiroconjugation*[94]. One important representative of spiroconjugated systems is spiro[4.4]nonatetraene **(SN4)**[95]. The molecular structures of spiro[4.4]nona-1,3,7-triene **(SN3)** and **SN4** have been determined by X-ray diffraction in order to detect the slight distortions expected by spiroconjugation. Comparison of bond lengths and angles reveals a slight shortening of the double bonds and a small lengthening of the single bonds connecting the spiro atom in **SN4**. The same effect is also found by *ab initio* calculations at the Hartree–Fock level 6-31G(d), although to a minor extent[96]. Table 10 shows the most important geometrical features of **SN3** and **SN4** together with the data of spirotetraenedione **(STD)**.

While **SN4** and **STD** exhibit essentially D_{2d} symmetry, **SN3** has C_S symmetry with a planar diene ring and an envelope-shaped cyclopentene ring. The maximum torsion in the folded ring of **SN3** is 20.2°. The spiro-connection of two five-membered ring systems leads to some strain at the spiroatom (101.4° to 101.8° at A1 compared to 109.5° for tetrahedral

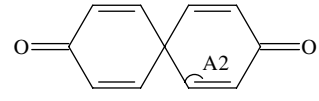
TABLE 10. Experimentally determined and calculated structure parameters for spiro[4.*n*]polyenes (distances in Å, angles in degrees)



(SN4)



(SN3)



(STD)

	B1	B2	B3	B4	A1	A2	Method[a]
SN4	1.516	1.338	1.469	—	101.7	109.6	XR[(S1)96]
	1.519	1.326	1.479	—	101.4	109.2	RHF/6-31G(d)[96]
SN3	1.505 1.514	1.347 1.343	1.470	1.334	101.8	108.9	XR[(S1)96]
	1.511 1.516	1.326 1.326	1.479	1.319	101.3	108.9	RHF/6-31G(d)[96]
STD	1.497	1.323	1.451	1.227	111.7	121.2	XR[(S2)97]

[a]In parentheses, esd's for bond lengths and angles in the last digit S1: 1–3, S2: 3–10.

environment). Derived from these data the structural effects of spiroconjugation seem to be extremely small, since bond lengths and angles are in normal ranges.

2. Annulated cyclopolyenes

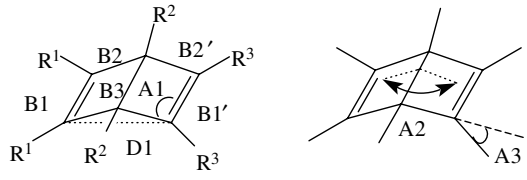
Two rings linked by sharing the same bond instead of the same atom lead to annulated bicyclic or tricyclic compounds, the propellanes. In the case of poly-unsaturated molecules, an interesting case is represented by the bicyclo[2.2.0] type. The parent compound Dewar benzene (bicyclo[2.2.0]hexa-2,5-diene) **(DEW)** is the smallest bicyclic diene which is an often discussed valence isomer of aromatic benzene C_6H_6. Unsubstituted **DEW** is a very small and strained molecule which is prepared photochemically. It is the first valence bond isomer of benzene ever isolated. The molecule is not planar; the interplanar angle of both adjacent four-membered rings varies between 115° and 118° (see Table 11). In this butterfly shape the π-systems are bent toward each other and can perform homoconjugation as well as hyperconjugation.

Very obvious is the long central single bond B3 observed by all experimental methods (1.57 to 1.63 Å). The double bonds reveal pyramidalization[98] (see Figure 5) which is defined by the angle A3 and describes the *out-of-plane* deviation of the substituents (1.5° to 2°). Hyperconjugational effects bias the sp^2-sp^3 single bond lengths which appear to be elongated. The effects of hyperconjugation and pyramidalization are illustrated in Figure 5.

If cyclohexa-1,3-diene is annulated with a three-membered ring at the 5,6- single bond, the norcaradiene system results. An opening of the cyclopropane ring at the common bond is observed by thermal rearrangement yielding cycloheptatriene. In the case of bisnorcaradiene **(BNOR)**, which is a [4.4.1]propellane, the ring opening leads to an energetically more favorable aromatic [10]annulene system. Substitution at the cyclopropane has an essential influence on the [10]annulene $\rightleftharpoons$ bisnorcaradiene equilibrium (Figure 6).

In contrast to the effect of π-systems in the cyclohexadiene systems, the introduction of π-acceptor substituents at the cyclopropane unit shortens the central bond. In the case of the cyano group, the influence of two substituents leads to a central bond B4 which

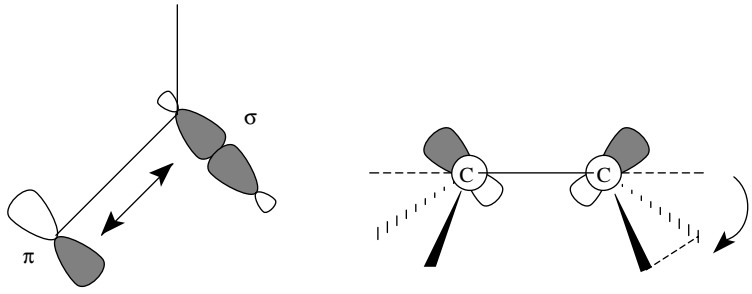
TABLE 11. Experimentally determined structure parameters for bicyclo[2.2.0]dienes (distances in Å, angles in degrees)



(DEW)

		B1 (B1')	B2 (B2')	B3	D1	A1 (A2)	Method[a]
DEW	$R^1 = R^2 = R^3 = H$	1.345	1.524	1.574	2.595	(117.3)	GED[(S3)99]
	$R^1 = R^2 = R^3 = Me$	1.352	1.523	1.629		(124.5)	GED[(S2)100]
	$R^1 = R^2 = H$	1.328	1.529	1.575	2.569	(114.9)	XR[(S1)101]
	$R^3 = CN$	(1.336)	(1.531)				
	$R^1 = R^3 = H$	1.346	1.531	1.594		95.1	XR[101]
	$R^2 = cy^b$					(115.9)	
	$R^1 = R^3 = H$	1.311	1.521	1.565		94.8	XR[(S1)102]
	$R^2 = cy^b$	(1.319)	(1.524)			(116.6)	
	$R^1 = R^3 = H$	1.316	1.533	1.572		(117.7)	XR[(S1)104]
	$R^2 = cy^b$						

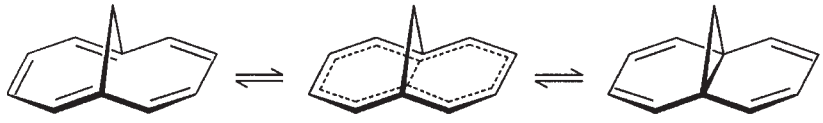
[a] In parentheses, esd's for bond lengths and angles in the last digit S1: 1–3, S2: 3–10, S3: >10.
[b] cy = cyclic bridged.



(A) **(B)**

FIGURE 5. Hyperconjugation **A** ($\pi-\sigma$(C−C)) and pyramidalization **B** of a C=C double bond

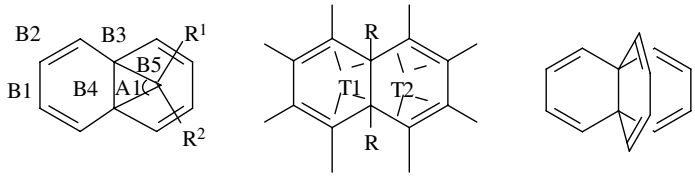
is even shorter than B5 (Table 12). In this case the norcaradiene form **C** is stabilized. A combination of a cyano and a methyl group has a weaker effect and, in the case of two methyl groups, the central bond is almost cleaved (1.771 Å and 1.827 Å for two independent molecules in the crystal lattice) and a significant equalization of the double and single bonds occurs in the rest of the molecule (form **B**). If there is no substitution, the bridged [10]annulene system **A** is observed with a distance of 2.235 Å for the former



(A) (B) (C)

FIGURE 6. Equilibrium of CH_2-bridged [10]annulene **A** and bisnorcaradiene **C**

TABLE 12. Experimentally determined and calculated structure parameters for bisnorcaradienes and annulated polyenes (distances in Å, angles in degrees)



(BNOR) (DHN) (PRO)

		B1	B2	B3	B4	B5 (T1)[b]	A1 (T2)	Method[a]
BNOR	$R^1 = R^2 = CN$	1.450	1.343	1.475	1.539	1.569 (151.0)	58.8 (4.3)	$XR^{(S1)105}$
	$R^1 = CN$ $R^2 = Me$	1.444	1.342	1.472	1.640	1.527 (145.7)	63.9 (5.8)	$XR^{(S1)106}$
	$R^1 = R^2 = Me$	1.419	1.335	1.458	1.771	1.508 (140.2)	71.8 (7.9)	$XR^{(S2)107}$
		1.431	1.348	1.453	1.827	1.507 (139.9)	74.6 (8.3)	$XR^{(S2)107}$
	$R^1 = R^2 = H$	1.418	1.377	1.405	2.235	1.486 (139.3)	97.6 (15.9)	$XR^{(S2)108}$
DHN	R = Me	1.470	1.337	1.537	1.553	(55.2)	(21.6)	$XR^{(S2)109}$
	R = COOMe	1.481	1.345	1.540	1.557	(53.2)	(20.5)	$XR^{(S2)109}$
PRO		1.457	1.341	1.528	1.567	(40.5)	(9.8)	$XR^{(S3)110}$

[a] In parentheses, esd's for bond lengths and angles in the last digit S1: 1–3, S2: 3–10, S3: >10.
[b] for **BNOR**: T1 = torsion angle C=C–C–C.

central bond. The aromatic character of the CH_2-bridged [10]annulene is weakened by folding of the conjugated system (see T1 and T2). Higher-level *ab initio* calculations on the MP2/6-31G(d) level could not predict a stable bisnorcaradiene form **C** as a minimum on the potential energy surface. The electron-withdrawing effect of both π-systems weakens the central bond in such a way that the energetic barrier between both forms disappears and the annulene structure is the only alternative. Table 12 shows geometrical parameters of different substituted bisnorcaradienes and related molecules.

Substituted 9,10-dihydronaphthalenes (**DHN**) adopt essentially C_2 symmetry, whereas the diene systems are strongly twisted (see torsion angles T1 and T2). The bond lengths are

in normal ranges. [4.4.4]Propellahexaene **(PRO)** has a remarkable propeller-like shape, close to D_3 symmetry. The torsion angles in the annulated six-membered rings are smaller than in the **(DHN)** structures. The central bond (1.567 Å) is only slightly longer than the normal value for sp^3-sp^3 single bonds.

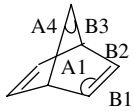
3. Bridged polyenes

Norbornadiene (bicyclo[2.2.1]hepta-2,5-diene) **(NOR)** appears also as a strained olefinic bicyclic molecule. The interplanar angle is smaller than in **DEW** with 113.9° to 115.1° (see Table 11). The same homoconjugational and hyperconjugational effects can be observed in **NOR**, whereas influences of homoconjugation mainly bias the electronic structure[111,112] and hyperconjugation biases the geometrical properties. The additive hyperconjugational interactions between π- and σ(C−C)-systems have a significant elongational effect on the single bonds (see Figure 5). The bond B2 is 0.024 Å (mean value) longer than a normal sp^2-sp^3 C−C single bond and B3 is observed about 0.013 Å (mean value) longer than normal C−C bonds of this type (sp^3-sp^3).

Bicyclic olefins of the **NOR** type were often discussed in terms of high reactivity and *exo*-selectivity in Diels-Alder reactions. A straightforward explanation for this effect can be given by the observed pyramidalization of the double bond into the *exo*-region of the unsaturated center (see Tables 13 and 14, angle A3). Another characteristic property of the bicylic systems of the **NOR** type is related to the globular shape of the molecules[113]. The nonpolarity and regular shape of molecules often lead to plastic phases[114] and polymorphism. The investigation of the molecular structure in the plastic high-temperature phase is not possible, caused by local disorder and inner rotation of the molecules. With the special method of *in situ* crystallization from solution using an IR laser beam[115] it is possible to circumvent the plastic phases. A single crystal of **NOR** in the ordered low-temperature phase could be achieved by this method; the X-ray data are given in Table 13.

In 7-isopropylidene-norbornene (**INOR1**) hyperconjugation also has a significant influence on the geometrical parameters. All single bonds which interact with the π-systems

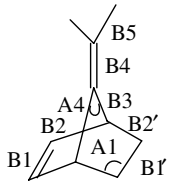
TABLE 13. Experimentally determined and calculated structure parameters for bicyclo[2.2.1]hepta-2,5-diene (distances in Å, angles in degrees)

	B1	B2	B3	A1 (A3)[b]	A2[b] (A4)	Method[a]
NOR	1.337	1.536	1.555	107.2 (∼ 4.5)	114.4 (92.5)	XR(S1)[116]
	1.339	1.533	1.571	—	— (92.2)	GED(S1)[117]
	1.336	1.530	1.557	107.1	— (91.9)	MW(S1)[118]
	1.319	1.539	1.550	107.7 (2.7)	115.1 (92.3)	RHF/6-31G(d)[116]
	1.345	1.533	1.552	107.0 (3.7)	114.8 (92.3)	MP2/6-31G(d)[116]

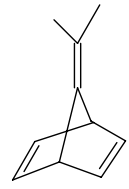
[a] In parentheses, esd's for bond lengths and angles in the last digit S1: 1–3.

[b] For the definition of A2 and A3, see Table 11.

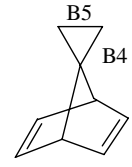
TABLE 14. Experimentally determined and calculated structure parameters for 7-substituted bicyclo[2.2.1]dienes and -polyenes (distances in Å, angles in degrees)



(INOR1)



(INOR2)



(SNOR)

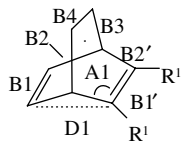
	B1 (B1')	B2 (B2')	B3	B4 (B5)	A1 (A3)[b]	A2[b] (A4)	Method[a]
INOR1	1.342 (1.553)	1.521 (1.566)	1.519	1.333	107.5 (∼ 4.2)	111.3 (96.0)	XR(S1)[116]
INOR2	1.337	1.538	1.533	1.330	107.6 (∼ 1.9)	114.5 (94.4)	XR(S1)[116]
	1.320	1.539	1.533	1.318	107.3 (1.7)	115.3 (93.7)	RHF/6-31G(d)[116]
	1.346	1.533	1.533	1.339	107.1 (2.4)	115.2 (94.4)	MP2/6-31G(d)[116]
SNOR	1.332	1.535	1.537	1.485 (1.525)	107.0 (∼ 2.9)	114.3 (93.7)	XR(S1)[116]
	1.320	1.539	1.537	1.483 (1.514)	107.2 (2.3)	114.9 (93.0)	RHF/6-31G(d)[116]
	1.346	1.533	1.537	1.489 (1.522)	107.0 (3.1)	114.9 (93.7)	MP2/6-31G(d)[116]

[a] In parentheses, esd's for bond lengths and angles in the last digit S1: 1–3.
[b] For the definition of A2 and A3, see Table 11.

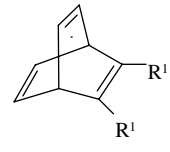
show longer bonds than usual. The six-membered ring is more puckered, with an interplanar angle of 111.3°, than in the cyclohexadiene system in **NOR**. The exocyclic double bond B4 shortens the central single bonds B3 and widens the angle A4 by hybridization effects and strain compared to **NOR**.

Strong homoconjugation effects are discussed for **INOR2**, where destabilizing interactions of the norbornadiene system and the exocyclic π-system take place[111]. As a consequence there is a slight tendency to achieve a bicycloaromatic state, in agreement with the observed polarization of the exocyclic bond B4 (obtained from ^{13}C-NMR data[112]). Structural influences, caused by pure homoconjugation, are hard to detect. They cannot be separated from the strong hyperconjugation effects, which again alter the σ(C−C) single bond system of **INOR2**. In **SNOR** the norbornadiene fragment is nearly identical to that in **INOR2**; here the spiro cyclopropane unit is part of the homoconjugated system[119]. Cyclopropyl homoconjugation in **SNOR** has a significant influence on the rather sensitive (bent) bonds of the three-membered ring. In addition to the effects of strain and hybridization, the vicinal bonds B4 are shortened and the distal bond B5 is elongated by electronic interactions with the π-systems. In contrast to cyclopropyl conjugation, this effect weakens the distal bond and the cyclopropyl group acts as an electron acceptor rather than an electron donor.

TABLE 15. Experimentally determined and calculated structure parameters for bicyclo[2.2.2]dienes and -polyenes (distances in Å, angles in degrees)



(DBAR)



(BAR)

		B1 (B1')	B2 (B2')	B3 B4	D1	A1	Method[a]
DBAR	$R^1 = H$	1.339	1.521	1.553		113.5	GED(S2)[121]
	$R^1 = CN$	1.325 (1.346)	1.512 (1.517)	1.559	2.444	111.8	XR(S1)[101]
BAR	$R^1 = H$	1.335	1.538			112.9	GED(S1)[122]
	$R^1 = CN$	1.311 (1.334)	1.531 (1.536)		2.430	111.4	XR(S1)[101]

[a]In parentheses, esd's for bond lengths and angles in the last digit S1: 1–3, S2: 3–10.

For **INOR1**, **INOR2** and **SNOR** a significant pyramidalization of the endocyclic double bonds can be observed by all methods. The out-of-plane deviations appear to be around 1.9° to 3.1° (see Table 14).

Barrelene **(BAR)** is an interesting molecule with high symmetry (D_{3h}) and three homoconjugated π-systems. The synthesis of the unsubstituted hydrocarbon **BAR** (which is rather stable at room temperature) was first reported by Zimmermann and Paufler in 1960[120]. The structural parameters of **BAR** (Table 15) show unusually long single bonds B2 (1.512–1.538 Å). In a direct comparison of bond B2 with dihydrogenated **DBAR** the difference caused by hyperconjugation is about 0.018 Å (Table 15), in good agreement with the observations from the bicyclo[2.2.1]systems.

4. Polycyclic polyenes

One of the most interesting small polycyclic hydrocarbons is tricyclodecatriene, better known as bullvalene **(BUL)**. It can be considered as a 1,2,3-trivinylcyclopropane, where the vinyl groups are linked by a common carbon (bridgehead) atom at each end. Undergoing Cope rearrangement, the molecule is able to transform a cyclopropyl atom into a bridgehead atom, and the bridgehead atom with two adjacent atoms into cyclopropyl atoms (see Figure 7). Several rapid rearrangements transfers each of the ten carbon atoms into a bridgehead atom, leading to a constant change of the π-bond positions in the molecule.

The molecular structure of the parent compound was investigated in the vapor and in the solid phase using X-ray, XN and GED methods. The reported data are shown in Table 16. In both phases a clear bond length separation could be detected with a localized three-membered ring and its three adjacent double bonds. The symmetry-equivalent cyclopropane bonds are rather long in C_{3v}-symmetric **BUL** (1.533–1.542 Å), which can be explained by the common electron-withdrawing effect of the π-systems in a *syn*-clinal conformation. For comparison, the unaffected bonds in unsubstituted cyclopropane are 1.499 Å in the crystal and 1.510 Å in the gas phase. Therefore, the bond lengths in **BUL**

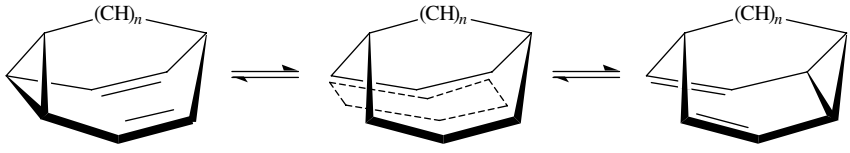
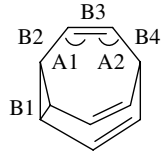
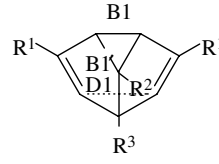


FIGURE 7. Cope rearrangement of bullvalene **(BUL)** ($n = 2$) and semibullvalene **(SEM)** ($n = 0$)

TABLE 16. Experimentally determined structure parameters for small polycyclic polyenes (distances in Å, angles in degrees)



(BUL)



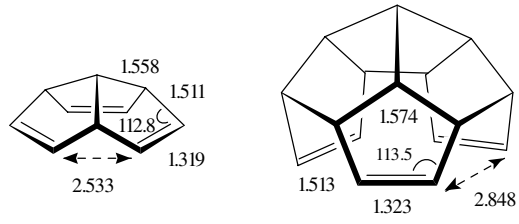
(SEM, SEM1, SEM2)

		B1 (B1')	B2	B3	B4 (D1)	A1	A2	Method[a,b]
BUL		1.542	1.465	1.346	1.523	122.6	126.3	GED[(S2)123]
		1.539	1.452	1.319	1.508	124.1	126.7	XR[(S1)124]
		1.533	1.473	1.342	1.516	123.7	126.5	XN[(S1)125]
SEM	$R^1 = R^2 = R^3 = H$	1.600 (1.530)	1.531	1.350	1.531	107.4	113.5	GED[(S2)126]
SEM1	$R^1 = R^3 = H$, $R^2 = CN$	1.577 (1.508)	1.475	1.375	1.524 (2.349)	111.0	111.8	XR[127]
SEM2	$R^1 = CN$, $R^2 = R^3 = Me$	1.835 (1.487)	1.402	1.354	1.498 (2.048)	110.7	111.2	XR[(S1)128]

[a] In parentheses, esd's for bond lengths and angles in the last digit S1: 1–3, S2: 3–10.
[b] XN = neutron diffraction.

are mainly influenced by cyclopropyl conjugation, where the weakening of the cyclopropane bonds is very helpful in terms of ring opening and the rearrangement mechanism.

In the related molecule tricyclooctadiene, which is also described as semibullvalene **(SEM)**, one vinyl group has been replaced by a direct bond to the former bridgehead atom ($n = 0$, see Figure 7). In **SEM** a very rapid Cope rearrangement also occurs, but in this case only two tautomeric forms are available. The structure of **SEM** could be investigated by GED; in the crystalline phase, however, only data of substituted derivatives are known. In the unsubstituted molecule the cyclopropane bonds are significantly different because of the interaction with both π-systems. In the case of bond B1, which is in the vicinal position for both double bonds, the cyclopropyl conjugation lengthens this bond to 1.600 Å, whereas for the other bonds vicinal and distal effects essentially cancel out each other (1.530 Å). In the rest of the molecule the single and double bonds are well localized and reveal normal values.



(1) **(2)**

FIGURE 8. Structures of triquinacene **(1)** and hexaquinacene **(2)** (distances in Å, angles in degrees)

Substitution of a single hydrogen atom by an electron acceptor group can show a very dramatic effect on the molecular structure of the **SEM** fragment. This is shown in Table 16. A cyano group at the central cyclopropane atom leads to a strengthening of bond B1; now the distal effect of the cyano group works in the opposite direction to that of the double bonds. As a result, the **SEM1** molecule is stabilized in its ground state for this tautomeric form. Double substitution at the double bonds **(SEM2)** by cyano groups has a destabilizing effect. The electron-withdrawing influence of the π-systems is now stronger and weakens the cyclopropane bond B1. The rearrangement is pushed forward by this substitution, leading to the same C_S symmetric molecule with substituents at the same positions for both tautomeric forms. The structural data reveal a very long ring bond B1 (1.835 Å) and, on the other side of the molecule, a shorter distance (D1) between the nonbonded atoms (2.048 Å). The bishomoaromatic character of this structure is also obvious by the other bond lengths of the molecule. The difference between the double bond length and the adjacent single bond length is only 0.056 Å. For this kind of substitution, there is an essential contribution of tautomeric form **B** (Figure 7).

The structure of the $C_{10}H_{10}$ hydrocarbon triquinacene (**1**), in which three multiply fused rings build a cup-shaped geometry with p$-\pi$ orbitals projected toward the center of the concave face, was investigated by X-ray analysis. The C_{3v}-symmetric hydrocarbon was discussed in terms of strong through-space interaction of the π-systems (homoconjugation) and homoaromatic character. The nonbonded distances of the almost-planar cyclopentene rings are 2.533 Å and are therefore too long for a $\pi-\pi$ overlap which leads to peripheral delocalization (see Figure 8). The bond distances for double and single bonds are quite normal. The fusion of three additional five-membered rings leads to the C_{16} hydrocarbon hexaquinacene (**2**), which represents a large fragment of a closed cage-like dodecahedrane ($C_{20}H_{20}$). The central cyclopentane rings are planar within the experimental error, but the cyclopentene rings are very slighty puckered outward. Analogous to **1**, the hydrocarbon **2** reveals C_{3v} symmetry but with the p$-\pi$ axes almost in the same plane. With nonbonded distance (2.848 Å) the magnitude of the p–p overlap integral is very small. Again, no essential homoaromatic influence can be detected by any distortion of the molecular geometry.

D. Alkylidenecycloalkanes and -alkenes

Exocyclic double bonds at cyclic systems, which contain cross-conjugated double bonds, cannot be considered as a subgroup of radialenes and shall therefore be treated separately, although many of the structural features are comparable. However, in these systems the exocyclic and endocyclic double bonds are competing with each other as sites for Diels–Alder reactions, cycloadditions and electrophilic attacks. The double bond character of both, as measured by its distance, can provide some evidence for the selectivities. If no strain and conjugation are expected, the double bonds should be comparable

to those found in ethene [1.314(1) Å XR[129] and 1.339(1) Å, GED[130]] or better in tetramethylethene [1.348(1) Å, XR[131] and 1.353(4) Å GED[132]]; the single bond distances are 1.507 Å and 1.511 Å. The H−C−H angle in ethene is 117.7°[129] and 117.4(1)[130]; the corresponding C−C−C angle in tetramethylethene is 112.1(1)°[131] and 112.2(5)°[132]. For isobutene, the GED values are in between these data: C=C 1.342(3), C−C 1.508(2) Å and C−C−C 115.8°[132]. Consequently, we expect for the exocyclic double bond at small cycloalkanes, such as in the extreme of a three-membered ring, the highest influence on the double bond distance. However, in methylenecyclopropane **(MCPA)** having an innercyclic angle at the central carbon atom of about 60°[133], this distance [1.316(1) Å] is almost unaffected compared to ethene (XR data), and even only slightly shortened if the gas-phase structures are taken. Here, it should be taken into account that both structure determinations deviate significantly. The same is found if the methylene double bonds of the GED structures of **MCPA** and methylenecyclobutane are compared (Table 17).

This comparison demonstrates that the exocyclic double bond length is little affected by the cyclic strain, which was also found for the radialenes; see Section II.E. However, significant deviations were found for conjugated systems, and the same holds for the linear and branched dienes and polyenes.

The smallest member of the family of alkylidenecycloalkenes is the highly sensitive methylenecyclopropene or triafulvalene **(MCPE)**, which was expected to exhibit either pseudoaromatic[136], nonaromatic[137] or antiaromatic[138] character. From the microwave spectrum of this compound only a 20% contribution of the zwitterionic state was suggested[139]. Surprisingly, the exocyclic bond distance was determined to be 1.332 Å, which is the same as in methylenecyclopropane **(MCPA)** determined by GED but significantly longer as determined by XR and MW. Because of the different electronic situation in the benzocyclopropa- and naphthocyclopropa-annulated systems[133], these will not be discussed further here although the exocyclic bond distances compare very well with those mentioned above and are in the range of 1.329–1.347 Å for a series of compounds[133].

1,2-Dimethylenecyclobutane, with the exocyclic double bonds as depicted in Table 18, should be comparable with butadiene. The double bond distances are virtually the same

TABLE 17. Structural parameters of ethene derivatives and small ring methylenecycloalkanes (distances in Å, angles in degrees)

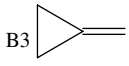
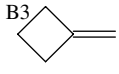
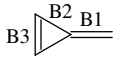
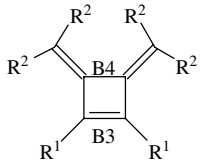
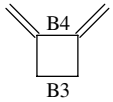
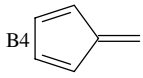
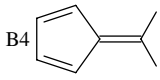
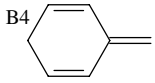
	B1	B2	B3	A1	Method
	1.314	—	—	117.7	XR[129]
	1.339	—	—	117.4	GED[130]
	1.342	1.508	—	115.5	GED[132]
	1.348	1.507	—	112.1	XR[131]
	1.353	1.511	—	112.2	GED[132]
	1.316	1.460	1.526	63.0	XR[133]
	1.322	1.457	1.542	63.9	MW[134]
	1.332	1.457	1.542		GED[135]
	1.331	1.517	1.565		GED[135]

TABLE 18. Structure parameters for free alkylidenecycloalkenes and -alkanes (distances in Å, angles in degrees)

		B1	B2	B3	B4	Method
		1.332	1.441	1.323	—	MW[139]
		1.332	1.446	1.328	—	MP2/6-31G(d)
	$R^1 = R^2 = H$	1.335	1.488	1.357	1.516	GED[142]
	$R^1 = R^2 =$ [15]	1.338	1.480	1.366	1.509	MP2/6-31G(d)
	$R^1 =$ *t*-Bu, $R^2 =$ Me	1.340	1.500	1.373	1.503[a]	XR[143]
		1.343	1.530	1.575	1.486	GED/MW[140]
		1.349	1.470	1.355	1.476	MW[144]
		1.349	1.468	1.357	1.476	MW[145]
		1.349	1.468	1.359	1.469	MP2/6-31G(d)[75]
		1.347	1.476	1.340	1.462	GED[146]
		1.354	1.433	1.343	1.460	XR[147]
		1.343	1.439	1.346	1.435	XR[148]
		MW spectrum consistent with planar ring				MW[149]

[a] Torsion angle C=C−C=C = 57.4°.

(1.343[140] and 1.349[26]) and again the highest distortion is found in the sp^2-sp^2 single bond (1.486 and 1.467 Å), which suffers the most from the ring strain and rehybridization. A spirocyclic substituted[141] derivative, determined by X-ray methods, shows the same features, 1.328[141] and 1.335 Å[4] for the double bonds and 1.479[141] and 1.456 Å[4] for the single bond.

3,4-Dimethylenecyclobut-1-ene has shortened exocyclic double bonds (1.335 Å[142]), which compare well with those of **MCPE** as a result of cross-conjugation. The difference between **MCPA** and **MCPE** for the exocyclic double bond, both determined by GED methods (0.010 Å), is the same as the difference between the ring-saturated dimethylenecyclobutane and the ring-unsaturated dimethylenecyclobutene (0.008 Å). Because of an enhanced conjugation of the methylene π-orbitals with the cyclic π-orbitals in the dimethylenecyclobutene, the conjugation between both methylene groups is reduced, leading to a longer distance in the bond between these groups (1.486 vs 1.516 Å, see Table 18). However, increased ring strain in the unsaturated ring has the same effect. For a derivative, the 1,2-di-*tert*-butyl-3,4-diisopropylidenecyclobut-1-ene[143], this conjugation is reduced due to a torsion of the ring system because of the bulky substituents, which leads to almost equalized single bonds in the ring (see Table 18).

The parent fulvene, 5-methylene-1,3-cyclopentadiene, was the subject of numerous calculations and conformational considerations. Both structures derived from microwave

spectra[144,145] agree with the *ab initio* data[75], the cross-conjugation from both sides reduces the length of the exocyclic double bond which is even shorter than the endocyclic double bonds. The consistency of two experimental and the *ab initio* data underline the reliability of the assumption that the exocyclic double bond should be shorter than the endocyclic ones. X-ray data from numerous derivatives, e.g. the 1,2,3,4,6-pentaphenylfulvene[150] or bicyclo[3.3.1]nonane-9-fulvene[151], however, give a nonuniform picture of the difference of the endocyclic and exocyclic bond distances. For the first mentioned, the exocyclic bond is 0.012 Å longer than the endocyclic double bond, and for the latter it is 0.008 Å shorter. Therefore these data are not considered for further discussion.

The GED data of isopropylidenecyclopentadiene or dimethylfulvene[146] deviate essentially from those of the parent compound; the exocyclic double bond is 0.007 Å longer than the endocyclic double bond. In an old X-ray determination[148] it is 0.003 Å shorter, and a very recent and accurate X-ray structure[147] gives a 0.011 Å longer distance, which is consistent with the inductive effect of the two methyl groups. The greatest discrepancy between the two X-ray determinations is found in the distal bond (0.025 Å), which is even shorter than the vicinal bond in the old crystal structure.

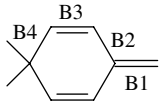
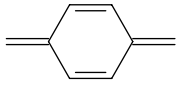
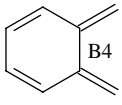
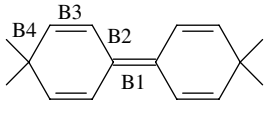
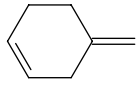
For the parent 6-methylene-1,4-cyclohexadiene a planar structure was found[149]; the 4,4′-dimethyl derivative, however, gave a dihedral angle of 8°[152], which should diminish slightly the cross-conjugation.

For the dimer, the bis(4,4-dimethyl-2,5-cyclohexadiene-1-ylidene), also referred to as pentaene, a second 'biphenyl case' exists, however not such a dramatic one. Biphenyl was found in the gas phase to be twisted by *ca* 42°[153] because of the repulsions of the *ortho*-hydrogen atoms. In favor of the molecular packing in the solid, these repulsions are overcome and a planar structure was found[154]. This example was frequently taken as a textbook example for the so-called 'packing effects' and considered as one of the most prominent examples for differences of structures in the gas phase and in the solid state. For pentaene, however, the central bond is even shorter than in biphenyl and therefore the *ortho*-hydrogen atoms should be even closer in a planar configuration. A torsion as in biphenyl is less likely, and therefore the structure as found in the gas phase[152] in a 'boat' — or 'chair' — fashion-like conformation with dihedral angles of about 9° is quite understandable. Semiempirical calculations confirm a chair-like structure[155] for the complete molecule, but the solid-state X-ray investigation[156] gave an essentially coplanar structure (slight 'stepped' form) with C_i symmetry and slender 'boat'-shaped phenyl rings (maximum torsion angles in the rings, 5.1°). Consequently, the central bond distance is longer than the double bonds in the rings (see Table 19).

p-Xylylene is very much related to the pentaene and polymerizes easily to poly-*p*-xylylene; the monomer should serve as a prototype for a biradical with the gain of aromaticity for the ring as the driving force. Although good *R*-values are achieved, the results from the GED experiments were claimed by the authors to be less reliable[157], endocyclic and exocyclic double bonds seem to be equal (1.381 Å) and the *ab initio* data reveal almost the same length (1.355, 1.358 Å). However, the difference between single and double bonds is much larger for the *ab initio* data (0.10 Å) than for the experiment (0.07 Å), which means that the conjugation is much less than originally anticipated from the experiment. This structure compares well with **DSD2** (Table 9), which has two spiroconnected cyclopropane rings instead of the exomethylene groups. There, the experimental difference between the single and double bond is larger (0.147 Å) than the calculated difference (0.125 Å).

4-Methylenecyclohex-1-ene (Table 19) is not planar and the MW data do not allow any detailed discussion on the distances because of the conformational behavior, which is consistent with a high barrier to ring conversion[159]. No X-ray structures

TABLE 19. Structure parameters for six-membered ring alkylidenecycloalkenes (distances in Å)

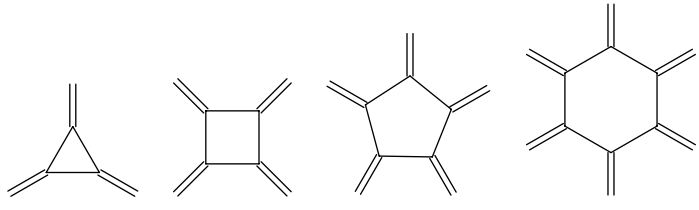
	B1	B2	B3	B4	Method[a]
	1.357	1.478	1.352	1.493	GED[152]
	1.381 1.358	1.451 1.458	1.381 1.355	— —	GED[157] MP2[75]
	1.356	1.458	1.357	1.484	MP2[75]
	1.382 1.37 1.374	1.472 1.46 1.462	1.350 1.33 1.327	1.496 1.50 1.499	GED[152] XR[156] XR[158]
	MW spectrum consistent with higher barrier to ring inversion				MW[159]

[a]MP2 = MP2/6-31G(d)

were found which provide more detailed information on the parent structure. For the 5,6-dimethylenecyclohexa-1,3-diene structure type (Table 19) no experimental data are available which give some idea about the delocalization in the ring. The *ab initio* data reveal a larger difference in bond distances (0.128 Å), which means that the conjugation in the ring should be even smaller than in the *p*-xylylene.

E. Radialenes

Radialenes are a class of compounds that have only relatively recently been synthesized and described[160–162]. They may also be described as all-*exo*-methylene-cycloalkanes, and the first four members of this group of molecules, which we for the convenience of the reader, will refer to by the number of ring atoms, are presented in Figure 9.



(3) **(4)** **(5)** **(6)**

FIGURE 9. Structures of radialenes

Numerous heteroradialenes, in which the *exo*-methylene groups are replaced by oxygen, nitrogen or sulfur atoms, have also been synthesized and studied because of their interesting electrical and magnetic properties. Heteroradialenes are, however, not included in this review.

Two questions related to the structure of radialenes are of special interest:

1. What kind of interaction exists between the π-electrons of the exocyclic C=C bonds?
2. Which factors determine the conformation of the radialene rings?

The radialene double bonds in a planar radialene ring will have overlapping π-orbitals, and it is reasonable to assume that the π-electrons in such a case will be delocalized and that this will have some influence on the lengths of the C−C and C=C bonds. Among the parent **3–6** radialene molecules **5** is not known, and so far only the planar molecule **3** has been the subject of an experimental structure investigation. It is therefore at present not possible to obtain experimental evidence about the structure and conformation of the parent **4**, **5** and **6** radialenes. For all these hydrocarbons a number of substituted species are known and have been studied (see below), but as the substituents result in increased nonbonded repulsions between the enlarged exocyclic groups, the preferred conformations of these species will probably differ from those of the parent compounds. In order to gain insight into the conformations of the parent radialene rings, one is therefore limited to information available from theoretical calculations. We have carried out MP2/6-31G(d,p) calculations with full geometry optimization for the parent radialene molecules **3**, **4**, **5** and **6**, and some of the results are shown in Table 20.

According to these calculations the minimum energy conformations of [3]- and [4]radialenes are planar, that of **5** is nearly planar, while the minimum energy conformer of **6** is a chair, which is flattened compared to that of cyclohexane (ring dihedral angles: 40.48°, vs 54°). It is reasonable to assume that coplanar structures might be advantageous for radialenes, if the total π-system of a ring is considered separately. The nonbonded repulsions involving hydrogen atoms of adjacent methylene groups will, however, be substantial for planar conformers of rings larger than **5**. The H---H distance for planar [6]radialene is, for example, estimated to be approximately 1.7 Å. The effect of nonbonded repulsions is illustrated by the calculated H---H distances presented in Table 20. In **3** this distance (3.8 Å) is so large that negligible interaction will occur. Also, in planar **4** this distance is

TABLE 20. Structure parameters obtained from MP2/6-31G(d,p) calculations (distances in Å, angles in degrees). Some similarly calculated data for 1,3-butadiene are shown for comparison

	3	**4**	**5**[e]	**5**[f]	**6**	**1,3-Butadiene**
C−C_{ring}	1.4448	1.4925	1.4848	1.4834	1.4829	1.4569
C=C	1.3387	1.3408	1.3456	1.3453	1.3456	1.3431
C−H	1.0813	1.0817	1.0810	1.0812[h]	1.0812	1.083[h]
∠C=C−H	121.04	121.26	121.59	121.53	120.97	121.45[h]
H··H[a]	3.808	2.875	2.241	2.3450[c]	2.805	
C−C−C−C_{ring}	0.0	0.0	0.0 (Ass.)	12.06[d]	40.48	
Bond bending[g]	27.8	14.0		5.6	1.3	
E[b]	−231.35543	−308.55248	−385.74467	−385.74552	−462.90302	

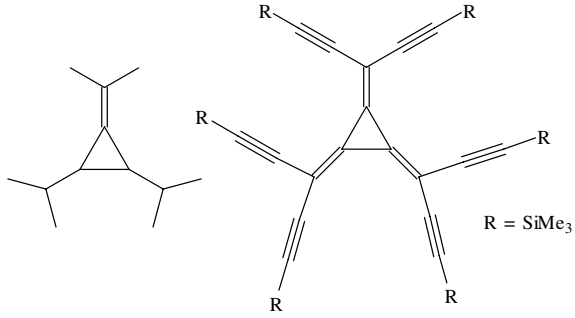
[a] Distance between nearest hydrogens in adjacent methylene groups.
[b] Total energies in Hartrees.
[c] Average value of 2.295; 2.295; 2.364; 2.406; 2.364[Å].
[d] Average absolute value of −5.75; 15.08; −18.64; 15.08; −5.75 (deg).
[e] Planar conformer.
[f] Twist-envelope conformer.
[g] Deviation between orbital direction and line of nuclear centers in the ring.
[h] Average value.

clearly larger than the sum of the Van der Waals radii of the two hydrogen atoms. The latter quantity is an ill-defined quantity that may be derived in a number of ways, and the results are not always consistent. We will here use Pauling's Van der Waals radius for hydrogen, 1.20 Å[163]. For a planar conformer of **5** the calculated shortest H---H distance, 2.24 Å, is somewhat smaller than the sum of the Van der Waals radii, while these distances are only slightly smaller than this value in the minimum energy twist-envelope conformer. A reasonable interpretation of these data is that a planar ring is preferred by the [5]radialene π-system, but since this conformation implies a certain degree of nonbonded repulsion between hydrogens on adjacent methylene groups, the total minimum energy conformation is achieved for a conformer based on a compromise between maximum π-orbital overlap and minimum nonbonded repulsion. The calculated energy is thereby reduced by *ca* 2.1 kJ mol^{-1}, relative to a planar **5** conformer.

The reason for the minimum energy conformer of **6** cannot be as simple as that proposed for **5**, as the former is far more puckered than what is necessary for minimizing the H---H nonbonded repulsions. Valence angle strain is another factor that might be important in this case. The similarity to the chair conformer of cyclohexane is striking, although the calculated [6]radialene conformation is less puckered.

The calculated difference between single and double CC bond lengths (**3**, 0.106 Å; **4**, 0.152 Å; **5**, 0.139 Å; **6**, 0.137 Å) is, with the exception of **3**, larger for the radialenes than for 1,3-butadiene (0.113 Å). This might indicate that the π-electron delocalization in the radialenes is reduced compared to that in 1,3-butadiene. An alternative explanation for the calculated bond length differences could be attributed to the deviations between the carbon orbital directions in the ring C−C bonds and the line connecting two neighboring ring carbon atoms in the radialenes (Table 20). The CC orbital overlap in a ring will be reduced proportionally to the magnitude of such deviations, resulting in increased C−C ring bond lengths. The electronic structure of **3** is sufficiently different from that of 1,3-butadiene to render a comparison between the structures of these two molecules meaningless.

Relatively few structural studies of radialenes have been carried out, and most of these are X-ray crystallographic studies. The first structure study of a radialene was, however, a gas electron diffraction study of **3** that appeared in 1968[164]. The molecule was found to be planar with D_{3h} symmetry, in agreement with information from IR and Raman spectroscopic measurements[165]. To the best of our knowledge only two structures of substituted [3]radialene have been reported since then. In both molecules all six hydrogens are equally substituted: in one case with methyl groups[166] **(7)** and in the other with trimethylsilylethynyl groups[167] **(8)**; see Figure 10. In hexamethyl[3]radialene **(7)** the D_{3h}



(7) **(8)**

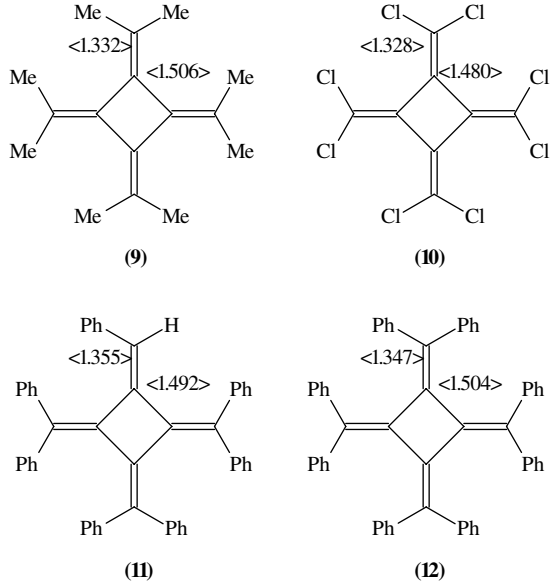
FIGURE 10. Structures of substituted [3]radialenes

symmetry of the parent system is not noticeably perturbed, while the deviation from this ideal symmetry is larger in the trimethylsilylethynyl **(8)** derivative, presumably because of crystal packing effects. The lengths of the C−C bonds in the ring are: **3**, 1.453(20) Å; **7**, 1.451(11) Å and **8**, 1.420(5)–1.431(3) Å. It therefore appears that the C−C bond in the hexakis(trimethylsilylethynyl) derivative is smaller than in the parent molecule. However, this cannot be stated with certainty, as the two structures have been obtained with different methods and because the GED results[164] have rather large error limits. The exocyclic double bonds of the three studies are: **3**, 1.343(20) Å; **7**, 1.331(1) Å; **8**, 1.350(4) Å, 1.355(4) Å, 1.358(3) Å. The exocyclic CC double bonds in **8** appear to be significantly longer than in **7**. This is, however, not surprising, as the exocyclic double bonds in **8** are cross-conjugated with the ethynyl substituents. The experimental results available for [3]radialenes are in good agreement with the calculated results for the parent compound (Table 20).

Considerably more structure data are available for [4]radialenes than for their smaller homologs[168–177]. The structure of the parent molecule **4** has not been determined yet, but its vibrational spectrum is in agreement with a planar molecule of D_{4h} symmetry[178]. Most [4]radialene structures are, however, found to be puckered: **9**, 22.1°[168]; **10**, 26.5°[172]; **11**, 19.2°[173]; **12**, 34.7°[174]. These include, for example the molecules shown in Figure 11.

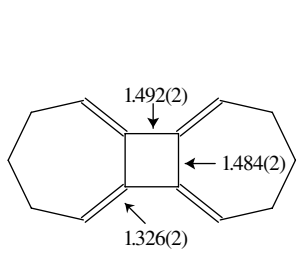
The nonplanarity of these [4]radialene molecules is obviously caused by nonbonded repulsions between the substituents on the methylene groups. On the other hand, the three [4]radialenes in Figure 12 are observed to have planar radialene systems **13**[169], **14**[170], **15**[166].

These molecules also have large substituents, and it might seem surprising that the radialene rings avoid puckered conformations in these species. The nonbonded repulsions are, however, reduced in these molecules because of external ring closures **(13)** or because two of the exocylic CC double bonds involve cumulated double bond systems (**14** and

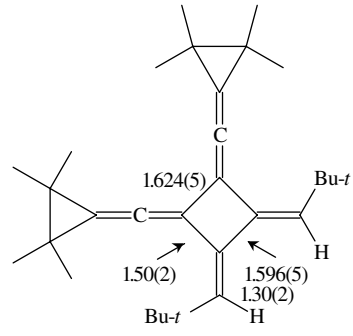


(9) **(10)** **(11)** **(12)**

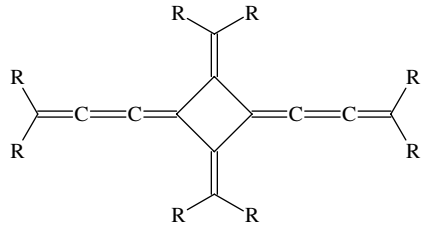
FIGURE 11. Structures of substituted puckered [4]radialenes (distances in Å)



(13)



(14)



(15)

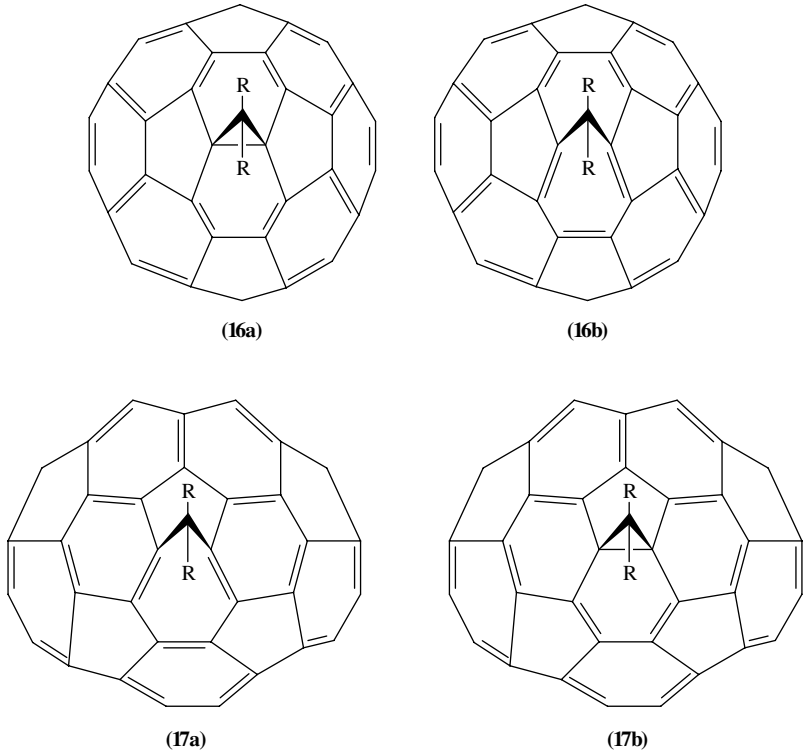
FIGURE 12. Structures of substituted planar [4]radialenes (distances in Å)

15), where the 'substituents' are pointing away from the adjacent methylene groups. Based on the available experimental information for [4]radialenes and the theoretically derived structure for **4**, one might therefore conclude that the preferred conformation for [4]radialene is planar, and that the ring is easily distorted by substitution due to nonbonded repulsions.

The parent [5]radialene **(5)** has so far evaded preparation. The decamethyl derivative is, however, known, and this molecule is found to have a half-chair conformation, with approximately C_2 symmetry[179]. There are, however, observations indicating that [5]radialene is a more interesting structural system than these meager data suggest. A [5]radialene-type bonding pattern is, for example, present in the newly discovered C_{60} molecule (buckminsterfullerene). A PM3 computational and experimental study of the [6,6]-closed **(16a)** and [6,5]-open **(17a)** methanofullerenes[180] demonstrated that the electronic basis for the experimentally preferred formation of **16a** and **17a** over the [6,6]-open **(16b)** and [6,5]-closed **(17b)** isomers of methanofullerenes (see Figure 13) is the preservation of the [5]radialene-type bonding pattern by these two structures.

The [6]radialenes are normally observed to have chair conformations[164,168,181,182], although a twist-boat conformation has been observed for a very highly substituted [6]radialene molecule[183]. A planar [6]radialene system has also been observed for thiophene-annulated cyclohexane **18**[184] and **19**[185] (Figure 14).

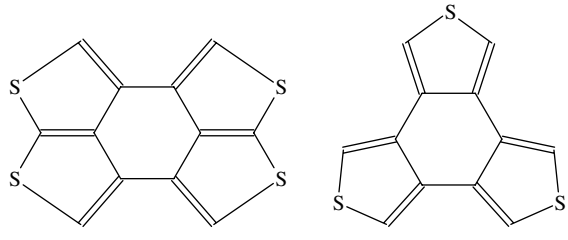
The latter two molecules are, however, special cases, where forces other than those inherent in the [6]radialene system are determining the preferred conformation. Hexakis(ethylidene)cyclohexane is the only radialene molecule where structure results obtained in the solid state[181], as well as in the gas phase[182], are available for comparison (Table 21).



(16a) **(16b)**

(17a) **(17b)**

FIGURE 13. Structures of methanofullerenes: [6,6]-closed (**16a**), [6,6]-open (**16b**), [6,5]-closed (**17b**) and [6,5]-open (**17a**)

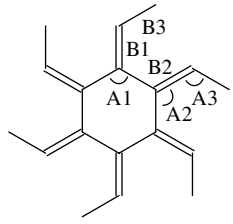


(18) **(19)**

FIGURE 14. Substituted [6]radialene (planar)

The molecule is found to be somewhat less puckered in the solid state than in the gas phase, presumably because of crystal packing effects. Apart from this, the structure parameters from the two studies are in excellent agreement. The C−C−C−C dihedral ring angles are observed to be ±46.2° in the crystal and ±53.0(6)° in the gas phase. The small differences in some of the angle parameters resulting from the two studies may generally be attributed to the flattening of the ring in the crystal state. The observed

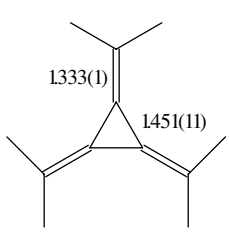
TABLE 21. Structural parameters for hexakis(ethylidene)-cyclohexane from gas electron diffraction (GED) and X-ray crystallography (XR) (distances in Å, angle in degrees)

	Parameter	GED[182]	XR[181]
	B1	1.347(1)	1.334(3)
	B2	1.494(2)	1.495(3)
	B3	1.508(3)	1.497(3)
	A1	112.1(2)	114.1(2)
	A2	121.3(4)	121.1(2)
	A3	127.0(6)	128.1(2)
	T1[a]	176.4	174.0
	T2[b]	±53.0	±46.2

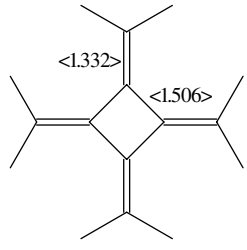
[a]T1 = torsion angle C−C=C−CH_3.
[b]T2 = torsion angle $(C-C-C-C)_{ring}$

C−C−C−C dihedral angle in gaseous hexakis(ethylidene)cyclohexane is 12.5° larger than the corresponding angle calculated for the parent radialene (**6**). This seems reasonable when the increased nonbonded repulsion due to the methyl substituents in the former is taken into account.

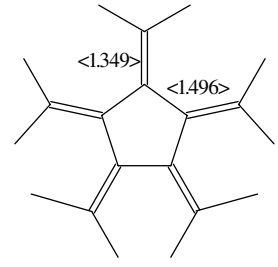
In order to get insight into the preferred orientations of the various radialene systems, we might consider the permethylated derivatives of the parent compounds, since



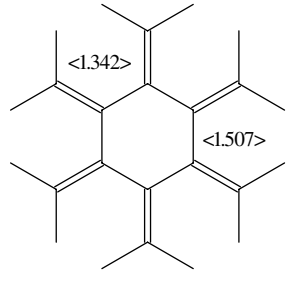
(7)



(9)



(20)



(21)

FIGURE 15. Structures of all-methyl substituted radialenes (distances in Å)

some structure data are available for all of them: **7**[166,171], **9**[164,168], **20**[179] and **21**[164,168] (Figure 15).

The endocyclic CC bonds in [3]radialenes are generally found to be about 0.05 Å shorter than those in the higher radialenes. This effect is also reproduced by the *ab initio* calculations (see Table 20), and is primarily attributed to the special bonding pattern in a three-membered ring. For exocyclic C=C bonds the correlation between ring size and bond length is more questionable. Hexamethyl[3]radialene is the only permethylated radialene with a planar radialene system. The nonplanarity of the other radialenes is clearly due to repulsions between neighboring methyl groups. The shortest distances between methyl carbon atoms on adjacent CC double bonds in planar conformations may be estimated to be 3.80, 2.56, 1.80 and 1.30 Å for permethylated [3]-, [4]-, [5]- and [6]radialenes (**7**, **9**, **20** and **21**), respectively. Only in the methylated [3]radialene **(7)** is a planar structure therefore possible without severe steric repulsions between the substituents.

Planar conformations of radialenes with five or more ring atoms will always be more or less destabilized due to nonbonded repulsions, unless special structural effects that stabilize a planar conformation are present. The available experimental data indicate, however, that radialene systems generally prefer planar conformations, if steric effects are not taken into account.

III. ACKNOWLEDGMENTS

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CHAPTER **3**

Thermochemistry of dienes and polyenes

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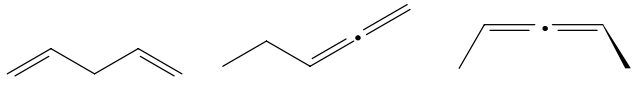
This study is dedicated to the memory of Prof. Thomas L. Jacobs who first introduced the author to cyclic acetylenes, dienes and cumulenes on an examination in 1963

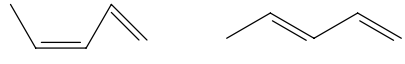
I. INTRODUCTION: SCOPE AND DEFINITIONS

A. What Do We Mean By Dienes and Polyenes?

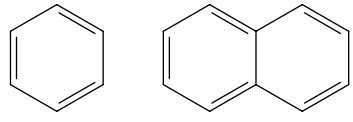
For this chapter we will define a diene as any organic compound that contains two carbon–carbon double bonds, whether the double bonds are nonconjugated as in 1,4-pentadiene, **1**; cumulated or 'allenic' as in 1,2- and 2,3-pentadiene, **2** and **3**; or conjugated as in (*Z*)- and (*E*)-1,3-pentadiene, **4** and **5**. Relatedly, a triene contains three carbon–carbon double bonds, a tetraene has four carbon–carbon double bonds, etc. We will use the generic term polyene to encompass trienes, tetraenes, etc., even though we admit now that the thermochemistry of tetraenes and more unsaturated species is sparse enough to make polyene and triene nearly synonymous in the current context. We will largely avoid discussion of 'buried' polyenes, since it does not particularly benefit our understanding of polyenes to include discussion of the numerous derivatives of benzene **(6)**, of naphthalene **(7)** or of any other polynuclear aromatic hydrocarbon, even though they could be named systematically as polyenes. Nonetheless, some of these compounds will appear occasionally in our chapter.



(1) **(2)** **(3)**

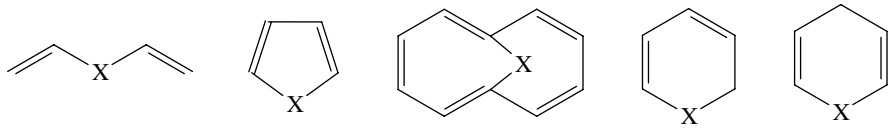


(4) **(5)**



(6) **(7)**

We will also forego discussion of any substituted polyene wherein the substituent is not hydrocarbyl (i.e. composed of any elements other than hydrogen and carbon). This decision does not arise out of lack of interest in these species *per se*, but rather, that discussion of many of the relevant compounds has been presented in earlier thermochemistry chapters elsewhere in other volumes in the 'Functional Groups' series. For example, the energetics of the X = O containing divinyl ether, **8**; furan, **9**; and 1,6-oxido[10]annulene (also known as 11-oxa-bicyclo[4.4.1]deca-1,3,5,7,9-pentaene), **10**; have been recently discussed in the Supplement E2 volume of this series[1] and therein were explicitly compared with those of their corresponding hydrocarbon analogs with X = CH_2, 1,4-pentadiene, cyclopentadiene and 1,6-methano[10]annulene, respectively. The −O− vs $-CH_2-$ comparison was shown to be generally interesting and informative where it can be made. The available thermochemical data are disappointingly sparse. For example, there are no thermochemical data for either pyran isomer, **11** or **12** with X = O, to include with discussions of the corresponding X = CH_2 species, the isomeric 1,3- and 1,4-cyclohexadienes that are discussed at some length in Section V.D of the current chapter. Indeed, not even all hydrocarbyl substituents and their ancillary functionalities and features will be discussed in the current chapter. We now acknowledge we will largely omit discussion of homoaromatic species such as cyclopropanated species and their comparison with the formally related compounds having C=C bonds. Inclusion of this interrelation is quite superfluous in the current chapter since it figured prominently in a recent review of the thermochemistry of cyclopropanes[2].



(8) **(9)** **(10)** **(11)** **(12)**

B. What Do We Mean By Thermochemistry?

As has been the approach for most of the author's other reviews on organic thermochemistry, the current chapter will be primarily devoted to the relatively restricted scope of 'enthalpy of formation' (more commonly and colloquially called heat of formation) and write this quantity as ΔH_f, instead of the increasingly more commonly used and also proper ΔH_f° and $\Delta_f H_m^\circ$. No discussion will be made in this chapter on other thermochemical properties such as Gibbs energy, entropy, heat capacity and excess enthalpy. Additionally (following thermochemical convention), the temperature and pressure are tacitly assumed to be 25 °C ('298 K') and 1 atmosphere (taken as either 101,325 or 100,000 Pa) respectively[3] and the energy units are chosen to be kJ mol^{-1} instead of kcal mol^{-1} (where 4.184 kJ ≡ 1 kcal, 1 kJ = 0.2390 kcal).

Again, following our earlier chapters as precedent, we continue to view intermolecular forces as 'complications' and 'nuisances'. We consider the molecule *per se* to be of sole interest and thus, unless explicitly noted to the contrary, any species discussed in this

chapter is to be assumed in the (ideal) gas phase. Admittedly, most organic compounds are 'naturally' liquids or solids under the thermochemically idealized conditions. They are likewise found in the condensed phase for most studies by synthetically or mechanistically inclined chemists. 'Corrections' to the gas are definitionally made by using enthalpies of vaporization (ΔH_v) and of sublimation (ΔH_s), defined by equations 1 and 2:

$$\Delta H_v \equiv \Delta H_f(g) - \Delta H_f(lq) \tag{1}$$

$$\Delta H_s \equiv \Delta H_f(g) - \Delta H_f(s) \tag{2}$$

where g, lq and s refer to gas, liquid and solid, respectively. Phase change enthalpies were obtained from whatever source available: our choice to maximize the use of gas phase data and minimize that from the liquid or solid requires numerous expediencies. In the absence of data from experimental measurements, enthalpies of vaporization for hydrocarbons will usually be estimated using the generally accurate (± 2 kJ mol^{-1}) two-parameter equation of Reference 4. We admit that the procedures for estimating enthalpies of sublimation are generally dependent on values obtained from experimental measurements (either those of enthalpies of fusion[5] or melting point[6]). Nonetheless, some effort will still be made to estimate enthalpies of sublimation.

C. Sources of Data

We have already acknowledged our intent to use relevant estimation approaches to enthalpies of vaporization and sublimation to maximize the usefulness of the data available. That dienes and polyenes have multiple double bonds that are potentially hydrogenatable to the totally saturated aliphatic or alicyclic hydrocarbons allows the employment of two other assumptions. The first assumption argues that the enthalpy of hydrogenation, ΔH_{H_2} measured in a nonpolar solvent is essentially equal to that which would be obtained in the gas phase[7]. The second assumption[8], implicitly employing the first, legitimizes the use of estimation techniques and even molecular mechanics to derive the enthalpy of formation of the totally saturated species. From this last number, the enthalpy of formation of the unsaturated diene or polyene of interest can be derived by equation 3 and simple arithmetic.

$$\Delta H_f \text{ (unsaturated)} + \Delta H_{H_2} = \Delta H_f \text{ (saturated)} \tag{3}$$

These latter assumptions make use of thermochemical data ancillary to the enthalpy of hydrogenation. These data are not just the enthalpies of formation of CO_2(g) and H_2O(lq), needed for his/her counterpart who measures enthalpies of combustion. The use of ancillary thermochemical information becomes imperative, e.g. the enthalpy of formation of an alkane that is the product of hydrogenating a diene of interest. It is an easy conceptual step to go from ancillary information to secondary sources of thermochemical data. This is consonant with our own bibliographic preferences and prejudices. In this paper we tacitly choose to cite secondary sources[9] over primary sources. This strongly simplifies the writing and reading of our text at the risk of offending an occasional author of an uncited primary research paper.

II. NONCONJUGATED DIENES AND POLYENES

A. Acyclic Species

It may appear that nonconjugated, acyclic dienes are the simplest and least interesting of all the classes of compounds to be discussed in the current chapter. The reader may wish to ask of the current author who has written numerous earlier reviews on organic

thermochemistry: 'Don't you get bored reading hour after hour, day after day, numbers and their derived problems?' To which, he responds 'Yes, and when I do I ask myself 'Why am I bored?' and then I have an interesting project'[10].

The simplest nonconjugated, acyclic diene is 1,4-pentadiene (**1**), with its enthalpy of formation of 105.6 kJ mol^{-1}. The obvious question is whether the two double bonds are truly independent. If they are, then the enthalpy of hydrogenation of one double bond as in (the identical) reactions 4a and 4b would be precisely one half of that of the hydrogenation of both as in reaction 5.

$$CH_2{=}CHCH_2CH{=}CH_2 + H_2 \longrightarrow CH_3CH_2CH_2CH{=}CH_2 \quad (4a)$$

$$CH_2{=}CHCH_2CH{=}CH_2 + H_2 \longrightarrow CH_2{=}CHCH_2CH_2CH_3 \quad (4b)$$

$$CH_2{=}CHCH_2CH{=}CH_2 + 2H_2 \longrightarrow CH_3CH_2CH_2CH_2CH_3 \quad (5)$$

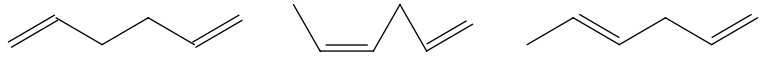
We would likewise deduce that the formal reaction in equation 6

$$CH_2{=}CHCH_2CH{=}CH_2 + CH_3CH_2CH_2CH_2CH_3 \longrightarrow 2CH_3CH_2CH_2CH{=}CH_2 \quad (6)$$

would then be thermoneutral. In fact, it is exothermic by merely 1.3 ± 2.1 kJ mol^{-1}, a result equal to the expected precise value of 0 within the experimental error bars.

We now turn to the isomeric hexadienes, of which three species qualify for consideration: the 1,5- and the (*Z*)- and (*E*)-1,4- compounds, species **13**, **14** and **15**, respectively. If interaction between the two double bonds in 1,4-pentadiene is so small, we expect this as well for the 1,5-hexadiene. One test of this is to consider reaction 7 by analogy to reaction 6.

$$CH_2{=}CH(CH_2)_2CH{=}CH_2 + CH_3CH_2(CH_2)_2CH_2CH_3 \longrightarrow 2CH_3CH_2(CH_2)_2CH{=}CH_2 \quad (7)$$



(13) **(14)** **(15)**

To do so, one can take the enthalpy of formation of *n*-hexane from Pedley, and with the phase independence assumptions in Reference 7, employ the enthalpies of hydrogenation of 1-hexene and 1,5-hexadiene from References 11 and 12 respectively. Alternatively[13], one can forget about the first quantity altogether and simply take the difference of the enthalpies of hydrogenation of the diene and twice that of the monoene. This reaction is endothermic by 1.1 ± 1.8 kJ mol^{-1}, a value statistically indistinguishable from the absence of any interolefin interaction in the diene. Relatedly, for the isomeric 1,4-hexadienes **14** and **15**, equation 8 may be used.

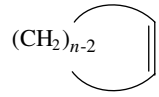
$$CH_3CH{=}CHCH_2CH{=}CH_2 + CH_3(CH_2)_4CH_3 \longrightarrow CH_3CH{=}CH(CH_2)_2CH_3 + CH_3(CH_2)_3CH{=}CH_2 \quad (8)$$

Again, one may take the difference of the enthalpies of hydrogenation of the diene and the sum of those for the two monoenes. Doing this separately for **14** and **15**, we find the reaction enthalpies for the *Z*- and *E*-dienes are -1.9 ± 1.2 and -1.8 ± 1.1 kJ mol^{-1}. These values are effectively zero. A stabilizing — or destabilizing — interaction was not expected for nonconjugated acyclic dienes and none was found.

B. Acyclic, Polymeric Polyenes

In this section we will discuss the thermochemistry of a collection of polymeric species of the generic repeat or monomeric formula $[-CH{=}CH-(CH_2)_{n-2}-]$. We admit that the state of many of the compounds at 298 K is ambiguous, or more precisely, that the sample's degree of crystallinity (cf the polymer chemist's terms 'amorphous solid' or even vaguer 'highly elastic') is ill-defined. As such, any attempts to correct for intermolecular interactions are suspect. We recall that it is easier to predict enthalpies of vaporization than of sublimation, and so conclude that general predictions for liquids are more reliable than for solids. As such, we will study the polymer in its liquid state even if the relevant temperature is not 298 K. No temperature corrections will be made and, given all of the above uncertainties, it seems an unnecessary additional effort to concern ourselves with the precise Z/E composition of the polymer[14]. The desired numbers in this section are enthalpies of hydrogenation and the final products are $n/2$ moles of polyethylene, i.e. $(CH_2CH_2)_{poly}$, with its derived enthalpy of formation[15] of *ca* -52 kJ mol^{-1}.

Starting with the $n = 4$ case, the desired polymer can be obtained by polymerization of either cyclobutene (**16**, $n = 4$) or butadiene. Using the cyclobutene polymerization enthalpy from Reference 16 and of the enthalpy of formation of monomer from Pedley, we find the enthalpy of formation of $[-CH{=}CH-(CH_2)_2-]$ is 12 kJ mol^{-1}. We conclude that the enthalpy of hydrogenation is -116 kJ mol^{-1}.



(16)

For the $n = 5$ case there is the unique starting material of cyclopentene (**16**, $n = 5$) and polymerization enthalpy[16] from which the enthalpy of formation of $[-CH{=}CH-(CH_2)_3-]$ is found to be -14 kJ mol^{-1}. The enthalpy of hydrogenation is thus *ca* -121 kJ mol^{-1}. Likewise, for $n = 6$, 7 and 8, the respective enthalpies of hydrogenation of $[-CH{=}CH-(CH_2)_{n-2}]$ are seen to be *ca* -83, -120 and -121 kJ mol^{-1}. Except for the $n = 6$ case, the various enthalpies of hydrogenation are around -120 kJ mol^{-1}, a value comparable to those found for numerous simple internal olefins reported in References 11 and 14. We can think of no reason why the $n = 6$ case should be so different from the others[17].

III. CUMULATED OR ALLENIC DIENES AND POLYENES (CUMULENES)

A. Allene

We start with a discussion of allene (propadiene), the simplest diene of all. Its gas phase enthalpy of formation is 190.5 ± 1.2 kJ mol^{-1}. We wish to compare this quantity with that of related monoenes. The first comparison addresses the 'relative stability' of one and two double bonds in a 3-carbon chain. Conceptually, this may be expressed as the enthalpy of the formal reaction 9

$$2MeCH{=}CH_2 \longrightarrow C_3H_8 + CH_2{=}C{=}CH_2 \qquad (9)$$

We find that allene is destabilized by *ca* 46 kJ mol^{-1}. Is this destabilization also found for other species with cumulated, or allenic, double bonds?

B. Dienes

Let us start with 1,2-butadiene. A particularly simple analysis is the comparison of allene and 1,2-butadiene using the formal methylation reaction 10

$$CH_2{=}C{=}CH_2 + MeCH{=}CH_2 \longrightarrow MeCH{=}C{=}CH_2 + CH_2{=}CH_2 \qquad (10)$$

This reaction has an accompanying endothermicity of *ca* 4 kJ mol^{-1}. Said differently, methylation of ethylene is some 4 kJ mol^{-1} more exothermic than of allene. How general is this greater exothermicity of alkylation of monoolefins over that of related allenes? Proceeding to the three cumulated 5-carbon dienes, we may consider the reactions

$$CH_2{=}C{=}CH_2 + EtCH{=}CH_2 \longrightarrow EtCH{=}C{=}CH_2 + CH_2{=}CH_2 \qquad (11a)$$

$$CH_2{=}C{=}CH_2 + 2MeCH{=}CH_2 \longrightarrow MeCH{=}C{=}CHMe + 2CH_2{=}CH_2 \qquad (11b)$$

$$CH_2{=}C{=}CH_2 + Me_2C{=}CH_2 \longrightarrow Me_2C{=}C{=}CH_2 + CH_2{=}CH_2 \qquad (11c)$$

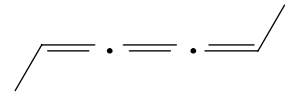
Using standard references and protocol, we find the three reactions are respectively endothermic by *ca* 2, 8 and 6 kJ mol^{-1}, or *ca* 2, 4 and 3 kJ mol^{-1} once one remembers to divide by 2 the last two numbers because the allene is dialkylated. So doing, from equations 10 and 11 we find an average *ca* 3 kJ mol^{-1} (per alkyl group) lessened stability for alkylated allenes than the correspondingly alkylated alkenes. This is a small difference that fits most naturally in the study of substituted cumulenes such as ketenes and ketenimines, i.e. not in this chapter. But it is also a guideline for the understanding of polyenes with more cumulated double bonds.

C. Trienes

The thermochemistry of totally cumulated trienes, i.e. species with the C=C=C=C substructure, is very limited. Indeed, the sole examples we know are those reported by Roth, namely (*Z*)- and (*E*)-2,3,4-hexatrienes MeCH=C=C=CHMe, species **17** and **18**. Their enthalpies of formation are identical to within experimental error, 265 kJ mol^{-1}. This equality is altogether reasonable given the small Me•••Me interaction across the 4-carbon, linear, cumulene chain in contradistinction to the 4.3 kJ mol^{-1} difference that is found for the isomeric (*Z*)-and (*E*)-2-butenes with their significantly smaller Me•••Me distance. Are cumulated trienes 'unstable' relative to cumulated dienes much as cumulated dienes are unstable relative to simple olefins? Briefly regressing to cumulated dienes, this assertion is corroborated by the finding that species **3**, i.e. 1,3-dimethylallene, has an enthalpy of 'decarbonization'[18] of 144.5 kJ mol^{-1} (reaction 12)

$$\mathbf{3} \longrightarrow (E)\text{-MeCH}{=}\text{CHMe(g)} + \text{C(s)} \qquad (12)$$

(17)



(18)

while the related reactions 13 of the two monosubstituted (R = Me and Et) and the unsubstituted allene (R = H)

$$RCH{=}C{=}CH_2 \longrightarrow RCH{=}CH_2(g) + C(s) \qquad (13)$$

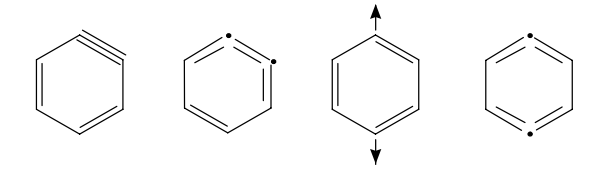
have enthalpies of 142.3, 140.6 and 139.0 kJ mol^{-1}. All of these decarbonization reactions are exothermic by *ca* 140 kJ mol^{-1}. Returning to the trienes, the related reaction 14

$$(\mathbf{17} \text{ or } \mathbf{18}) \longrightarrow \mathbf{3} + \mathrm{C(s)} \tag{14}$$

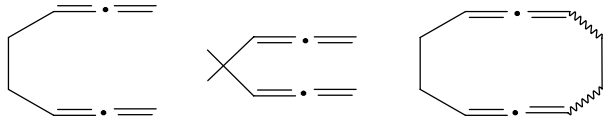
has the contrasting endothermicity of but 123 kJ mol^{-1}. Are the trienes so different from the dienes? These two sets of results become consonant once we observe the conjugated — and hence stabilizing — diene substructure (note the $\Delta^{2,3}$–$\Delta^{4,5}$ interaction) that is lying within the cumulated double bonds of **17** and **18**.

D. Tetraenes

We know of no substance containing four completely cumulated double bonds for which the enthalpy of formation is available, and but few species that fill that structural description at all. Likewise, we know of no substance containing three cumulated double bonds and an either affixed conjugated or nearby, but unconjugated, double bond for which enthalpy of formation data are available except for the disingenuous benzyne **(19)** recognized if it is drawn in its unconventional resonance structure **20**. However, besides the equally inappropriate *p*-benzyne **(21**, **22)**, we find in Roth the desired thermochemical numbers for three other tetraenes. All of these latter species are bis-allenes, the acyclic 1,2,6,7-octatetraene **(23)** and 4,4-dimethyl-1,2,5,6-heptatetraene **(24)**, and the cyclic 1,2,6,7-cyclodecatetraene **(25)**. There is no reason to believe that either **23** or **24** is particularly strained. Table 1 documents our optimism by numerically taking one-half of the difference of the enthalpies of formation of these acyclic bis-allenes and more 'conventional' species[19], namely the corresponding olefins and acetylenes. Nearly constant differences were found. We should expect both the cumulene **25** and its olefin counterpart, 1,5-cyclooctadiene, **26**, to be strained, and their comparison is further complicated by the ambiguity of having to choose between the *meso* or *dl* isomers for the former (**27** and **28**, respectively), and among the (*Z*,*Z*), (*E*,*Z*) or (*E*,*E*) isomers for the latter (**29**–**31**, respectively). There are two measurements from which one can derive the desired enthalpy of formation of the cumulene. The first is Roth's enthalpy of hydrogenation that results in a value of 360 kJ mol^{-1} for explicitly the *meso* compound, **27**. The second is the nearly contemporaneous determination of the enthalpies[20] of combustion and of vaporization (for what appears to be isomer **27** as well) resulting in 356.1 ± 3.8 kJ mol^{-1}. We have arbitrarily decided to consider the (*Z*,*Z*) isomer of **26**, species **29**, because it is the most stable of the 1,5-cyclooctadienes (see Section V.F). So doing, the desired difference quantity is



(19) **(20)** **(21)** **(22)**



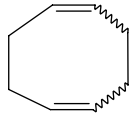
(23) **(24)** **(25)**

TABLE 1. Enthalpies of formation of bis-allenes, the related bis-olefins and bis-acetylenes and their acyclic analogs

−R−	2Et−	$-CH_2CH_2-$	$Me_2C<$
ΔH_f ($CH_2{=}CH{-}R{-}CH{=}CH_2$)	0	84	52[a]
$1/2\delta$ (bis-allene, bis-olefin)	141	142	139
ΔH_f ($CH_2{=}C{=}CH{-}R{-}CH{=}C{=}CH_2$)	282	368	330
ΔH_f ($HC{\equiv}C{-}R{-}C{\equiv}CH$)	330	415[b]	382[b]
$1/2\delta$ (bis-allene, bis-acetylene)	−24	−23	−26

[a]The necessary enthalpy of formation of $Me_2C(CH{=}CH_2)_2$ was derived by assuming the reaction $Me_2CEt_2 + CH_2(CH{=}CH_2)_2 \longrightarrow Me_2C(CH{=}CH_2)_2 + CH_2Et_2$ is thermoneutral.
[b]The liquid phase enthalpy of formation of this species is from Pedley; the necessary enthalpy of vaporization was estimated.

found to be *ca* 130 kJ mol^{-1}. Considering all of the above uncertainties and the relatively exotic structure of **25**, we conclude that the bis-allene **25** is *not* so strange after all[21].



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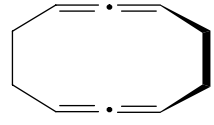

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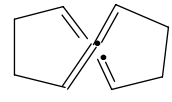

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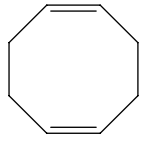

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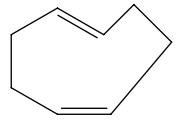

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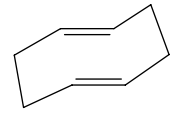
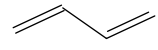


(31)

IV. CONJUGATED ACYCLIC DIENES

A. Consequences of Conjugation

It is part of the folklore of organic chemistry that the conjugated 1,3-butadiene, **32**, enjoys stabilization beyond that were there no interaction between the two double bonds. Indeed, conjugated dienes represent an archetypical example for organic chemists when discussing resonance stabilization accompanying the interaction of two functional groups, and so it may be argued that a new functional group arises.



(32)

What is relevant to this chapter is that a conjugated diene has higher thermodynamic stability than one would expect in the absence of conjugation. Leaving off all hydrogens and substituents in the name of simplicity, several interrelated definitions that document

this stabilization are apparent. The first compares the enthalpy of hydrogenation corresponding to total saturation of the diene; cf reaction 15a with the hydrogenation enthalpies of the related monoenes, cf reactions 15b and 15c. The difference of the first enthalpy, ΔH_r (equation 15a), and the sum of the second and third [ΔH_r(equation 15b) + ΔH_r (equation 15c)], provides a definition for the conjugation energy, E_{16} (equation 16).

$$C{=}C{-}C{=}C + 2H_2 \longrightarrow C{-}C{-}C{-}C \tag{15a}$$

$$C{=}C{-}C{-}C + H_2 \longrightarrow C{-}C{-}C{-}C \tag{15b}$$

$$C{-}C{-}C{=}C + H_2 \longrightarrow C{-}C{-}C{-}C \tag{15c}$$

$$E_{16} \equiv \Delta H_r(\text{equation 15a}) - [\Delta H_r(\text{equation 15b}) + \Delta H_r(\text{equation 15c})] \tag{16}$$

We immediately recognize this quantity (E_{16}) as equal to the exothermicity of reaction 17:

$$C{-}C{-}C{=}C + C{=}C{-}C{-}C \longrightarrow C{=}C{-}C{=}C + C{-}C{-}C{-}C \tag{17}$$

The result for 1,3-butadiene is -15.7 ± 1.9 kJ mol^{-1}, a value comparable to conventional expectations save the sign[22]. We can now define the difference of the value for an arbitrary conjugated diene of interest and this 15.7 kJ mol^{-1} as E_{18} (equation 18).

$$E_{18} = -15.7 - E_{17} \tag{18}$$

That is, we can compare the 'new diene' with the archetypical 1,3-butadiene where a positive number suggests that it is more stabilized than the paradigm.

The above definition of the enthalpic effects of conjugation is not unique. A second definition decouples the two double bonds by an alternative hydrogenation process (equation 19).

$$C{=}C{-}C{=}C + H_2 \longrightarrow C{=}C{-}H + H{-}C{=}C \tag{19}$$

It is found that this reaction, more properly called a hydrogenolysis than a hydrogenation, is only *ca* 5 kJ mol^{-1} exothermic for simple species such as 1,3-butadiene and its mono and dimethylated derivatives[12,23,24]. This is surprisingly close to thermoneutrality. Nonetheless, we have decided to define E_{20} by equation 20,

$$E_{20} = 5.1 - E_{19} \tag{20}$$

where 5.1 ± 1.2 kJ mol^{-1} is the precise hydrogenolysis value for 1,3-butadiene. Again, comparison can be made with 1,3-butadiene where a positive number for E_{20} implies the new diene is more stable than the archetype. A third definition totally hydrogenates the diene to the saturated hydrocarbon (cf equation 15a), and the difference of this enthalpy and that for the unsubstituted butadiene results in E_{21} (equation 21):

$$E_{21} = -225.7 - E_{20} \tag{21}$$

In this equation the -225.7 ± 1.3 kJ mol^{-1} is the hydrogenation enthalpy of 1,3-butadiene to *n*-butane. This last expression speaks to substituent/diene interactions and to substituent–substituent interactions. Both electronic and steric effects contribute. Again, this allows calibration of a substituted diene with 1,3-butadiene itself. A positive sign can be interpreted as the substituted species being more stabilized than the archetype.

TABLE 2. Conjugation enthalpies of gaseous substituted butadienes relative to butadiene itself

Substituents	E_{18}	E_{20}	E_{21}
(*E*) 1-Me	6	2	3
(*Z*) 1-Me	−3	−3	−3
2-Me	0	3	−4
(*E*) 1-Et[a]	7[b]	3	4
(*Z*) 1-Et[a]	7[b]	−1	0
2-Et[c]	−12[d]	−6	−10
(*E*, *E*) 1,4-Me_2[e]	5[b]	1	14
(*E*, *Z*) 1,4-Me_2[e]	5[b]	−3	11
(*Z*, *Z*) 1,4-Me_2[e]	−2[b]	−7	6
2,3-Me_2	−5[b]	0	2
(*E*, *E*) 1,2,3,4-Me_4[f]		−7	15
(*E*, *Z*) 1,2,3,4-Me_4[f]		−14	17
(*Z*, *Z*) 1,2,3,4-Me_2[f]		−15	10
2,3-*t* − Bu_2[g]		−44[h]	−12[i]

[a]The enthalpies of formation of the isomeric 1-ethylbutadienes (or more properly named 1,3-hexadienes) are taken from Reference 12.

[b]The enthalpies of formation of the monoolefin hexene products are derived from Reference 11.

[c]The enthalpy of formation of the 2-ethylbutadiene is taken from Reference 8.

[d]The enthalpy of formation of the monoolefin products, 3-methyl-1-pentene and 2-ethyl-1-butene, are derived from Reference 11.

[e]The enthalpies of formation of the isomeric dimethylbutadienes (or more properly named 2,4-hexadienes) are taken from Reference 12.

[f]The enthalpies of formation of the isomeric tetramethylbutadienes (or more properly named 3,4-dimethyl-2,4-hexadienes) are taken from Reference 23.

[g]The enthalpy of formation of the di-*t*-butylbutadiene is taken from Reference 23.

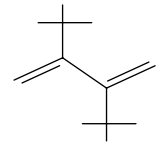
[h]This is the solvent and vaporization-corrected enthalpy of hydrogenation of the diene from Reference 23. There is no need in the current context for the enthalpy of formation of the hydrogenation product 2,3-di-*t*-butylbutane (or more properly named 2,2,3,4,5,5-hexamethylhexane), unlisted in our archives, and derived in Reference 23 by molecular mechanics.

[i]The enthalpy of formation of the hydrogenolysis product, 3,3-dimethyl-1-butene, was derived from the data in Reference 11b.

However, because a given alkyl group replacing hydrogen on saturated and unsaturated carbon results in different enthalpy of formation changes, we hesitate to compare dienes with different number of substituents on the butadiene backbone. Indeed, that 1,3-butadiene is a di-terminal double-bond system allows for the conclusion that butadiene is not a good species for comparison. Indeed, Table 2 presents the accumulated values of E_{18}, E_{20} and E_{21} for all of the acyclic dienes (all unsystematically named therein as substituted derivatives of butadiene) that are known to the author for which there is relevant gas phase enthalpic data[25]. It is very disconcerting that these definitions and descriptions of conjugation energy and substituent effects for our set of dienes result in no obvious generalities or guidelines.

The description of conjugated dienes as shown by equation 17 and the associated comparison with butadiene in equation 18 corresponds most closely to the conventional definition. The results are plausible in that groups on one double bond that are *cis*-situated relative to the other encourage nonplanarity, cause destabilization and result in lessened conjugation energy. Or so we say. The biggest debit of this approach is that the thermochemistry of the monoenes related by single addition of H_2 is often absent. An example

is the case of 2,3-di-*t*-butylbutadiene **33**, and so the energetics of this species could not be examined in the current light.



(33)

Because reaction 19 is so close to thermoneutrality for unstrained olefins and dienes, it represents a convenient way of estimating and benchmarking enthalpies of formation for dienes and polyenes[26] even if it is not isodesmic[27] whereas reaction 17 is. However, it is 'full of surprises' such as the finding that the related oxygen reaction (equation 22) involving α-dicarbonyl compounds is also nearly thermoneutral[24,28].

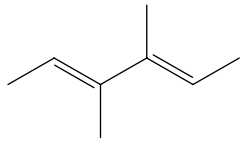
$$2\text{RCHO} \longrightarrow \text{RCOCOR} + \text{H}_2 \tag{22}$$

However, it is not obvious how much understanding the energetics of this last reaction will provide a key to understanding of dienes.

Reaction 14 is the simplest process associated with the measurement of the hydrogenation of the diene. No other unsaturated compounds such as the monoolefins formed by addition of a single equivalent of H_2, not reactions 7a, 7b or 12, need be considered. This is a virtue from the vantage points of not having to 'interrupt' the reaction, analyze the products or needing to synthesize any additional species. However, all comparison with monoolefins has been lost and that is the interrelationship conjugation energy speaks to. Perhaps with more data we will gain greater understanding.

B. What Other Data Are There

We admit to comparatively little experience in quantitatively understanding solvent and entropic effects. For example, consider the 1,2,3,4-tetramethylbutadienes presented in Table 2. From Reference 23, we find the relative solution phase Gibbs energies for the (*E*,*E*)-, (*E*,*Z*)- and (*Z*,*Z*)-isomers (**34–36**, respectively) increase in the order $(E, E) < (E, Z) \approx (Z, Z)$. By contrast, the gas phase enthalpies of formation increase in the order $(Z, Z) < (E, E) < (E, Z)$. Somehow it seems inappropriate to include the other C_8H_{14} hydrocarbons of Reference 23 in the current study when we only know their relative Gibbs energies in solution[29].



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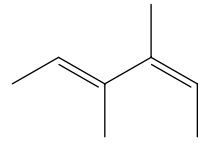

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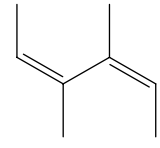
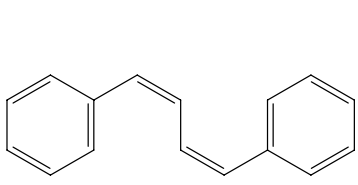


(36)

Data are sparse. Let us thus relax the earlier phase restriction to the gas phase. We therefore briefly discuss some conjugated dienes for which we have enthalpy of formation data solely in the condensed phase. The first pair of species are the isomeric (*Z*,*Z*)-and

(*E*,*E*)-1,4-diphenylbutadienes, **37** and **38**. Pedley tells us that the difference of enthalpies of formation is *ca* 20 kJ mol^{-1} in the solid. Pedley's chronicled data to the contrary, we would have thought that the value should be larger than the comparable archival difference for **39** and **40**, the (*Z*)- and (*E*)-diphenylethylenes (stilbenes)[30]. We likewise find that solid 1,2,3,4-tetraphenylbutadiene, **41**, is *ca* 30 kJ mol^{-1} less stable than its 1,1,4,4-isomer, **42**. One natural comparison is with the saturated tetraphenylbutanes but there are seemingly no data available for 1,2,3,4-tetraphenylbutane. Another comparison involves formal cleavage of the central single bond to form two molecules of diphenylethylene, but the absence of *Z*/*E* assignments for the double bonds in 1,2,3,4-tetraphenylbutadiene makes this approach irrelevant.



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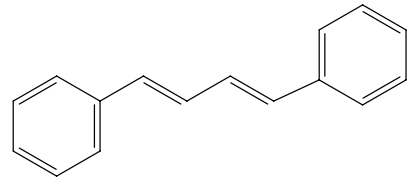

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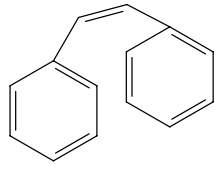

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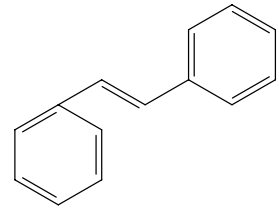

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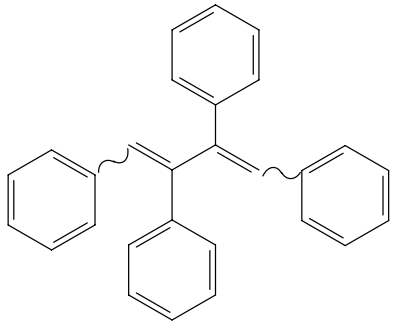

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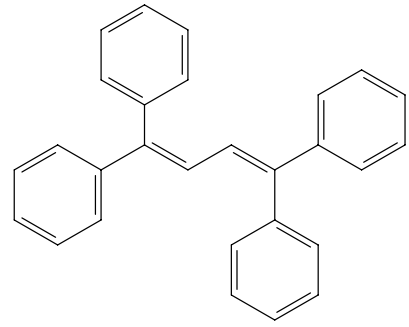


(42)

V. CYCLIC DIENES

A. What Types of Species Qualify?

There are three generic types of species with this description: those cyclic dienes in which both double bonds are found totally within, or *endo* to, the ring; those in which

both double bonds are found *exo* to the ring, and those with one *endo* and one *exo* double bond. We start with the first class of compounds.

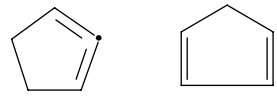
B. Doubly *Endo* Micro-rings

The first member of this class of compounds would appear to be cyclopropadiene, **43**, but it is immediately recognized that this species is more accurately drawn with the alternative resonance structure corresponding to cyclopropenylidene, **44**. As such, this C_3H_2 species does not truly belong in the current chapter and so will be ignored here[31]. There are two isomers for cyclobutadiene, the 1,2- and 1,3-, species **45** and **46** respectively. We are not surprised there are no enthalpy of formation data for the former and it is tempting to conclude that this cyclic allene is seemingly 'too small' to even allow for reaction calorimetry of any kind. There are no enthalpy of formation data for the latter or for any of its derivatives either[32], although the generally believed antiaromaticity of cyclobutadienes would have argued against inclusion of the data even had we found it much as the thermochemistry of cyclohexatrienes (i.e. substituted benzenes) is all but ignored in this chapter.

(43) **(44)** **(45)** **(46)**

C. Cyclopentadiene

Turning now to cyclopentadienes, there are the isomeric 1,2-and 1,3-cyclopentadiene [**47** and **48** (**9**, $X = CH_2$)]. The thermochemical community has ignored **47**, a cyclic allene, and indeed, it has seemingly ignored all cyclic allenes[33] despite the reasonable number of reasonable, i.e. isolable and isolated, species[34]. The latter is among the most normal looking species in this chapter: **48** is customarily called cyclopentadiene without any locants for the two double bonds. Pedley chronicles its enthalpy of formation to be 134.3 ± 1.5 kJ mol^{-1} from measurements of its enthalpy of a gas phase hydrogenation reaction resulting in cyclopentane. Roth cites this value and also one derived of their own from solution phase hydrogenation measurements, 138.9 kJ mol^{-1}, that resulted in the same product. The 4.6 kJ mol^{-1} discrepancy is quite disconcerting because:



(47) **(48)**

(a) if it really reflects a difference of gas phase and condensed phase enthalpies of hydrogenation, the earlier enunciated assumption that results from nonpolar media mimic those in the gas phase is suspect;

(b) most compounds have never been studied by thermochemists. Those compounds that have been investigated have rarely been studied by more than one group;

(c) we may define the conjugative stabilization in cyclopentadiene as the exothermicity of the cyclopentene 'disproportionation' (reaction 23).

$$2\text{cyclo-}[(CH_2)_3(CH)_2] \longrightarrow \mathbf{48} + \text{cyclo-}[(CH_2)_5] \qquad (23)$$

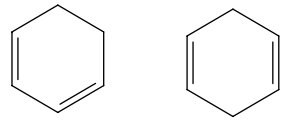
Using Pedley's suggested enthalpy of formation, this reaction is seen to be exothermic by 9.9 kJ mol^{-1}. This number is quite small noting that a related but strain-free reaction (an alternative acyclic paradigm for conjugation), i.e. reaction 24

$$2(E)\text{-MeCH=CHPr} \longrightarrow (E,E)\text{-MeCH=CHCH=CHMe} + n - C_6H_{14} \qquad (24)$$

is exothermic by nearly 20 kJ mol^{-1}. Indeed, this result would appear to reflect the oft-asserted instability of *cis*-oid (alternatively written *Z*- or s-*cis*) dienes[35]. Using Roth's value for the enthalpy of formation of cyclopentadiene, the exothermicity of reaction 23 has now shrunk to 5.3 kJ mol^{-1}. If this value is taken, the conjugative stabilization of cyclopentadiene has all but vanished[36].

D. 1,3- and 1,4-Cyclohexadiene

It is perhaps unexpected to have an entire section devoted solely to two normal-looking cyclic dienes, 1,3- and 1,4-cyclohexadiene, species **49** and **50** (**11** and **12** with $X = CH_2$). While an entire volume has been written on stereochemical aspects of substituted cyclohexadienes[37], this interest alone would not suggest that more than a perfunctory discussion of the enthalpies of formation of the parent species need be made. Our expectations are simple. The former diene is conjugated; the latter is not. A difference of *ca* 15 kJ mol^{-1} favoring the former is expected. Our archives are surprisingly mute: Pedley gives us the enthalpy of formation of only the 1,3-species, 106.2 ± 0.9 kJ mol^{-1}, derived from a 60-year-old gas phase enthalpy of hydrogenation measurement[38]. Roth gives us that value as well as one derived from a 23-year-old solution hydrogenation enthalpy measurement[39]. As with cyclopentadiene, this latter value differs from the earlier one by some 5 kJ mol^{-1}. Though more recent, that measurement which was made in the polar solvent, glacial AcOH, requires the need for solvent effect corrections. This suggests that the earlier value is preferable. Interestingly, the latter reference[39] also reports the hydrogenation enthalpy of 1,4-cyclohexadiene. This value is *ca* 1 kJ mol^{-1} higher than the corresponding enthalpy found for its 1,3-isomer. Since the hydrogenation product is the same for both dienes, in the absence of any particular solvent effect for **49** or **50**, we conclude that the enthalpies of formation of these two cyclohexadienes are nearly the same with the formally conjugated species the slightly more stable. Direct equilibration of **49** and **50** showed[40] the former 1,3-isomer to be more stable by 1.6 ± 0.8 kJ mol^{-1}. Disappointingly, this reaction was performed in polar media (*t*-BuOK in DMSO) and so the same skepticism enunciated for the solution phase hydrogenation study could be enunciated here[41].



(49) **(50)**

What about measurements of enthalpies of combustion of condensed phase species **49** and **50** and accompanying enthalpies of vaporization? Enthalpies of formation of the gaseous hydrocarbons can be directly obtained from these studies as well. There are two recent studies that provide us with useful information. The first[42] results in the values of 104.6 ± 0.6 and 104.8 ± 0.6 kJ mol^{-1} respectively. The second accompanies the earlier cited cyclic bisallene (and polycyclic monoolefin) study, in which the authors[20]

reported the value of 100.4 ± 3.1 kJ mol^{-1} for the 1,4-isomer. This value is quite different from what was reported above and so, regrettably, we find no corresponding combustion measurements on its isomer in Reference 20 as well. It is tempting to ignore this last result because the comparison of the stabilities of the 1,3- and 1,4-cyclohexadienes cannot be directly addressed from this latter paper.

Summarizing all of the above, it would appear that 1,3- and 1,4-cyclohexadiene have nearly identical enthalpies of formation. Does this mean that the 1,3-isomer is destabilized and/or that the 1,4-isomer is stabilized? Let us accept an enthalpy of formation of *ca* 105 kJ mol^{-1} for the enthalpy of formation of both isomers. In the absence of any stabilization or destabilization, we would expect the cyclohexene 'disproportionation' reaction 25

$$2\text{cyclo-}[(CH_2)_4(CH)_2] \longrightarrow (\mathbf{49} \text{ or } \mathbf{50}) + \text{cyclo-}[(CH_2)_6] \qquad (25)$$

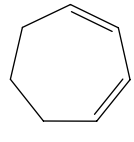
to be nearly thermoneutral. In fact, our analysis suggests that this reaction is exothermic by 8 kJ mol^{-1}. Accordingly, 1,3-cyclohexadiene is less stable than we would have derived from results of 2,4-hexadiene (but again remember *cis*-oid conjugated dienes). Conversely, 1,4-cyclohexadiene is more stable on the basis of conventional assumptions about the thermochemistry of nonconjugated dienes and acyclic paradigms.

E. Cycloheptadienes

As was seen for 1,3-cyclohexadiene, the data in Pedley and Roth report conflicting measurements for the enthalpy of formation of 1,3-cycloheptadiene, **51**. The values differ by some 3 kJ mol^{-1}. This is often a non-negligible difference, but either result is plausible: the disproportionation reaction 26

$$2\text{cyclo-}[(CH_2)_5(CH)_2] \longrightarrow \mathbf{51} + \text{cyclo-}[(CH_2)_7] \qquad (26)$$

corresponding to earlier reactions 23 and 25, is exothermic by either *ca* 6 or 9 kJ mol^{-1}. However, the difference becomes almost irrelevant when comparing these findings with those for 1,4-cycloheptadiene, **52**. As with the isomeric cyclohexadienes **49** and **50**, Reference 39 presents solution phase hydrogenation (glacial AcOH solvent) for the two cycloheptadienes. Remembering that the difference of the solution phase enthalpies of hydrogenation, and hence of formation, difference of the isomeric cyclohexadienes was within a kJ mol^{-1} of that found from the chosen combustion measurements, encourages us to trust the difference found for **51** and **52**. But here, the conjugated isomer is reported to be more stable than its unconjugated counterpart by almost 30 kJ mol^{-1}. This difference is significantly larger than the acyclic paradigm for the stabilization effects due to conjugation of double bonds. We strongly suggest reinvestigation of the thermochemistry of the cycloheptadienes — and the cyclohexadienes as well.



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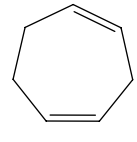
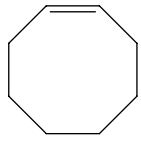


(52)

F. Cyclooctadienes

As with the isomeric cyclohexadienes, there are a variety of data to present. Let us start with the 1,5-isomer, **26** and remind the reader there are three 'forms' of this species,

the (*Z*,*Z*), (*E*,*Z*) and (*E*,*E*) isomers, **29–31**, respectively. Pedley presents enthalpy of formation data for only the first. By contrast, Roth enigmatically gives data only for the last two. Taken as a totality, the three numbers are 101.1 ± 1.3 kJ mol^{-1}, 158.2 and 196.2 kJ mol^{-1}. When there are two double bonds in an 8-membered ring, at least for the 1,5-isomer, changing from a (*Z*)-conformation to (*E*) seems to be accompanied by *ca* 50 ± 10 kJ mol^{-1} per double bond increase in enthalpy of formation. This is consistent with isomerization of the monoolefin, cyclooctene, as well. Pedley suggests the enthalpy of formation of (*Z*)-cyclooctene, **53**, to be -27.0 ± 4.2 kJ mol^{-1}. Roth cites enthalpies of formation of (*E*)-cyclooctene, **54**, ranging from 9.2 to 20.1 kJ mol^{-1} based on three distinct hydrogenation measurements. We thus deduce a E/Z difference of 42 ± 6 kJ mol^{-1}. Likewise, using numbers from Roth, we find that (*Z*,*Z*)-1,3-cyclooctadiene, **55a**, is some 60 kJ mol^{-1} more stable than its (*E*,*Z*)-isomer, **55b**.



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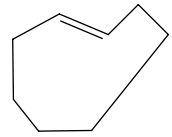

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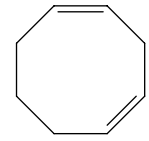
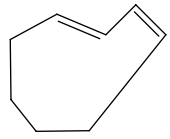


(55a)



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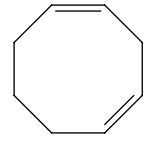


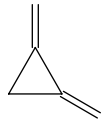
(56)

From a consistent set of hydrogenation enthalpies in glacial AcOH, the cyclooctadienes decrease in stability 1,5- (**29**) < 1,4- (**56**) < 1,3- (**55a**) with sequential differences of 13.0 **(29**, **55a)** and 6.7 **(55a**, **56)** kJ mol^{-1}. For comparison — despite our earlier enunciated skepticism about isomerization reactions performed in polar media (*t*-BuOK in DMSO) — the following enthalpies of reaction, and thus enthalpies of formation, differences were found[43]: 16.4 ± 1.4 and 2.8 ± 0.8 kJ mol^{-1}. Consistency, if not precise numerical agreement, is found for the energetics of the isomeric cyclooctadienes.

G. Doubly *Exo* Cyclic Dienes

Except for the still thermochemically uninvestigated 1,2-bismethylenecyclopropane[44], **57**, all bismethylenecycloalkanes can further be divided into two categories — those in which the *exo*-methylene groups are on adjacent carbons and those further apart. The two isomeric bismethylenecyclobutanes have been studied. Roth presents an enthalpy of formation for the 1,2-isomer, **58**, of 204.2 kJ mol^{-1}. In the absence of any additional strain-induced destabilization or conjugative/delocalization-induced stabilization, we would expect the disproportionation reaction 27 of methylenecyclobutane **(59)**

$$2[\mathbf{59}] \longrightarrow \mathbf{58} + \text{cyclo-}[(CH_2)_4] \qquad (27)$$



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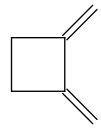
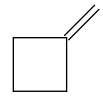


(58)



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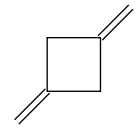


(60)

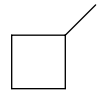
to be thermoneutral. In fact it is exothermic by *ca* 10 kJ mol^{-1}, reflecting — as in our earlier discussion of cyclopentadiene — the destabilization induced by forcing a *cis*-oid conformation on a conjugated diene. Reaction 28

$$2[\mathbf{59}] \longrightarrow \mathbf{60} + \text{cyclo-}[(CH_2)_4] \tag{28}$$

relatedly for the 1,3-bismethylene isomer, **60**, would also be expected to be thermoneutral in the absence of additional stabilization or destabilization effects. No direct enthalpy of formation measurements exist for **60**. Reaction 28 may be roughly recast in terms of hydrogenation enthalpies. Twice this quantity for the singly methylenated **59** would equal that of **60** in the absence of any other significant stabilizing or destabilizing factor, if we make the reasonable assumption that the saturated counterpart, reaction 29, is essentially thermoneutral.

$$2[\mathbf{61}] \longrightarrow \mathbf{62} + \text{cyclo-}[(CH_2)_4] \tag{29}$$

In fact, using data for **59** and **60** with the same solvent and *a fortiori* from the same paper[45], we deduce that **60** is seemingly destabilized by 5 kJ mol^{-1}.



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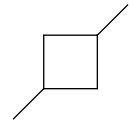
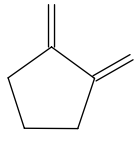


(62)

Does the 10 kJ mol^{-1} stabilization for adjacent exomethylene groups in cyclobutane arise from conjugative interactions? Is the 5 kJ mol^{-1} destabilization for nonadjacent exomethylenes in cyclobutane general for other cycloalkane derivatives?

Consider now other bismethylenecycloalkanes. We start with 1,2-dimethylenecyclopentane, **63**, and acknowledge there are no accompanying thermochemical data for its 1,3-isomer, **64**. We can write the formal reaction 30

$$2\text{cyclo} - [(CH_2)_4C{=}CH_2] \longrightarrow \mathbf{64} + \text{cyclo-}[(CH_2)_5] \tag{30}$$



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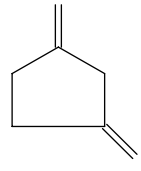

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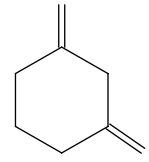

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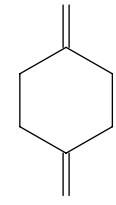


(66)

From enthalpy of formation data of **63** from Roth, and for the other species from Pedley, we find reaction 30 is exothermic by 6 kJ mol^{-1}. Consider now the isomeric 1,3-and 1,4-dimethylenecyclohexane, **65** and **66**; no thermochemical data for its 1,2-isomer are seemingly available. We can write the related formal reactions 31a and 31b.

$$2\text{cyclo} - [(CH_2)_5C{=}CH_2] \longrightarrow \mathbf{65} + \text{cyclo-}[(CH_2)_6] \quad (31a)$$

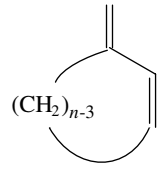
$$2\text{cyclo} - [(CH_2)_5C{=}CH_2] \longrightarrow \mathbf{66} + \text{cyclo-}[(CH_2)_6] \quad (31b)$$

From enthalpy of formation data of **65** from Roth, of **66** from Reference 46, and for the other species from Pedley, we find reactions 31a and 31b are exothermic by nearly 19 and 9 kJ mol^{-1} respectively. We have no understanding of why 1,3-dimethylenecyclohexane is so stable relative to its 1,4-isomer, or how to predict stabilization of any bismethylenecycloalkane as a function of ring size.

H. *Endo, Exo* Cyclic Species

As the ring size gets bigger, there are an increasing number of isomers of this general description. For the sake of brevity, we will consider only the formally conjugated species, generically **67** where n is the ring size[47]. No problems or surprises are expected here: consider thus the straightforward hydrogenation reaction 32

$$\mathbf{67} + 2H_2 \longrightarrow \text{cyclo-}[(CH_2)_{n-1}CHMe] \quad (32)$$



(67)

Taking the enthalpy of formation of **67** with $n = 5$ from Roth and the product methylcyclopentane from Pedley, this reaction is found to be 222 kJ mol^{-1} exothermic. This result is consonant with that of the acyclic reaction 33

$$CH_2{=}CHC(Me){=}CH_2 \longrightarrow CH_3CH_2CHMe_2 \quad (33)$$

which has an exothermicity of 228 kJ mol^{-1}, some 6 kJ mol^{-1} higher. It is not, however, consonant with the enthalpy of reaction 32 with $n = 6$ for which a reaction enthalpy of some 177 kJ mol^{-1} is found using numbers from Pedley[48]. Other than assuming that an experimental measurement is wrong, no explanation is apparent[49].

I. Bicyclic Dienes and 'Beyond'

There are many bicyclic dienes and polyenes. If for no other reason than to show that seemingly homologous series often show profound complications, in Table 3 we present the enthalpies of formation of the bicyclo[2.2.n]alka-2,5-dienes, bicyclo[2.2.n]alk-2-enes and bicyclo[2.2.n]alkanes, species **68**, **69** and **70**, respectively, wherein we limit our attention to the cases of $n = 0$, 1 and 2. It is seen that the enthalpies of formation of the bicycloalkadiene, bicycloalkene and bicycloalkane always become more negative in that

TABLE 3. Recommended enthalpies of formation of bicyclo[2.2.*n*]alka-2,5-dienes, bicyclo[2.2.*n*]alk-2-enes and bicyclo[2.2.*n*]alkanes for $n = 0$, 1 and 2

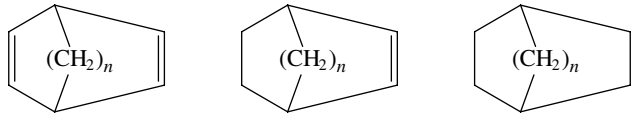
	$n = 0^a$	$n = 1^b$	$n = 2^c$
Bicycloalkadiene	335	240	141
Bicycloalkene	261	90	35
Bicycloalkane	125	−52	−99

[a] See Reference 50.
[b] See Reference 51.
[c] See Reference 52.

order and that, for a given degree of unsaturation, the enthalpies of formation also always become more negative in the order $n = 0, 1$ and 2. These results are sensible. It is the exceptional double bond[53] for which saturation (hydrogenation) is an endothermic reaction. Recognizing the monocyclic structural fragments amidst the bicycles, we also expect the strain energies to decrease in the order of 4-membered ring > 5-membered ring > 6-membered ring. The deviation from thermoneutrality of the formal reaction 34

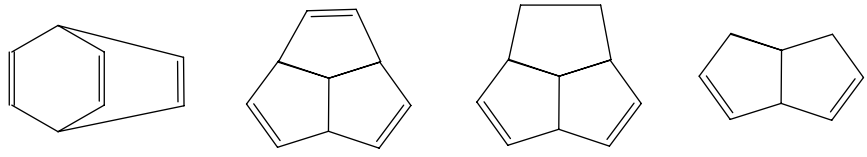
$$2[\mathbf{69}] \longrightarrow \mathbf{68} + \mathbf{70} \tag{34}$$

speaks to the interaction of the two double bonds in the bicycloalkadiene[54]. For $n = 0$, 1 and 2, these reactions are respectively 62 *endo*, 2 *exo* and 28 kJ mol^{-1} *exo*-thermic.



(68) **(69)** **(70)**

Hardly feigning completeness under the general rubric of 'beyond', we now briefly discuss bicyclo[2.2.2]octatriene or barrelene, **71**, with its recommended[52] enthalpy of formation of 303 kJ mol^{-1}. The difference of this enthalpy of formation and the bicyclic species with one fewer double bond (**68**, $n = 2$) is 162 kJ mol^{-1}, *ca* 20 kJ mol^{-1} less than any other difference we find in Table 3. It is thus clear that this bicyclic triene is considerably destabilized. By contrast, the corresponding difference for **72**, the tricyclic triquinacene, and the corresponding diene **73**, is *ca* 20 kJ mol^{-1} lower[55] than for the diene as well as for **74**, a related bicyclic diene[56]. Having promised to avoid discussion of homoaromaticity in the beginning of this chapter and other exotic interactions of double bonds, we avoid mention of the mechanisms of seeming stabilization, destabilization and normalcy for **72**, **71**, and of **73** and **74**, respectively.

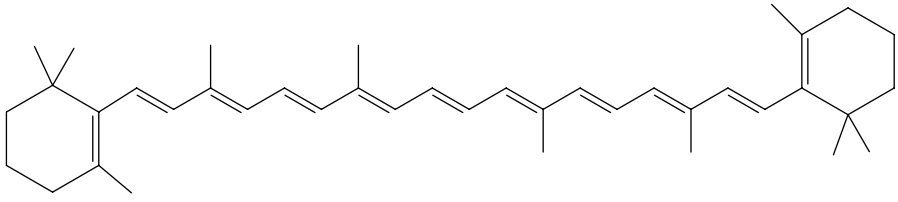


(71) **(72)** **(73)** **(74)**

VI. CONJUGATED POLYENES

A. What Sparse Data Are There

We have earlier discussed the thermochemistry of acyclic conjugated dienes. In this section the enthalpy of formation of conjugated trienes will be discussed along with a few compounds with more than three double bonds. For all of the activity in the chemical and biochemical community in conjugated polyenes — whether derived from interest in antioxidants (e.g. β-carotene, **75**), the visual process (e.g. retinal, **76**) or conducting polymers (e.g. polyacetylene, **77**) — there are surprisingly little thermochemical data for species with conjugated three or more double bonds. Nonetheless, we remind the reader that following our earlier enunciated prejudices, we will still ignore substituted species such as the partially conjugated ergosterol, **78**, with its solid and gaseous phase enthalpies of formation of -789.8 ± 24.7 and -670.9 ± 25.5 kJ mol^{-1}, respectively.



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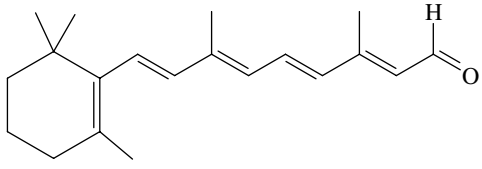

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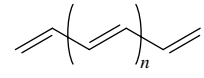

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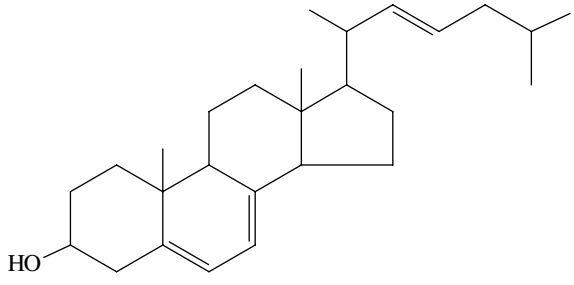
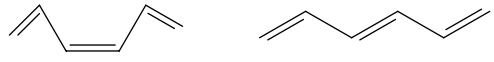


(78)

B. Acyclic Species

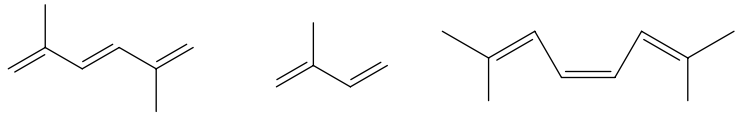
We start with the simplest conjugated triene, 1,3,5-hexatriene, for which there are the two isomers, the (*Z*)- and (*E*)-, species **79** and **80**, respectively. Nearly 30 years ago[57], the enthalpy of combustion of the former, as liquid, was reported. From this number,

the customary ancillary values of the enthalpies of formation of H_2O and CO_2, and our standard estimation approach for enthalpies of vaporization, we obtain the desired enthalpy of formation of gaseous **80** as 175 ± 14 kJ mol^{-1}. Somewhat later, considerably more precise enthalpies of hydrogenation[39] were reported for both compounds. These studies were performed in glacial AcOH with an unmeasured correction for solvent effects. Ignoring this solvent correction and accepting these enthalpies of hydrogenation and of formation of the common hydrogenation product, gaseous *n*-hexane, we derive the desired enthalpies of formation of **79** and **80** to be 169.7 ± 1.1 and 165.1 ± 1.5 kJ mol^{-1}. The two results for (*E*)-1,3,5-hexatriene are in agreement. One can do better than merely ignore the solvent correction for the hydrogenation measurement by positing[56] a constant correction per double bond of *ca* 2.9 kJ mol^{-1}, and thereby result in the modified value of *ca* 174 kJ mol^{-1} for the (*E*)-triene. Needless to say, it would be more correct to measure the solvent correction directly[12]. Alternatively, one can perform the hydrogenation in a nonpolar solvent and so mimic the gas phase result[7]. Within the last few years, this quasi-gas-phase hydrogenation measurement were reported[12] albeit on a **79/80** (or *Z*/*E*-hexatriene) mixture of known stoichiometry. Accepting the earlier difference of enthalpies for the two isomers results in the enthalpies of formation of **79** and **80** of 172.0 ± 2.5 and 167.8 ± 2.5 kJ mol^{-1} respectively. Admitting some numerical 'sloppiness', a corollary of the earlier observation[37,38] that the enthalpy of formation of a strainless conjugated diene is *ca* 5 kJ mol^{-1} more than the sum of the component monoenes is that the enthalpy of formation of a strainless conjugated triene is *ca* 10 kJ mol^{-1} more than the sum of the component monoenes. A value of 167.5 kJ mol^{-1} is 'predicted' in good agreement with experiment for the (*E*)-isomer; we may understand the *ca* 5 kJ mol^{-1} discrepancy for the (*Z*)-isomer in terms of strain in the latter as a 3.2 ± 1.1 kJ mol^{-1} difference is found[11] for the *Z*/*E* difference for 3-hexene, the related monoolefin with an internal double bond.



(79) **(80)**

Agreement is somewhat poorer for substituted hexatrienes. Consider now the (*E*)-isomer of 2,5-dimethyl-1,3,5-hexatriene **(81)** for which Roth gives an enthalpy of formation of 95.8 kJ mol^{-1}. Simple olefin additivity, as done above for the parent hexatriene, results in a value of 103 kJ mol^{-1}. Modifying the above 5 to 3.5 kJ mol^{-1} as found for the relatedly branched conjugated diene (isoprene, **82**) gives a new value of *ca* 100 kJ mol^{-1} for the enthalpy of formation of **81**. The discrepancy has shrunk to *ca* 4 kJ mol^{-1}.



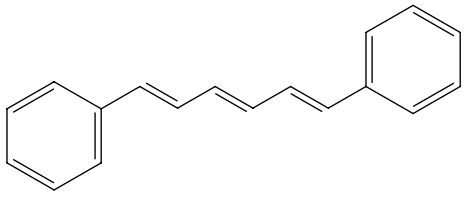
(81) **(82)** **(83)**

Consider now the 1,1,6,6-tetramethylated derivative of (*Z*)-1,3,5-hexatriene **(83)**, a species more properly named (*Z*)-2,6-dimethyl-2,4,6-octatriene and occasionally and trivially called '*cis*-allo-ocimene'. To estimate its enthalpy of formation, let us use simple olefin additivity along with:

(a) the same 3.5 (instead of 5 kJ mol^{-1}) correction as above,
(b) the Z/E correction for the central hexatriene double bond as with the parent triene,
(c) the same Z/E difference as found for the substructure C=C−C=C−Me as found in the pentadienes **4** and **5**,

Numerically, the above sum to *ca* 40 kJ mol^{-1}. The experimentally measured enthalpy of formation for liquid **83**, derived from a combustion measurement, is −24 kJ mol^{-1}. Using our standard protocol to estimate the necessary enthalpy of vaporization results in an additional 50 kJ mol^{-1}. A value of 26 kJ mol^{-1} is thus predicted for the enthalpy of formation of gaseous **83**. The source of the 14 kJ mol^{-1} discrepancy evades us[58].

The final acyclic conjugated triene we will discuss is 1,6-diphenylhexatriene, presumed (*E*,*E*,*E*) and hence species **84**. Ignored by Pedley, an earlier archive[59] presented the enthalpy of formation of the solid to be 211 kJ mol^{-1}, a value *ca* 10 kJ mol^{-1} lower than that would be obtained by extrapolating from the enthalpies of formation of solid (*E*)-stilbene **(40)** and (*E*,*E*)-1,4-diphenylbutadiene **(38)**. Admitting the caveats given by a yet earlier compendium[60], we estimate with some callousness the necessary enthalpy of sublimation to obtain the desired gas phase enthalpy of formation. A value of *ca* 120 kJ mol^{-1} is found by averaging the values of other C_{18} hydrocarbons[61], while using only polynuclear aromatic hydrocarbons[62] would have given us 110 kJ mol^{-1}. This suggests that the enthalpy of formation of the gaseous species is between *ca* 320 and 330 kJ mol^{-1}. By contrast, the simple olefinic additivity logic would have resulted in *ca* 360 kJ mol^{-1}. The 30–40 kJ mol^{-1} difference is without explanation. Given the interest in α,ω-diphenylpolyenes (generically **85**), we recommend the remeasurement of the enthalpy of formation of **84**.



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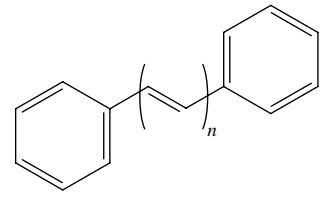
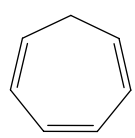


(85)

C. Totally Monocyclic Species

By this description we mean all of the conjugated double bonds are found in a single ring. Two thermochemically characterized examples we know of are tropilidene (1,3,5-cycloheptatriene) **(86)** and 1,3,5-cyclooctatriene **(87)**. We have already mentioned that 1,3,5-cyclohexatriene and its derivatives will not be directly considered in this chapter because of the 'special' aromaticity of benzene and its derivatives. Were there no additional strain or resonance effects, then the enthalpy of formation of benzene and tropilidene would differ by −20.6 kJ mol^{-1}, the so-called 'universal' methylene increment[63]. Ignoring an uncertainty of *ca* 5 kJ mol^{-1} inherent in deciding between Pedley's (180.9 kJ mol^{-1}) and Roth's (186.6 kJ mol^{-1}) recommended values of the enthalpy of formation of tropilidene, the difference for benzene and tropilidene is *ca* 100 kJ mol^{-1} with benzene having the less positive value. It is unequivocal that the 120 kJ mol^{-1} discrepancy reflects the aromatic stabilization of benzene — one cannot use this discrepancy to suggest tropilidene is markedly destabilized.



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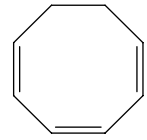
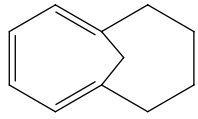


(87)

Relatedly, one would have expected 1,3,5-cyclooctatriene to have a more negative enthalpy of formation than tropilidene by the same -20.6 kJ mol^{-1}. By contrast, the difference for these enthalpies of formation of species **86** and **87** as derived from experimentally measured enthalpies of formation is *ca* $+12$ kJ mol^{-1}. From this we may deduce that tropilidene enjoys considerable stabilization due to homoaromatic interactions. While this conclusion is not new[64], nonetheless we find it encouraging to see it corroborated.

D. Totally Bicyclic Species

We also know the enthalpies of formation of the triene, 1,6-(butane-1,4-diyl)-tropilidene (bicyclo[4.4.1]undeca-1,3,5-triene, **88**) as well as of the related tetraene [1,6-(2-butene-1,4-diyl)-tropilidene, **89**] and pentaene [1,6-(1,3-butadiene-1,4-diyl)-tropilidene, **90**], respectively[65]. Choosing Roth's suggested value for the enthalpy of formation of the parent tropilidene so that all four species are taken from the same primary source[66], we find that attachment of these varying 4-carbon chains increase the enthalpy of formation by -40, 74 and 136 kJ mol^{-1}, respectively. Upon affixing these same 4-carbon chains to benzene to form tetralin, 1,4-dihydronaphthalene and naphthalene (**91, 92** and **7**, respectively) the corresponding enthalpy of formation changes[67] by -57, 51 and 68 kJ mol^{-1}.



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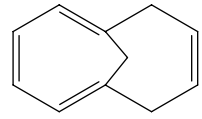

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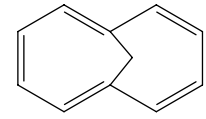

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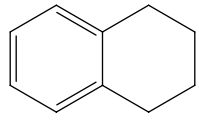

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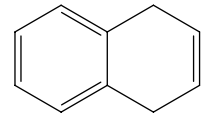
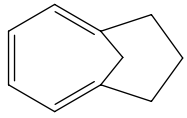


(92)

That there is less stabilization associated with attachment of $-(CH_2)_4-$ to tropilidene than to benzene suggests the greater sensitivity of homoaromatic species to distortion with concomitant loss of stabilization. This is not altogether surprising. Attachment of a propane-1,3-diyl chain to tropilidene does not result in the homoaromatic species **93** but instead the ring closes to the [4.3.1]-propelladiene, **94**. By contrast, we suspect few readers would want to consider the corresponding 1,2-(propane-1,3-diyl)-benzene, **95**, as non- or even homoaromatic. After all, this stable species has long been known as either indane or hydrindane. Relatedly, replacement of CH_2 by CF_2, CMe_2 or CH_2CH_2 shifts the equilibrium to the appropriate [4.3.1] or [4.3.2] propellane (species **96–98**, respectively).

It is interesting that attachment of $-(CH_2)_4-$ and $-CH_2CH{=}CHCH_2-$ to benzene results in nearly the same enthalpy of formation change but it is not obvious how fortuitous this equality is: we have reasons for considerable skepticism of its validity[68]. That formation of naphthalene from benzene is accompanied by a lessened enthalpy of formation increase than that of 1,6-methano[10]annulene (yet another name for species **90**) from tropilidene would appear to be more of a strain than a resonance derived effect. From Roth, we find the resonance energy increase on going from tropilidene to 1,6-methano[10]annulene is 55 kJ mol^{-1} and from benzene to naphthalene the increase is nearly the same, nearly 59 kJ mol^{-1}. By contrast, the 1,5-methano[10]annulene **(99)** is less stable by 77 kJ mol^{-1} than the species it appears most naturally to be compared with, namely the isomeric **90**.



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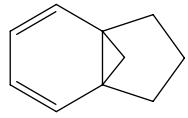

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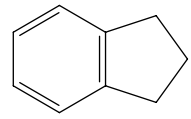

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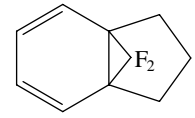

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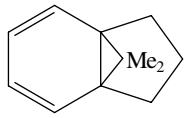

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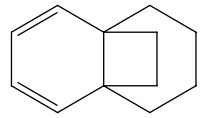

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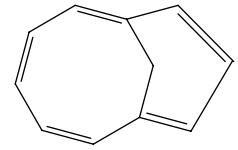
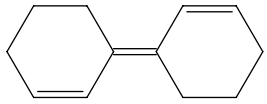


(99)

E. Semicyclic Species

This class of compounds is defined to have some of the three conjugated double bonds found in the ring and others not. This class includes the isomeric 3,3′-bis(cyclohexenylidenes), **100** and **101**. Roth shows us that the two isomers have the same enthalpy of formation within *ca* 1 kJ mol^{-1}, a difference somewhat smaller than the 4 kJ mol^{-1} found for the totally acyclic 1,3,5-hexatrienes, **79** and **80** respectively. Naively these two sets of trienes should have the same $(E)/(Z)$ enthalpy difference. Given experimental uncertainties, we will not attempt to explain the difference[69]. We may compare **100** and **101** with phenylcyclohexane, **102**, an isomeric species which also has the same carbon skeleton. There is nearly a 110 kJ mol^{-1} enthalpy of formation difference between the semicyclic and cyclic trienes. We are not surprised, for the word 'cyclic' is customarily replaced by 'aromatic' when in the context of the previous sentence.



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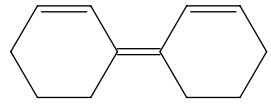

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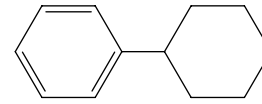


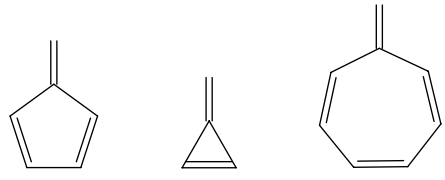
(102)

Strictly speaking, compounds such as fulvenes, isotoluenes and 3,4-dimethylenecyclobutene also qualify as semicyclic trienes. However, they will be discussed in the following section of this chapter because of their relation to aromatic hydrocarbons.

VII. CONJUGATED SPECIES WITH *EXO*-METHYLENE GROUPS: FULVENES, ISOTOLUENES, XYLYLENES AND RELATED SPECIES

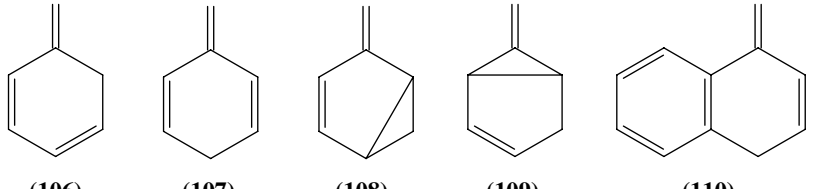
A. Trivial Names and Nontrivial Compounds

The classes of compounds discussed in this section have 'trivial' but 'generic' names that hark back to a more primitive understanding of organic chemistry. The class name 'fulvenes' addresses the yellow color of some of their initially discovered examples. Strictly speaking, these compounds are derivatives of methylenecyclopentadiene, **103**. In Section VII.C below on fulvenes we will extend the discussion to include the energetics of the ring-contracted methylenecyclopropene, **104**, and ring-expanded methylenecycloheptatriene, **105**, and thereby include the so-called triafulvenes and heptafulvenes. (These latter names suggest a more correct name for the derivatives of **103** is pentafulvenes, an alternative we will not use in this chapter.)

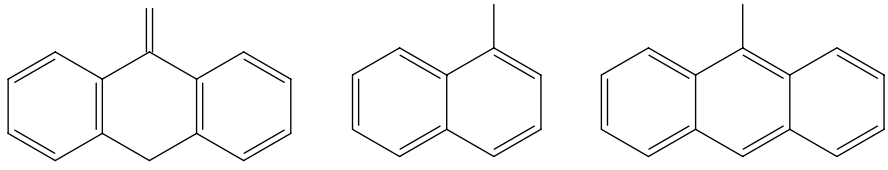


(103) **(104)** **(105)**

'Isotoluenes', discussed below in Section VII.D, are tautomeric isomers of alkylbenzenes wherein the aromatic ring has been sacrificed to form an exocyclic double bond, and so there is the archaic term 'semibenzenes' that has elsewhere been used for these species. Strictly speaking, the name 'isotoluene' itself refers to the two derivatives of cyclohexadiene (cf **49** and **50**) with a single exomethylene group, and so there are the *o*-, **106**, and *p*-, **107**, isomers. We also recognize the bicyclic species, **108** and **109**, that may both be casually considered *m*-isotoluenes, as well as tautomers of other alkylarenes such as **110** and **111**, that being suitably isomeric to 1-methylnaphthalene **(112)** and 9-methylanthracene **(113)** also qualify as isotoluenes.

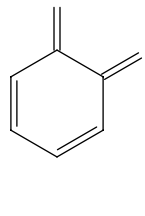


(106) **(107)** **(108)** **(109)** **(110)**



(111) **(112)** **(113)**

'Xylylenes', to be discussed in Section VII.E, have the same formal relation to xylenes as ethylene does to ethane, namely two fewer hydrogens with a compensatory, additional double bond. More properly then, *o*- and *p*-xylylene, **114** and **115**, are recognized as derivatives of 1,3- and 1,4-cyclohexadiene (**49** and **50**) with two exomethylene groups. (They are also recognized as derivatives of *o*- and *p*-benzoquinone, **116** and **117**, and so there is the alternative name of quinodimethans.) There is also a species called *m*-xylylene that has been alternatively drawn as **118, 119** and **120**. We will also consider the ring-contracted 3,4-dimethylenecyclobutene, **121**, under the generic category of xylylenes as well.



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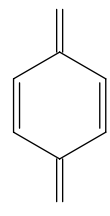

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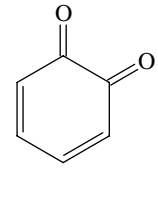

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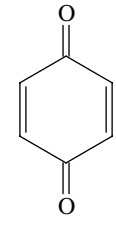

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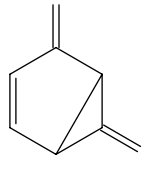

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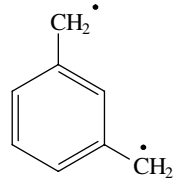

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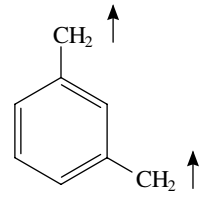

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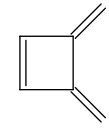


(121)

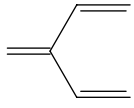
The compounds in this section — fulvenes, isotoluenes, xylylenes — are characterized by trivial names. Our various reference citations document their nontrivial chemistry: isomerization, polymerization and oxidation befall the unwary experimentalist who would study them.

B. Conjugation and Cross-conjugation

In the title to this section we referred to fulvenes, isotoluenes and xylylenes as conjugated species. Strictly speaking, we should have referred to them as cross-conjugated. Let us thus begin with a definition. By cross-conjugated, we mean species with the substructure $C{=}C(-C{=}C)_2$ as opposed to $C{=}C{-}C{=}C{-}C{=}C$, that is, they are formal derivatives of 1,1-divinylethylene as opposed to 1,2-divinylethylene. It is a common assumption in the study of energetics of organic compounds that cross-conjugation results in less resonance stabilization than conventional conjugation. Is this assumption quantitatively corroborated by the thermochemical literature?

The simplest cross-conjugated polyene is **122**, 3-methylene-1,4-pentadiene or 1,1-divinylethylene itself. Accepting the analysis in Reference 2 that was made using Roth's data, we find this species to be some 23 $kJ\,mol^{-1}$ less stable than the simplest conjugated polyene, **80**, (*E*)-1,3,5-hexatriene or 1,2-divinylethylene. The next simplest cross-conjugated polyenes are 3-methylene-1,4,6-heptatriene, **123**, and 3,4-dimethylene-1,5-hexadiene, **124**, that would naturally be compared with (*E*,*E*)-1,3,5,7-octatetraene,

125. While we know of no experimental thermochemical data for **123**, Roth informs us that the enthalpy of formation of **124** is 259 kJ mol^{-1}. There are no experimental thermochemical data for **125** either, but it is easy to estimate the desired enthalpy of formation. We may either use the standard olefin approach with ethylene, 1,3-butadiene and (*E*)-1,3,5-hexatriene (i.e. with CH_2=CH_2, **33** and **79**) or linearly extrapolate these three unsaturated hydrocarbons. From either of these approaches, we find a value of *ca* 225 kJ mol^{-1}. Cross-conjugation costs some 35 kJ mol^{-1} in the current case. Interestingly, the directly measured cross-conjugated 1,1-diphenylethylene **(126)** is only *ca* 10 kJ mol^{-1} less stable than its directly measured conjugated (*E*)-1,2-isomer **(40)** despite the expected strain effects that would additionally destabilize the former species.



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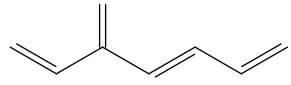

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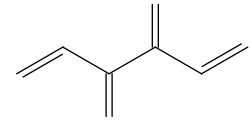

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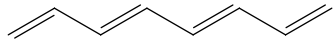

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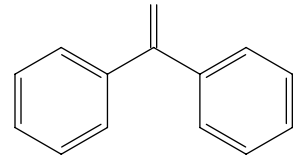
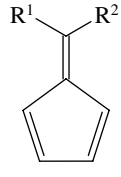


(126)

C. Fulvenes

Part of the folklore of nonbenzenoid hydrocarbons suggests fulvenes are on the nonaromatic/aromatic border. It is thus not obvious whether these species really belong in this chapter. Yet, because their aromaticity is so much less than that found for their isomeric benzenoid derivatives[70] we feel confident to proceed. Other than the parent hydrocarbon[71] species **103** [i.e. **127** wherein (R^1, R^2) = (H, H) most of the other thermochemically characterized fulvenes have substitution on the exomethylene carbon; cf (R^1, R^2) = (H, Me)[71], (Me, Me)[72] and (Ph, Ph)[73]: for reference, the suggested enthalpies of formation of the (H, H), (H, Me), (Me, Me) and (Ph, Ph) species are 224, 185, 144 and 402 kJ mol^{-1}, respectively. Were all differences in steric interactions and contributions from the dipolar resonance structures of the generic type **128** negligible, then ΔH_f (**127**, R^1, R^2) and $\Delta H_f(CH_2{=}CR^1R^2)$ would be linearly related. We find that a nearly perfect straight line



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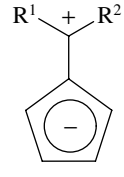

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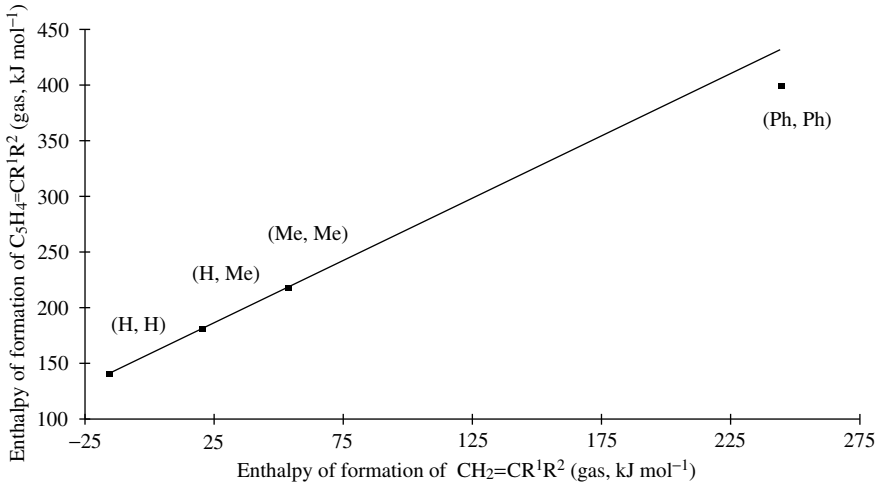


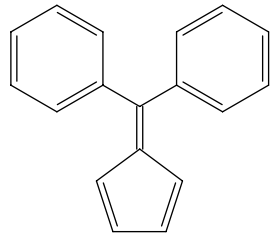
FIGURE 1. Enthalpies of formation of C_5H_4=CR^1R^2 vs CH_2=CR^1R^2

for olefins vs fulvenes (equation 35) can be drawn[74] through the (H, H), (H, Me) and (Me, Me) points:

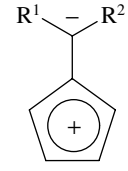
$$\Delta H_f(\mathbf{127}, R^1, R^2) \pm 1.3 = (1.152 \pm 0.026)\Delta H_f(CH_2{=}CR^1R^2) + (163.0 \pm 0.9) \quad (35)$$

The r^2 for this line is 0.9995 with a standard deviation of *ca* 0.9 kJ mol^{-1} (Figure 1). The deviation for $R^1 = R^2 =$ Ph **(129)** is some 43 kJ mol^{-1} below the line. If the *exo*-methylene/ring bond is quite polar and resonance structures **128** are significant (**130** is easily ignorable), then ΔH_f (**127**, R^1, R^2) and ΔH_f(O=CR^1R^2) would be more likely to be linearly related. Another nearly perfect line, that of carbonyls vs fulvenes, can be drawn through the (H,H), (H,Me) and (Me,Me) points (equation 36).

$$\Delta H_f(\mathbf{127}, R^1, R^2) \pm 2.7 = (0.734 \pm 0.075)\Delta H_f(O{=}CR^1R^2) + (304.8 \pm 5.9) \quad (36)$$



(129)



(130)

The r^2 is but 0.998 with a standard deviation of *ca* 1.0 kJ mol^{-1} (Figure 2). Again the diphenyl species **129** is sorely deviant, this time above the line by some 59 kJ mol^{-1}, i.e. in the opposite direction. Despite the nearly ±15 kJ mol^{-1} uncertainty reported for the measurement for enthalpy of formation of diphenylfulvene, these results suggest the

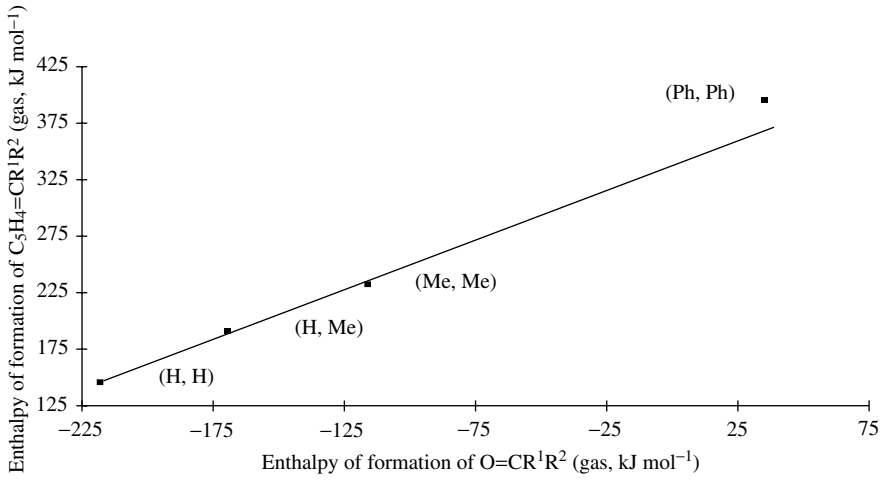


FIGURE 2. Enthalpies of formation of C_5H_4=CR^1R^2 vs O=CR^1R^2

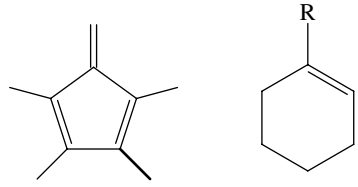
fulvene *exo*-methylene/ring bond is of polarity intermediate between those of 'normal' olefins and ketones. This conclusion is consistent with the general idea of some — but not 'that much' — polarity in fulvenes.

Consider now the one ring-substituted fulvene for which we have a measured enthalpy of formation, namely the ring tetramethylated derivative **131** with its value of 83 kJ mol^{-1}. If benzene is the appropriate paradigm for fulvene, then reaction 37 is expected to be essentially thermoneutral.

$$\mathbf{103} + 4\text{PhMe} \longrightarrow \mathbf{131} + 4C_6H_6 \tag{37}$$

If an olefinic paradigm is appropriate for fulvene, then reaction 38 would be more likely to be thermoneutral.

$$\mathbf{103} + 4(\mathbf{132}, \text{R} = \text{Me}) \longrightarrow \mathbf{131} + 4(\mathbf{132}, \text{R} = \text{H}) \tag{38}$$



(131) **(132)**

From the enthalpies of formation from Roth for the fulvenes and from Pedley for the other hydrocarbons in equations 37 and 38, we find the former reaction is exothermic by 12 kJ mol^{-1} while the latter is endothermic by 12 kJ mol^{-1}. Ionic resonance structures analogous to **128** are expected to be of less importance for the ring alkylated species than for the parent species **103**: negatively charged carbon is destabilized by adjacent

electron-donating groups. Nonbonded Me•••Me and Me•••CH_2 repulsion further destabilize the tetramethyl species. As such, reactions 37 and 38 are more endothermic than the above numbers suggest. We conclude that the understanding derived from equation 37 is untenable. Equivalently, fulvene is more olefinic than benzenoid, a result we have already concluded.

The parent triafulvene, **104**, is the sole representative of this hydrocarbon class for which there is a suggested enthalpy of formation[75], namely 423 kJ mol^{-1}. If the conjugative interactions of the *exo*-methylene with cyclopropene and cyclopentadiene were the same, then equation 39 would be thermoneutral.

$$\mathbf{103} + \text{cyclo-}[CH_2(CH)_2] \longrightarrow \mathbf{104} + \text{cyclo-}[CH_2(CH)_4] \tag{39}$$

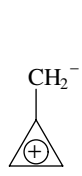
In fact, it is some 56 kJ mol^{-1} endothermic. Part of small ring folklore[76] asserts that introduction of trigonal carbons into 3-membered rings is energetically expensive compared to acyclic paradigms. In that 5-membered ring compounds are generally 'normal', much the same is expected when comparing the directly relevant 3- and 5-membered rings; cf equations 40 and 41:

$$\text{cyclo-}[(CH_2)_3] + \text{cyclo-}[(CH_2)_4C{=}CH_2] \longrightarrow \text{cyclo-}[(CH_2)_2C{=}CH_2] + \text{cyclo-}[(CH_2)_5] \tag{40}$$

$$\text{cyclo-}[(CH_2)_2C{=}CH_2] + \text{cyclo} - [(CH_2)_3(CH)_2] \longrightarrow \text{cyclo-}[CH_2(CH)_2] + \text{cyclo-}[(CH_2)_4C{=}CH_2] \tag{41}$$

These reactions, going from no sp^2 carbon to one in a 3-membered ring, and from one to two respectively, are endothermic by *ca* 59 and 55 kJ mol^{-1}. This suggests that going from two to three sp^2 carbons in a three-membered ring will also be endothermic by *ca* 50–60 kJ mol^{-1}. Correcting for this suggests equation 39 would be essentially thermoneutral were there no special strain effects in 3-membered rings. As such, we conclude that the conjugative effects of the *exo*-methylene on cyclopropene and cyclopentadiene in the formation of triafulvene and fulvene, respectively, are nearly the same. This is a surprising result given the reversed polarity of these hydrocarbons; cf ionic resonance structures **128** and **133**.

What, then, can be said about heptafulvene, **105**? No direct measurement of the enthalpy of formation of **105** has been reported. However, there are chronicled[77] measurements of its enthalpy of hydrogenation[78], −386 kJ mol^{-1}. The enthalpy of formation of the hydrogenation product, methylcycloheptane **(134)**, remains unmeasured. However, the difference of this value and of the demethylated counterpart, cycloheptane, is not likely to be significantly dissimilar from the differences found for the pairs methylcyclohexane and cyclohexane, methylcyclopentane and cyclopentane, and even the acyclic isobutane ('2-methylpropane') and propane. These last differences average *ca* 30 kJ mol^{-1} and thus we deduce ΔH_f(**134**, g) = −148 kJ mol^{-1} and ΔH_f(**105**, g) = 238 kJ mol^{-1}. Is this last value plausible? Let us compare **105** with tropone, **135**. The enthalpy of formation of **105** is found to be 194 kJ mol^{-1} more positive than that of **135**. By contrast, the difference of enthalpies of formation of methylenecyclohexane and cyclohexanone, methylenecyclopentane and cyclopentanone, and isobutene ('methylenepropane') and acetone (propanone) average some 203 kJ mol^{-1}. This does not make sense in that we might have thought that tropone would enjoy more resonance stabilization than heptafulvene. Yet we recall that conjugated α,β-unsaturated carbonyl compounds have less resonance stabilization than the sterically comparable and isoelectronically related dienes[79].



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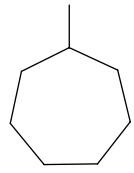

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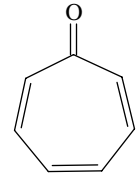
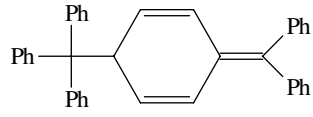


(135)

D. Isotoluenes

It is interesting to note that 100 years ago the first isotoluene was discovered[80] and 60 years ago its thermochemistry was investigated[81]. However, this compound has generally remained misnamed and so its interesting structural feature was ignored by most chemists. Then again, the incorrect name itself evinces interest (hexaphenylethane) — by contrast, the mere length (and, implicitly, the complexity) of its more 'systematic' name 4-(triphenylmethyl)-1-(diphenylmethylidene)-2,5-cyclohexadiene, **136**, disguises its unusual structural features[82]. Much more recently, the enthalpies of formation of both *o*- and *p*-isotoluene (**106** and **107**, respectively) have been determined: the former by both positive[83] and negative[84,85] ion chemistry, the latter only by the latter[84,85]. The positive ion experiment suggests an enthalpy of formation of 172 kJ mol^{-1}. The negative ion experiments suggest the enthalpies of formation of the isotoluenes lie some 100 ± 17 kJ mol^{-1} above that of toluene and so are numerically *ca* 150 ± 17 kJ mol^{-1}. Are any of these values reasonable? The following outlines our confusion.



(136)

The first observation is that the two isotoluenes have nearly the same enthalpy of formation as had been seen for the isomeric cyclohexadienes in Section V.C. This suggests that conjugation energy in both of these species is small because the *o*- and *p*-isotoluenes are formally conjugated and cross-conjugated trienes, respectively. Yet, there is considerable conjugation energy in the isotoluenes as demonstrated by the 25 (using data from Reference 83) or 50 kJ mol^{-1} (using data from Reference 84 and 85) exothermicity of the formal reactions 42a and 42b.

$$\mathbf{49} + \text{cyclo-}[(CH_2)_5C{=}CH_2] \longrightarrow \mathbf{106} + \text{cyclo-}[(CH_2)_6] \quad (42a)$$

$$\mathbf{50} + \text{cyclo-}[(CH_2)_5C{=}CH_2] \longrightarrow \mathbf{107} + \text{cyclo-}[(CH_2)_6] \quad (42b)$$

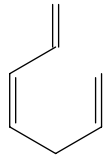
Remembering that a typical endothermicity of very approximately 5 kJ mol^{-1} is found when there is no strain accompanying combination of two olefins to form a conjugated diene[23,24], the cyclization reaction of (*Z*)-1,3,6-heptatriene, **137** (equation 43)

$$\mathbf{137} \longrightarrow \mathbf{107} + H_2 \quad (43)$$

is naively expected to be endothermic by that *ca* 5 kJ mol^{-1} as well. From a plausible enthalpy of formation of *ca* 162 kJ mol^{-1} for the acyclic triene, we deduce the enthalpy

of formation of **106** to be 163 kJ mol^{-1}. Considering all the assumptions, it is not unreasonable that a value as small as 150 kJ mol^{-1} may arise[86].

Finally, our earlier experience[87] suggests the difference of the enthalpy of formation of benzo-*p*-isotoluene, **110**, and *p*-isotoluene, **107**, should be comparable to that of the cyclohexadienes **49** and **50** to the dihydronaphthalenes, **138** and **92**, and to cyclohexene, **139**, to tetrahydronaphthalene, **91**, and thus to the *ca* 31 kJ mol^{-1} found for general benzoannelation. Admitting there are complications with the enthalpies of formation of the former pair of species (see Section V.C), let us use those of the latter pair and their difference of 31 kJ mol^{-1}. From Reference 85 (using both negative and positive ion chemical techniques and logic), we find **110** has an enthalpy of formation some 65 kJ mol^{-1} higher than that of 1-methylnaphthalene, **112**. From Reference 88, we find the latter number, 113 kJ mol^{-1}, and so derive the enthalpy of formation of **110** to be 180 kJ mol^{-1}. From this we conclude that the enthalpy of formation of *p*-isotoluene, **107**, is *ca* 150 kJ mol^{-1}. This is consistent with one of the suggested experimental numbers, but violates our intuition as noted above[89].



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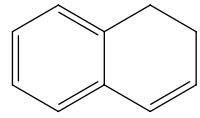

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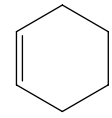

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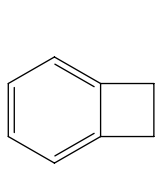
E. Xylylenes

As with the isotoluenes, there are two sets of independent, but also indirect, measurements from which the enthalpy of formation of *o*-xylylene, **114**, can be derived. One study interrelated this species by varied equilibration measurements involving the isomeric benzocyclobutene **140** and the hydrogenation enthalpy of the latter hydrocarbon to bicyclo[4.2.0]octane, **141**. The value of 254 kJ mol^{-1} was derived by Roth from this study. The second study[90] employed what are now relatively primitive quantum chemical calculations to assist in their understanding of ion–molecule reactions, most notably proton affinity measurements involving the 2-methylbenzyl cation, **142**. An alternative value of 234 ± 17 kJ mol^{-1} was initially derived here. One can be convinced these independent values are roughly consonant if the suggested error bars are employed. Yet it should be admitted that the authors of Reference 90 suggested a value of 230 ± 17 kJ mol^{-1} for the *p*-isomer, **115**, from related analysis involving the 4-methylbenzyl cation, **143**. However, this value was amended to 203 ± 17 kJ mol^{-1} in a relatively recent compendium[91] by use of experimentally measured enthalpies of halide transfer reactions[92]. In turn, use of a new and nearly completed proton affinity scale[93] results in a value somewhat less than 200 kJ mol^{-1} for ΔH_f **(115)**. The same analysis suggests a comparable enthalpy of formation for the *o*-isomer, **114**. So, which value is to be preferred for the enthalpy of formation of (either) xylylene, *ca* 200, 230 or 250 kJ mol^{-1}? The origin of the discrepancy evades us, as does any explanation for the observation that the two xylylenes should have nearly the same enthalpy of formation[94].

Let us now turn to the ring-contracted xylylene 3,4-dimethylenecyclobutene **(121)**. Does Roth's preferred enthalpy of formation value of 336 kJ mol^{-1} look plausible? In the absence of both 'special' strain and resonance energy contributions, the difference of the



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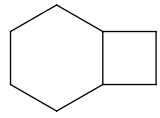

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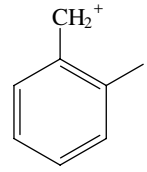

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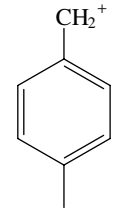


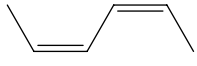
(143)

enthalpies of formation of **121** and benzene would equal the difference of the enthalpies of formation of 2,3-dimethyl-1,3-butadiene and 2,4-hexadiene. That is, the following reaction would be essentially thermoneutral;

$$\mathbf{121} + \mathrm{MeCH{=}CHCH{=}CHMe} \longrightarrow \mathbf{6} + \mathrm{CH_2{=}CMeCMe{=}CH_2} \qquad (44)$$

Taking the former value from Pedley (45.1 ± 1.1 kJ mol^{-1}) and the average of the values for the (*Z*,*Z*)-, (*E*,*Z*)- and (*E*,*E*)-2,4-hexadienes (species **144, 145** and **146**, *ca* 48 kJ mol^{-1} from Reference 12), we derive the enthalpy of formation of **121** is 86 kJ mol^{-1}. The discrepancy is 250 kJ mol^{-1}, a large but mostly sensible number. That is, we recover all but *ca* 30 kJ mol^{-1} of this exothermicity by summing the new destabilization arising from the strain energy of a 4-membered ring (*ca* 109 kJ mol^{-1}) and the loss of resonance energy of benzene as defined by Roth (fortuitously also, *ca* 109 kJ mol^{-1}). Relatedly, the exothermicity of the formal reaction 45

$$\mathbf{121} + \text{cyclo-}[(\mathrm{CH_2})_3(\mathrm{CH})_2] \longrightarrow \mathbf{103} + \text{cyclo-}[(\mathrm{CH_2})_3\mathrm{C{=}CH_2}] \qquad (45)$$



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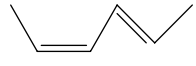

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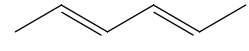


(146)

is *ca* 25 kJ mol^{-1}. Using the more classical calorimetric measured value for the enthalpy of formation of *o*-xylylene, a comparable exothermicity is found for the following putative thermoneutral reaction (equation 46) involving this species along with 1,3-cyclohexadiene and cyclobutene:

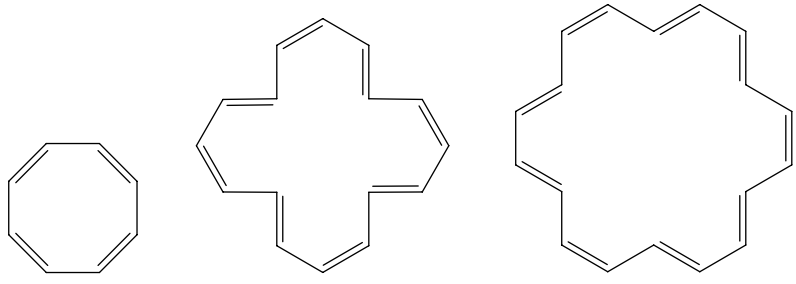
$$\mathbf{121} + \mathbf{49} \longrightarrow \mathbf{103} + \text{cyclo-}[(\mathrm{CH_2})_2(\mathrm{CH})_2] \qquad (46)$$

That equations 44, 45 and 46 find species **121** equally destabilized suggests either an error in the measurement and/or an error in our understanding of the energetics of 3,4-dimethylenecyclobutene.

VIII. ANNULENES: AROMATICITY AND ANTIAROMATICITY

A. If We Study Cyclooctatetraene, Why Not Benzene?

When starting this chapter we promised ourselves and the reader not to consider benzene and its derivatives. Cyclooctatetraene [or more properly (*Z*,*Z*,*Z*,*Z*)-1,3,5,7-cyclooctatetraene, **147**] is generally recognized as a polyene and so this latter compound would appear to belong here. How can we do one and not the other? Therefore, in this concluding section of the chapter, we briefly discuss the enthalpies of formation of some of the



(147) **(148)** **(149)**

[*n*]annulenes, those cyclic conjugated polyenes with the generic formula C_nH_n. There are experimentally determined values for $n = 6$ (benzene), 8 (cyclooctatetraene), 16 and 18, species **6, 147, 148** and **149**, respectively[95].

B. How Aromatic or Antiaromatic are [8] and [16]Annulenes?

Regardless of how we wish to define the resonance stabilization of the $n = 6$ case of benzene, it is unequivocal that this substance enjoys considerable stabilization relative to 'classical' expectations related to acyclic and/or less unsaturated precedent. Rather than discussing the plethora of models and even greater experimental evidence that documents this 'aromaticity', we consider benzene itself as the paradigm. We will return to olefinic paradigms later in this section.

More precisely, let us consider the enthalpies of reaction for the formal process 47:

$$n/6[C_6H_6] \longrightarrow C_nH_n \tag{47}$$

We start with the $n = 8$ case and thus species **147**. For the liquid and gas, the enthalpies of reaction are 189.1 and 185.7 kJ mol^{-1} endothermic, respectively, while for the solid with temperature-uncorrected enthalpies of fusion, the reaction is found to be 189.9 kJ mol^{-1} endothermic. These numbers are essentially indistinguishable and this near-equality encourages us to consider data for reaction 47 from any of the three phases as equivalent to each other and equal to *ca* 188 kJ mol^{-1}. For the $n = 16$ case, there are thermochemical data only for the solid phase of [16]annulene, **148**. Using this enthalpy of formation of **148**, 547.5±11.7 kJ mol^{-1}, and that of solid benzene by use of a temperature-uncorrected enthalpy of fusion, this reaction is found to be some 373 kJ mol^{-1} endothermic. That 373 is greater than 188 does not mean that [16]annulene is more destabilized than its 8-carbon analog. Numbers associated with aromaticity and antiaromaticity have usually been normalized by dividing by the number of carbon atoms and/or π-electrons. Accordingly, dividing these two destabilization numbers by 16 and 8, respectively, results in the more significant stabilization per carbon (or per π-electron). These last two numbers, 23.3 and 23.6 kJ mol^{-1}, are essentially equal. We thus conclude that the aromaticity — more precisely, the antiaromaticity — of species **148** and **147**, [16] and [8]annulene, are essentially equal.

C. [18]Annulene and Acyclic Polyenes

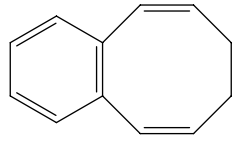
Let us turn to [18]annulene, **149**, for which there are two sets of measurements. The first set consists of direct enthalpy of combustion and thus of formation[96]. From the

latter datum, 163.4±16.7 kJ mol^{-1} for solid **149** and our phase change independence assumption, we find reaction 48 to be exothermic by some 46 kJ mol^{-1}. Equivalently, benzene is *ca* 2.5 kJ mol^{-1} more aromatic per carbon than [18]annulene. As noted by the authors of Reference 96, this difference seems too small: [18]annulene does not behave *that* aromatic. These latter authors redetermined the enthalpy of formation of **149** by analyzing the enthalpy of the decomposition reaction to form benzene and 1,2-benzo-1,3,7-cyclooctatriene, **150**, in reaction 48:

$$\mathbf{149} \longrightarrow \mathbf{6} + \mathbf{150} \tag{48}$$

On the basis of some judicious measurements and relevant estimations, the enthalpy of formation of gas phase [18]annulene was derived[97] to be *ca* 519±22 kJ mol^{-1}. From this we conclude that benzene is *ca* 15 kJ mol^{-1} more aromatic per carbon than [18]annulene. This value seems too large.

Although we cannot as yet converge on a desired enthalpy of formation of gaseous [18]annulene[98], it is quite apparent that this last number is suspect in terms of at least two acyclic paradigms for aromaticity. Recall the Dewar–Breslow definition[99] for aromaticity and antiaromaticity of an [*n*]annulene in terms of the corresponding acyclic polyene with *n*/2 double bonds. There is no experimental measurement of the enthalpy of formation of all-(*E*)-1,3,5,7,9,11,13,15,17-octadecanonaene, species **151**. However, we should be surprised if this value seriously differed from that of nine ethylenes and 8(5) kJ mol^{-1}, the 5 kJ mol^{-1} being taken as the enthalpy of reaction 19 for unstrained olefins and dienes[100]. The enthalpy of formation of **151** is thus *ca* 513 kJ mol^{-1}. This is somewhat less than the value for [18]annulene and so we would conclude that the cyclic species is essentially nonaromatic[101]. Alternatively, consider the series of acyclic polyenes, ethylene, 1,3-butadiene, 1,3,5-hexatriene, ... The gas phase enthalpies of formation are respectively 52.5, 110.0, 165.1, ... corresponding to an enthalpy of formation of an acyclic and unstrained −CH=CH− (or alternatively =CH−CH=)[102] group of *ca* 56 kJ mol^{-1}. Were [18]annulene totally strainless and totally without aromaticity (as opposed to delocalization), one could say that it was composed of nine such groups. The enthalpy of formation of **151** would then equal *ca* 9•56 or 504 kJ mol^{-1}. This number is less positive than the recommended enthalpy of formation of [18]annulene. Do we want to consider this species to be antiaromatic[103]? The source of the error is not apparent.



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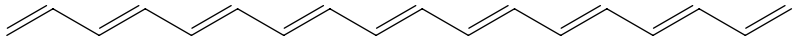

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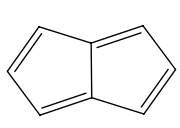
D. Annulenoannulenes

We close this chapter with a brief discussion of [*n*]annuleno[*n*′]annulenes, those species composed of two *ortho*-fused annulenes. Using the same closed shell criterion as for

[*n*]annulenes themselves, we find that there are but five species that fulfill this description for which thermochemical data are derivable from experiment: pentalene **(152)**, naphthalene **(7)**, azulene **(153)**, bicyclo[6.2.0]deca-1,3,5,7,9-pentaene **(154)** and octalene **(155)**. We obtain the enthalpy of formation of **152** by assuming reaction 49 involving it and its 1,3,5-tri-*t*-butyl derivative, **156**, is thermoneutral,

$$\mathbf{156} + 3\text{PhH} \longrightarrow \mathbf{152} + 3^{t}\text{-BuPh} \tag{49}$$



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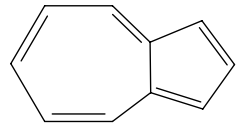
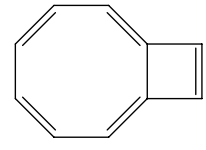
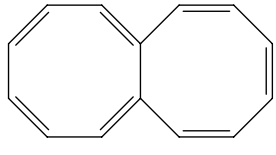


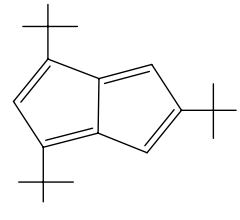
(153)



(154)



(155)

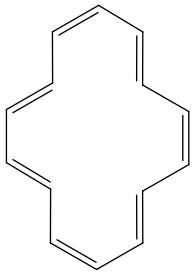


(156)

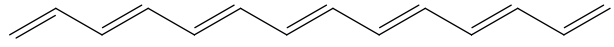
Is this value of 330 kJ mol^{-1} plausible? Were pentalene a normal polyene, we would anticipate an enthalpy of formation of *ca* 4•52.5+5•5 or *ca* 235 kJ mol^{-1}. There is thus *ca* 100 kJ mol^{-1} of destabilization. Is this due to antiaromaticity since we recognize pentalene as a derivative of planar [8]annulene? We think not, for there are two five-membered rings in pentalene each contributing *ca* 30 kJ mol^{-1} of strain apiece[104].

The next three annulenoannulenes — species **7**, **153** and **154** — are isomers with enthalpies of formation 150.3, 307.5 and (from Roth) 514.2 kJ mol^{-1}. In terms of combining ethylenes to form polyenes, their shared acyclic reference energy[105] would be 293 kJ mol^{-1}. It is clear that naphthalene is aromatic and viewing it as a polyene is ill-advised. It is clear that species **154** is strained by at least *ca* 100 kJ mol^{-1} as befits the presence of a four-membered ring. We find further disentangling the competing roles of destabilizing strain and stabilizing aromatic delocalization is problematic.

Turning now to octalene, were species **155** a normal polyene, its enthalpy of formation would be *ca* 407 kJ mol^{-1}. Instead, the experimentally determined value is 551 kJ mol^{-1}. This suggests considerable destabilization much as found in its component cyclooctatetraene rings: after all, cyclooctatetraene itself is destabilized by *ca* 60 kJ mol^{-1} relative to the acyclic octatetraene. Octalene is not a simply modified derivative of [14]annulene **(157)** or even of all-(*E*)-1,3,5,7,9,11,13-tetradecaheptaene, **158**. Regrettably, it evades us how to make the necessary 'wiggle-worm corrections' to relate general polyenes, annulenes and annulenoannulenes. But we do not wring our hands. Perhaps in time to contribute to a future supplement to this volume we will have gained the necessary insights to make these interrelations, comparable in qualitative and quantitative understanding of the other dienes and polyenes that fill this chapter.



(157)



(158)

IX. ACKNOWLEDGMENTS

The author wishes to thank Suzanne W. Slayden for her numerous scientific and editorial comments on this study, and to the Chemical Science and Technology Laboratory of the US National Institute of Standards and Technology for partial support of his research.

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1. S. W. Slayden and J. F. Liebman, in *The Chemistry of Functional Groups, Supplement E2*: *The Chemistry of Hydroxyl*, *Ether and Peroxide Groups* (Ed. S. Patai), Wiley, Chichester, 1993.
2. J. F. Liebman, in *The Chemistry of the Cyclopropyl Group*, Vol. 2 (Ed. Z. Rappoport), Wiley, Chichester, 1995.
3. D. D. Wagman, W. H. Evans, V. B. Parker, R. H. Schumm, I. Halow, S. M. Bailey, K. L. Churney and R. L. Nuttall, *The NBS Tables of Chemical Thermodynamic Properties*: *Selected Values for Inorganic and C_1 and C_2 Organic Substances in SI Units*, *J. Phys. Chem. Ref. Data*, **11** (1982), Supplement 2.
4. J. S. Chickos, A. S. Hyman, L. H. Ladon and J. F. Liebman, *J. Org. Chem.*, **46**, 4294 (1981).
5. J. S. Chickos, R. Annunziata, L. H. Ladon, A. S. Hyman and J. F. Liebman, *J. Org. Chem.*, **51**, 4311 (1986).
6. J. S. Chickos, D. G. Hesse and J. F. Liebman, in *Energetics of Organometallic Species* (Ed. J. A. Martinho Simões), NATO ASI, Series C, Vol. 367, Kluwer, Dordrecht, 1992.
7. D. W. Rogers, O. A. Dagdagan and N. L. Allinger, *J. Am. Chem. Soc.*, **101**, 671 (1979).
8. W. R. Roth, O. Adamczak, R. Breuckmann, H.-W. Lennartz and R. Boese, *Chem. Ber.*, **124**, 2499 (1991).
9. Unless otherwise said, our preferred sources for enthalpies of formation of hydrocarbons are Reference 8 by Roth and his coworkers, and J. B. Pedley, R. D. Naylor and S. P. Kirby, *Thermochemical Data of Organic Compounds* (2nd ed.), Chapman & Hall, New York, 1986. In this chapter these two sources will be referred to as 'Roth' and 'Pedley', respectively, with due apologies to their coworkers. We will likewise also occasionally take enthalpies of fusion from either E. S. Domalski, W. H. Evans and E. D. Hearing, 'Heat Capacities and Entropies of Organic Compounds in the Condensed Phase', *J. Phys. Chem. Ref. Data*, **13**, 1984, Supplement 1, or E. S. Domalski and E. D. Hearing, *J. Phys. Chem. Ref. Data*, **19**, 881 (1990), and refer to either work as 'Domalski'.
10. This is a paraphrase of the dialogue involving the humanistic psychologist Carl Rogers: "being asked 'Don't you get bored listening hour after hour, day after day to people telling you their problems', replied, 'Yes, and when I do I ask myself "Why am I bored?" and then I have an interesting experiment'." This episode was recounted by Irvin Greenberg, another humanistic psychologist, to the author of the current study.
11. (a) D. W. Rogers and E. L. Crooks, *J. Chem. Thermodyn.*, **15**, 1087 (1983).
    (b) D. W. Rogers, E. Crooks and K. Dejroongraung, *J. Chem. Thermodyn.*, **19**, 1209 (1987).
12. W. Fang and D. W. Rogers, *J. Org. Chem.*, **57**, 2297 (1992).
13. By Hess's Law, these two approaches must yield the same energy of interaction between the two double bonds. The virtue of this latter approach is that enthalpy of formation data for the

hydrogenated or saturated species need not be available. The use of Hess's law discourages us from employing enthalpies of formation obtained by using molecular mechanics. So does our prior experience (e.g. References 1 and 2) in making estimates to accommodate for missing enthalpies of formation. In the current study we use molecular mechanics in the following, relatively limited sense. In Reference 8, Roth empirically measured enthalpies of hydrogenation and accompanied these numbers by molecular mechanically calculated enthalpies of formation of saturated hydrocarbons to derive the enthalpies of formation of the dienes and polyenes of direct interest in this chapter. The current author did not deem it necessary or even desirable to estimate *de novo* the enthalpies of formation of the saturated species.

14. For simple alkenes there is a *ca* 4 kJ mol^{-1} difference in the enthalpy of hydrogenation for their single internal double bond. See References 11 for the isomeric hexenes; D. W. Rogers and K. Dejoongruang, *J. Chem. Thermodyn.*, **20**, 675 (1988) for isomeric heptenes; and D. W. Rogers, K. Dejoongruang, S. D. Samuel, W. Fang and Y. Zhao, *J. Chem. Thermodyn.*, **24**, 561 (1992) for isomeric octenes.
15. We take here twice the 'universal methylene increment' (cf Reference 1) as found in the liquid state, i.e. 20.6 + 4.7 where 20.6 is the usually proposed (gas phase) value and 4.7 is (within a sign) the enthalpy of vaporization or condensation per carbon for an arbitrary organic compound as suggested in Reference 4.
16. B. Lebedev and N. Smirnova, *Macromol. Chem. Phys.*, **195**, 35 (1994).
17. Said differently, in the absence of interolefin interactions within and between polymer molecules, the enthalpy of polymerization should reflect the release of strain energy of the precursor monomer cycloalkene. From our earlier knowledge of cycloalkenes [e.g. J. F. Liebman and A. Greenberg, *Chem. Rev.*, **76**, 311 (1976) and A. Greenberg and J. F. Liebman, *Strained Organic Molecules*, Academic Press, New York, 1978], we conclude cyclohexene is less strained than cyclobutene, cyclopentene, cycloheptene and cyclooctene. Another reason for suspicion is that the enthalpies of polymerization and of hydrogenation of cyclohexene and its 4-methyl derivative are not expected to be particularly different, yet the polymerization of the former is reported (under all conditions) to be some 30 kJ mol^{-1} more negative than the latter. Reference 27 gives us the enthalpies of formation and polymerization of 4-methylcyclohexene, -75 ± 4 and -1 kJ mol^{-1}, respectively: the enthalpy of formation of poly(4-methylcyclohexene) is thus -76 kJ mol^{-1}. We can roughly estimate the enthalpy of formation of the saturated counterpart of the polymer, i.e. [$-(CH_2)_5CHMe-$] in two ways. The first starts with [$-(CH_2)_6-$], the saturated counterpart of polymerized cyclohexene. We would predict its enthalpy of formation to be $-54{\bullet}6/2 = -162$ kJ mol^{-1}. From the values in Pedley, we find the average difference of the enthalpies of formation of liquid *n*-alkanes and arbitrary monomethyl derivatives is *ca* $-$ 31 kJ mol^{-1} and so ΔH_f([$-(CH_2)_5CHMe$], lq) ≈ -193 kJ mol^{-1}. Alternatively, we can start with liquid [$-(CH_2)_7-$] and its enthalpy of formation of $-54{\bullet}7/2 = -189$ kJ mol^{-1} and 'correct' it to -193 kJ mol^{-1} by the *ca* $-$ 4 kJ mol^{-1} that accompanies isomerization of a $-CH_2CH_2-$ unit in a liquid *n*-alkane to $-CHMe-$. We thus find the hydrogenation enthalpy of poly(4-methylcyclohexene) is *ca* $-$ 117 kJ mol^{-1}, an entirely reasonable and adequately precedented value. Summarizing, save the possibility of experimental error in the enthalpy of formation of the polymer of cyclohexene, the source of the discrepancy remains evasive.
18. The reader should not be bothered by the presence of solid carbon among the formal products of reaction 12. However, we can correct for it by explicitly considering the enthalpy of formation of 'gaseous graphite' or, equivalently, the sublimation enthalpy of graphite. One estimate of this quantity assumes a value of 6.1 kJ mol^{-1} as suggested for polynuclear aromatic hydrocarbons [S. E. Stein, D. M. Golden and S. W. Benson, *J. Phys. Chem.*, **81**, 314 (1977)]. [Alternatively, following from the estimate of the enthalpy of formation of 'gaseous diamond' [D. Van Vechten and J. F. Liebman, *Isr. J. Chem.*, **21**, 105 (1981)], we derive a value of between 4.7 and 9.4 kJ mol^{-1}.] Replacing C(s) by gaseous graphite results in endothermicity of reaction 12 of *ca* 135 kJ mol^{-1}.
19. We choose 'one-half' so that the difference quantity corresponds to the enthalpy difference for one allene unit, where we remind the reader that the difference of the enthalpies of formation of an allene and the corresponding olefin is the same as the enthalpy of the 'formal decarbonization' reaction of the allene that forms the olefin and solid, graphitic carbon.
20. V. A. Luk'yanova, L. P. Timofeeva, M. P. Kozina, V. N. Kirin and A. V. Tarakanova, *Russ. J. Phys. Chem.*, **65**, 439 (1991).

21. We can narrow the difference from 10 kJ mol^{-1} even further once it is remembered that in the comparison of *meso*-bisallene, **27**, and (*Z*, *Z*)-diene, **29**, there are two extra alkylallene and alkylolefin interactions for which a stabilization of *ca* 3 kJ mol^{-1} for the latter was already suggested. Admittedly, comparison with the corresponding 1,5-cyclooctadiyne suggests strain-derived anomalies. From the enthalpy of hydrogenation, and thus derived enthalpy of formation, of this diyne from W. R. Roth, H. Hopf and C. Horn, *Chem. Ber.*, **127**, 1781 (1994), we find 1/2δ (bis-allene, bis-acetylene) equals *ca* $-$ 80 kJ mol^{-1}. We deduce that the discrepancy of this last δ quantity from the others is due to strain in the cyclic diyne.
22. We can return to 'normalcy' by reversing the sign and speaking of 15.7 kJ mol^{-1} as the conjugation energy of butadiene. This seeming ambiguity of sign is very much like that electron affinity. 'Everyone knows' that butadiene enjoys stability over that of two ethylenes. 'Everyone knows' that atomic chlorine wants another electron to form Cl^-. Conjugation energies, like electron affinities, are thus naturally negative. Therefore, since we have but one sign to consider in the current context, it is often ignored.
23. W. R. Roth, H.-W. Lennartz, W. v. E. Doering, W. R. Dolbier, Jr. and J. C. Schmidhauser, *J. Am. Chem. Soc.*, **110**, 1883 (1988).
24. J. F. Liebman, *Struct. Chem.*, **3**, 449 (1992).
25. We admittedly ignore some of the dienes discussed in Reference 23 for which free energies are available. Not knowing entropies and solvent effects precisely, and acknowledging that rather small effects are relevant to the current discussion, we conclude that free energies are not free. More work is needed for the use of Gibbs energies than for enthalpies.
26. See References 12 and 23, and elsewhere in this chapter.
27. W. J. Hehre, R. Ditchfield, L. Radom and J. A. Pople, *J. Am. Chem. Soc.*, **92**, 4796 (1970).
28. We might have thought that α-diketones would have less stabilization by this definition than conjugated dienes. After all:
    (a) with its positive oxygen, the resonance structure $^+O{-}C{=}C{-}O^-$ looks less stabilizing than the one with positive carbon $^+C{-}C{=}C{-}C^-$;
    (b) the carbon oxygen bond in ketones is polarized $C^{\delta+}{-}O^{\delta-}$ and thus there is coulombic repulsion in the diketone;
    (c) to mollify (b) by decreasing the partial positive charge on carbon, the diketone 'enjoys' less ionic/covalent resonance than the monoketone fragments.
    We are surprised.
29. We admit some cowardice. Most of our earlier estimates of entropy invoked symmetry numbers and/or were studies of bond cleavage reactions dominated by translational effects. We hesitate to compare isomers with the same carbon or heavy atom skeleton when effects of a few kJ mol^{-1} are crucial.
30. We are being somewhat disingenuous in that we are taking the difference here of the enthalpy of formation of the 'naturally' liquid (*Z*)-isomer and of the liquid (*E*)-isomer obtained by summing the value for the solid and the *ca* 27 kJ mol^{-1} enthalpy of fusion (at 398 K) from Domalski. We know of no measurement of the enthalpy of fusion for (*Z*)-stilbene at any temperature from which to derive an enthalpy of formation for the solid.
31. Because of its carbene functionality, our decision to consider only the parent hydrocarbons would mean that cyclopropenylidene would be ignored here even if monoolefins were of relevance. This philosophy accounts for our ignoring the energetics of the isomeric carbenes, propargylene (HCCCH) and propenylidene (CH_2CC), in the earlier section on cumulenes in the current chapter.
32. It is interesting to note that there are enthalpy of formation data for solid and gaseous tetra-*t*-butyltetrahedrane, but not for its more stable valence isomer, tetra-*t*-butylcyclobutadiene; cf G. Maier, *Angew. Chem., Int. Ed. Engl.*, **27**, 309 (1988). This review cites unpublished enthalpy of combustion measurements (M. Månsson) and enthalpy of sublimation measurements (C. Rüchardt, H.-D. Beckhaus and B. Dogan). We admit our surprise that details of these measurements remain unpublished.
33. The reader may recall that the enthalpy of formation of a cyclic bis-allene has been determined (see Section III.D).
34. See, for example, the two reviews with enticing compounds by R. P. Johnson:
    (a) in *Molecular Structure and Energetics*: *Studies of Organic Molecules* (Eds. J. F. Liebman and A. Greenberg), VCH, Deerfield Beach, 1986.
    (b) *Chem. Rev.*, **89**, 1111 (1989).

We now make the *a posteriori* 'obvious' suggestion that determinations of enthalpies of hydrogenation be made.

35. This has been quantitated for 1,3-butadiene itself:
(a) M. E. Squillacote, R. S. Sheridan, O. L. Chapman and F. A. L. Anet, *J. Am. Chem. Soc.*, **101**, 3657 (1979).
(b) P. W. Mui and E. Grunwald, *J. Am. Chem. Soc.*, **104**, 6562 (1982).
(c) Y.-P. Sun, D. F. Sears, Jr. and J. Saltiel, *J. Am. Chem. Soc.*, **110**, 6277 (1988).
36. This seeming lack of stabilization is disconcerting when it is noticed that the antisymmetric combination of the two methylene C−H σ bonds is of the right symmetry to 'mix in' with the π system. As such, cyclopentadiene can be said to enjoy the possibility of 6π, and hence aromatic stabilization.
37. P. W. Rabideau (Ed.) *The Conformational Analysis of Cyclohexenes, Cyclohexadienes and Related Hydroaromatic Compounds*, VCH, New York, 1989.
38. G. B. Kistiakowsky, J. R. Ruhoff, H. A. Smith and W. E. Vaughn, *J. Am. Chem. Soc.*, **58**, 146 (1936).
39. R. B. Turner, B. J. Mallon, M. Tichy, W. von E. Doering, W. R. Roth and G. Schröder, *J. Am. Chem. Soc.*, **95**, 8605 (1973).
40. E. Taskinen and K. Nummelin, *J. Org. Chem.*, **50**, 4833 (1985). These authors performed the isomer equilibration at several temperatures and so could use the experimentally derived equilibrium constant to derive the enthalpy of rearrangement. There was no need for assuming the entropy of isomerization is 0 or just determined by symmetry number corrections.
41. Taskinen and Nummelin (op. cit.) reported many other isomer equilibria in their paper. Most of these used cyclohexane as the solvent and I_2 as the catalyst and so are not confounded by solvent effects. However, these authors noted that hydrogen atom transfer induced disproportionation (to form the aromatic benzene) dominates this reaction for the case of **49/50** isomerization and so they needed alternative reaction conditions.
42. (a) W. V. Steele, R. D. Chirico, A. Nguyen, I. A. Hossenlopp and N. K. Smith, *Determination of Some Pure Compound Ideal-Gas Enthalpies of Formation*, NIPER-319, IITRI, Bartlesville, OK, June 1989.
(b) W. V. Steele, R. D. Chirico, A. Nguyen, I. A. Hossenlopp and N. K. Smith, *Am. Inst. Chem. Eng. Symp. Ser.*, **85** (271), 140 (1990).
43. E. Taskinen and K. Nummelin, *Acta Chem. Scand.*, **B39**, 791 (1985).
44. We know of three species containing the bismethylenecyclopropane substructure for which enthalpies of formation are available: the annelated benzocyclopropene and naphtho[*b*]cyclopropene, and the tris-methylene species, [3]-radialene [see J. F. Liebman and A. Greenberg, *Chem. Rev.*, **89**, 1225 (1989)]. However, none of these data seems particularly useful in the current context.
45. R. B. Turner, P. Goebel, B. J. Mallon, W. von E. Doering, J. F. Coburn, Jr. and M. Pomerantz, *J. Am. Chem. Soc.*, **90**, 4315 (1968).
46. W. R. Roth, F.-G. Klärner and H. W. Lennartz, *Chem. Ber.*, **113**, 1818 (1980).
47. To be honest, this self-imposed limitation was also employed because we lack the desired enthalpy of formation of any other type of *exo*, *endo*-cyclic dienes.
48. It is to be remembered that the cyclic diene contains a *cis*-/internal olefinic linkage while the acyclic diene contains a terminal one. Were the carbon skeleton the same, the difference in the enthalpies of hydrogenation of (*Z*)-/internal and terminal olefins should be reflected in the difference of their enthalpies of formation. For the isomeric butenes, the difference is 7.2 kJ mol^{-1} and for the pentenes, the difference is 9.6 kJ mol^{-1}. Furthermore, strictly speaking, the data Pedley gives for the 3-methylenecyclohexene is for the liquid while for the methylcyclohexane we have enthalpies of formation of both the liquid and gas. The following strategies were employed here:
(a) Estimate the enthalpy of formation of vaporization of the diene. This gives an enthalpy of formation of the gaseous diene of 23 kJ mol^{-1} and a hydrogenation enthalpy of 177 kJ mol^{-1}.
(b) Assume the diene and its hydrogenated product have the same enthalpy of vaporization. Equivalently, the enthalpy of hydrogenation of the liquid diene will be the same as that of the gaseous species. This also gives a hydrogenation enthalpy of 177 kJ mol^{-1}.
49. We wish to argue that experimental error is the case. Pedley cites liquid phase enthalpies of formation of -12.7 and -58.7 kJ mol^{-1} for the isomeric 3-methylenecyclohexene and 2-methyl-1,3-cyclohexadiene. The difference of these two numbers, -46 kJ mol^{-1}, is meaningfully

distinct from those of the related species with but one double bond, methylenecyclohexane and 1-methylcyclohexene, -20 kJ mol^{-1}. This is plausible: after all, we have seen unusual ring size effects with the *endo*, *endo* and *exo*, *exo* dienes presented earlier in this section. Consider now the 2-methyl-1,3-cyclohexadiene measurement. Regardless of the precise choice made for the enthalpy of formation of liquid 1,3-cyclohexadiene (cf the earlier discussion of the gas), a value of *ca* 70 kJ mol^{-1} appears plausible. This would imply that methylation affects the enthalpy of formation of a 1,3-cyclohexadiene by some -130 kJ mol^{-1}. The change upon methylation of liquid cyclohexene is -42.7 kJ mol^{-1}, while for liquid benzene the change is -36.6 kJ mol^{-1}. Something is seriously wrong with the archival enthalpy of formation of 2-methyl-1,3-cyclohexadiene, and by inference with the value of 3-methylenecyclohexene as well.

50. D. W. Rogers, F. J. McLafferty, W. Fang and Y. Qi, *Struct. Chem.*, **4**, 161 (1993).
51. D. W. Rogers, F. J. McLafferty, W. Fang, Q. Yang and Y. Zhao, *Struct. Chem.*, **3**, 53 (1992).
52. D. W. Rogers, F. J. McLafferty and K. Channamallu, *Struct. Chem.*, **3**, 291 (1992).
53. The only experimentally thermochemically characterized case we know of is benzene, which while formally valid is admittedly disingenuous.
54. We are not distinguishing between through-space, through-bond, or 'simply' steric mechanisms, nor discussing concepts such as homoantiaromaticity or any other 'prefixed' or 'hyphenated' aromaticity phenomena as explanations for stabilization or destabilization of any of the aforementioned species.
55. J. F. Liebman, L. A. Paquette, J. R. Peterson and D. W. Rogers, *J. Am. Chem. Soc.*, **108**, 8267 (1986).
56. D. W. Rogers, S. A. Loggins, S. D. Samuel, M. A. Finnerty and J. F. Liebman, *Struct. Chem.*, **1**, 481 (1990). Admittedly, the authors did not separate **74** from the isomeric bicyclo[3.3.0]octa-2,6-diene but it is unlikely that these two species are *that* different.
57. D. Kreysig, R. Friere, H. Aparowsky and J. Schirmer, *J. Prakt. Chem.*, **37**, 329 (1968).
58. Had the compound been less stable than we would predict the discrepancy would have been easier to explain. One could argue that the *gem*-dimethyl groups would have resulted in destabilization because of 'buttressing'. It is tempting to argue that the triene was contaminated by 'polymer' and/or peroxide, both of which have lower enthalpies of formation. But we have no documentation of this.
59. D. R. Stull, E. F. Westrum, Jr. and G. C. Sinke, *The Chemical Thermodynamics of Organic Compounds*, Wiley, New York, 1969.
60. M. Kharasch, *Bur. Stands. J. Res.*, **2**, 359 (1929).
61. We used all of the C_{18} hydrocarbons in Pedley and derived their enthalpies of sublimation by subtracting the recommended enthalpies of formation of the solid and the corresponding gaseous species. There was considerable variation in the sublimation enthalpies, as seemingly befits the diverse choice of compounds (and associated crystal packing) including such species as naphthacene, 6,6-diphenylfulvene, 3,4,5,6-tetramethylphenanthrene, [3.3]paracyclophane and *n*-octadecane.
62. See Stein and coworkers cited in Reference 18.
63. While there is some dispute about how universal the 'universal methylene increment' really is (cf Reference 1), it is nonetheless generally conceded that a methylene group affixed to two carbons usually contributes *ca* $-$ 21 kJ mol^{-1} to the gas phase enthalpy of formation.
64. See W. R. Roth, F. G. Klärner, G. Siepert and H. W. Lennartz, *Chem. Ber.*, **125**, 217 (1992) and D. W. Rogers, A. Pododensin and J. F. Liebman, *J. Org. Chem.*, **58**, 2589 (1993) and many references cited therein.
65. Species **88–90** are also recognized to be bicyclo[4.4.1]undecane derivatives.
66. Roth gives two values for the enthalpy of formation of **90**. We adopt the value from his laboratory for our current study.
67. Pedley is the major source of information for all of these 4-carbon bridged benzenes, where we acknowledge that the enthalpy of the gaseous 1,4-dihydronaphthalene was found by combining Pedley's value for the liquid with our estimated enthalpy of vaporization.
68. Our uncertainty is derived in part from the lack of a measured enthalpy of vaporization, cf Reference 67. However, what triggered our skepticism is the observation that the isomeric 1,2-and 1,4-dihydronaphthalenes have reported enthalpies of formation that differ by *ca* 13 kJ mol^{-1} while the corresponding species lacking the benzene ring, the isomeric 1,3- and 1,4-cyclohexadienes, are almost isoenergetic (see Section V.D of this chapter). From J. F. Liebman, in *The Cyclophanes* (Eds. P. M. Keehn and S. M. Rosenfeld), Academic Press, New York, 1983,

we find that benzoannelation normally has a quite constant effect on enthalpies of formation of nonaromatic species. For example, benzoannelation of cyclopentene, cyclopentadiene and cyclohexene are accompanied by increases of *ca* 27, 29 and 31 kJ mol^{-1}, respectively. Taking a value of *ca* 30 kJ mol^{-1} for the increase, we can think of no reason why the enthalpy of formation of either dihydronaphthalene should be outside the 130–140 kJ mol^{-1} range.

69. We recall that Fang and Rogers, op. cit., measured the enthalpy of hydrogenation of the acyclic trienes in a nonpolar solvent instead of acetic acid as earlier reported. However, they did not remeasure the *Z*- and *E*-isomers separately but instead assumed the earlier measured difference is correct. Said differently, they assumed that the effect on the enthalpy difference of the *Z*- and *E*-hexatriene is essentially independent of solvent. This is plausible but remains untested.
70. See, for example, R. S. Hosmane and J. F. Liebman, *Tetrahedron Lett.*, **33**, 2303 (1992). We additionally note that in the absence of any conjugative interaction, the difference of the enthalpies of formation of fulvene (*vide infra*) and benzene would very nearly equal the difference of the enthalpies of formation of methylenecyclopentane and cyclohexene. The former difference is 161 kJ mol^{-1} while the latter difference is but 17 kJ mol^{-1}.
71. The desired enthalpy of formation of fulvene and of its 6-methyl derivative were determined by Roth by measurement of the appropriate enthalpy of hydrogenation. The facile polymerization of this compound precludes conventional bomb calorimetry.
72. The desired enthalpy of formation of 6,6-dimethylfulvene was determined by Roth citing measurement of hydrogenation enthalpies, and chronicled by Pedley citing enthalpies of combustion and vaporization. The two results differ by 7 kJ mol^{-1}. We have opted for Roth's value because it is in better agreement with a value calculated using Roth's force field method. It is also to be noted that measurement cited by Pedley for the neat condensed phase could be flawed by the presence of partially polymerized fulvene and neither elemental abundance of the compound nor analysis of the combustion products would have disclosed this. Likewise, the measured enthalpy of vaporization would not have necessarily uncovered this contaminant.
73. As documented by Pedley, only enthalpies of combustion and sublimation have been reported for 6,6-diphenylfulvene. We recommend the measurement of the enthalpy of hydrogenation to form α-cyclopentyl diphenylmethane to acquire a more precise enthalpy of formation.
74. The author thanks Suzanne W. Slayden for suggesting and doing this statistical analysis, as well as providing the accompanying figures.
75. The number and requisite analysis used to derive it is taken from Liebman and Greenberg (Reference 44).
76. J. F. Liebman and A. Greenberg, in *The Chemistry of the Cyclopropyl Group*, Vol. 1 (Ed. Z. Rappoport), Wiley, Chichester, 1987.
77. R. B. Turner, W. R. Meador, W. von E. Doering, L. H. Knox, J. R. Mayer and D. W. Wiley, *J. Am. Chem. Soc.*, **79**, 4127 (1957).
78. Unlike many of the early hydrogenation studies, this measurement was made in a relatively nonpolar polyether solvent (with the admittedly misleading name 'diethylcarbitol'). Because the solvent is nonpolar, the results for this species are expected to adequately mimic those that would be found in the gaseous phase.
79. This conjugated enone/diene difference is more definitively seen in the 184 kJ mol^{-1} decrease in enthalpy of formation on going from 1-pentene to butanal, in contrast to the 177 kJ mol^{-1} going from (*E*)-1,3-pentadiene to *trans*-crotonaldehyde. For further discussion, see J. F. Liebman and R. M. Pollack, in *The Chemistry of Enones* (Eds. S. Patai and Z. Rappoport), Wiley, Chichester, 1989.
80. J. M. McBride, *Tetrahedron*, **38**, 2009 (1976).
81. H. E. Bent and G. R. Cuthbertson, *J. Am. Chem. Soc.*, **58**, 170 (1936).
82. Admittedly, $Ph_3C{-}CPh_3$ (literally, hexaphenylethane as drawn) has largely uncharacterized features as well. For example, the considerable weakness of the central C–C bond is not paralleled by the 'central' C–C bond in tetraphenylmethane and 1,1,1,2-tetraphenylethane, the sole thermochemically characterized species in which there is a $C{-}(C_B)_3$ (C^*) structural group. [The enthalpy of formation of the latter species is from H.-D. Beckhaus, B. Dogan, J. Schaetzer, S. Hellmann and C. Rüchardt, *Chem. Ber.*, **133**, 137 (1990).]
83. T. Bally, D. Hasselmann and K. Loosen, *Helv. Chim. Acta*, **68**, 345 (1983).
84. J. E. Bartmess, *J. Am. Chem. Soc.*, **104**, 335 (1982).
85. J. E. Bartmess and S. S. Griffith, *J. Am. Chem. Soc.*, **112**, 2931 (1990).

86. This value was obtained by summing the enthalpies of formation of 1,4-pentadiene, ethylene and *ca* 5 kJ mol^{-1} as in References 23 and 24 and by assuming thermoneutrality for the reaction

$$EtCH{=}CH_2 + (Z){-}EtCH{=}CHCH{=}CH_2 \longrightarrow C_3H_8 + \mathbf{137}$$

where the enthalpy of formation of the hexadiene is from Reference 12.
87. See J. F. Liebman cited in Reference 68.
88. R. Sabbah, R. Chastel and M. Laffitte, *Thermochim. Acta*, **10**, 353 (1974).
89. We feel it is about time that we quote the wondrous aphorism 'things are counterintuitive only when you have intuition' (Deborah Van Vechten, personal communication).
90. S. K. Pollack, B. C. Raine and W. J. Hehre, *J. Am. Chem. Soc.*, **103**, 6308 (1981).
91. S. G. Lias, J. E. Bartmess, J. F. Liebman, J. L. Holmes, R. D. Levin and W. G. Mallard, *Gas-Phase Ion and Neutral Thermochemistry*, *J. Phys. Chem. Ref. Data*, **17** (1988), Supplement 1.
92. R. B. Sharma, D. K. S. Sharma, K. Hiroaka and P. Kebarle, *J. Am. Chem. Soc.*, **107**, 3747 (1985).
93. E. P. Hunter, 1996 NIST Proton Affinity Scale, in preparation. We thank Edward Hunter for sharing his numbers with us.
94. We admit that the two isomeric cyclohexadienes have very nearly the same enthalpies of formation. However, it is doubtful that replacement of $>CH_2$ by $>C{=}CH_2$ is without significant steric and electronic consequences. The latter group is larger and both [intermethylene C−H] and [(1,4)-π-electron] antibonding derived repulsion suggests destabilization arising from vicinal $>C{=}CH_2$ groups. We thus expect *o*-xylylene to be significantly less stable than its *p*-isomer. We wonder if these two C_8H_8 species found with nearly the same enthalpy of formation are really the same compound, although it appears unlikely that it be either styrene or heptafulvene.
95. We naturally exclude here the cyclopropenyl, cyclopentadienyl and cycloheptatrienyl radicals, all of which can also be recognized as cyclic C_nH_n species much as we did not include in our discussion the enthalpies of formation of allyl and pentadienyl radical as part of our analysis of polyenes such as butadiene and hexatriene.
96. A. E. Beezer, C. T. Mortimer, H. D. Springall, F. Sondheimer and R. Wolovsky, *J. Chem. Soc.*, 216 (1965).
97. J. F. M. Oth, J.-C. Bünzli and Y. de Julien de Zélicourt, *Helv. Chim. Acta*, **58**, 2276 (1974).
98. We suspect fewer problems would have arisen had Oth and coworkers (see Reference 97) decided to perform enthalpy of hydrogenation measurements on [18]annulene. Nonetheless, we note that Oth's suggested value for the enthalpy of formation of benzo-1,3,5-cyclooctatriene is within 2 kJ mol^{-1} of that estimated summing Roth's enthalpy of formation of 1,3,5-cyclooctatriene and Liebman's (cited in Reference 68) benzoannelation constant.
99. (a) R. Breslow and E. Mohachsi, *J. Am. Chem. Soc.*, **85**, 431 (1963).
(b) A. L. H. Chung and M. J. S. Dewar, *J. Chem. Phys.*, **42**, 756 (1965).
100. We admit to being somewhat sloppy because we are not distinguishing between (*Z*)- and (*E*)-polyene subunits. However, the reader will recall from Section VI.A that in Reference 23 it was shown that the difference in enthalpies of formation of (*Z*)- and (*E*)-1,3,5-hexatriene was *ca* 4 kJ mol^{-1}.
101. Benzene remains 'safely' aromatic by this definition. After all, its enthalpy of formation is 82.6 kJ mol^{-1} while that of the reference acyclic species is 167.5 kJ mol^{-1}, considerably higher.
102. In our own notes, we find that we have occasionally written the −CH=CH− group as <−CH=CH−> and where the < and > indicate it was a single bond that was deleted or 'X'd' out in the generation of the group. In a related way, =CH−CH=, $-CH_2-$ and $CH_2{=}$ are written <=CH−CH=>, $<-CH_2->$ and $CH_2{=}>$; Mahnaz Motevalli-Oliner and Joel F. Liebman, hitherto unpublished symbolism.
103. Benzene remains 'safely' aromatic by this definition as well. After all, its enthalpy of formation is 82.6 kJ mol^{-1} while that of the 'real' 1,3,5-hexatriene, the reference acyclic species, is 165.1 kJ mol^{-1}, considerably higher.
104. This is by analogy to cyclopentane, cyclopentene and methylenecyclopentane, all from References 17 by Greenberg and Liebman.
105. We have summed the enthalpy of formation of five ethylenes for the five formal double bonds and 6(5) for the six formal single bonds by analogy to our discussion of [18]annulene.

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CHAPTER **4**

Conformation and chiroptical properties of dienes and polyenes

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I. INTRODUCTION

Circular dichroism (CD) spectroscopy (and the nowadays less used optical rotatory dispersion, ORD) is a well-recognized and powerful tool for the stereochemical investigation of chiral molecules[1]. When dealing with the vast class of dienes and polyenes and their derivatives, it is essential to refer to a specific arrangement of the double bonds. Cumulated systems have been thoroughly reviewed in 1980 by Runge for this same series[2]. Double bonds separated by two or more carbon–carbon single bonds can be successfully described in terms of additive effects arising from the individual olefinic chromophores. In contrast, a conjugated system must be treated as a single chromophore. We shall limit the present discussion to alternating dienes and polyenes only.

A distorted conjugated pair of double bonds is an intrinsically chiral chromophoric system, and its overall chiroptical properties depend on the reduced symmetry of the chromophore itself as well as on the perturbing action of a dissymmetric environment.

The aim of the present chapter is to discuss in some detail the mechanisms giving rise to optical activity in these molecules and to examine the main rules formulated for correlating structure and CD, critically analysing their use and limitations with suitable examples. Further information can be found in the original literature and in two recent review articles, by Gawroński and Walborsky[3] and by Buchecker and Noack[4], covering the diene and polyene (limited to carotenoids) fields, respectively.

II. CONJUGATED DIENES

A. Diene Conformations

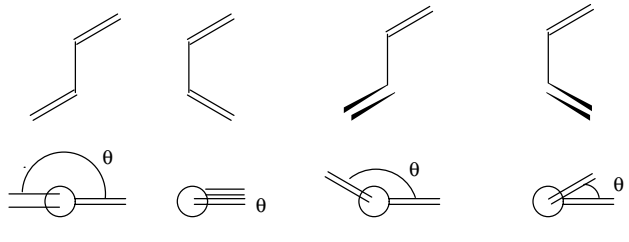
1,3-dienes can exist in two limiting planar conformations defined as *s-trans* and *s-cis* with respect to the single bond C_2-C_3 and in non-planar skewed form, often called *cisoid* or *transoid*, with reference to the nearer planar form. The dihedral angle θ describes this internal degree of freedom, as depicted in Scheme 1.

We shall conventionally define as positive the clockwise rotations from the double bond nearer to the observer to the one farther away.

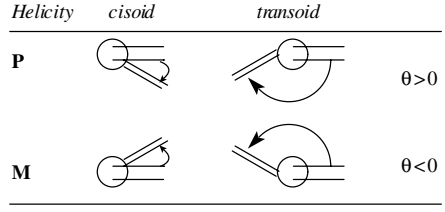
As shown in Scheme 2, positive angles define P-helicity while negative θ values define M-helicity.

B. Electronic Absorption Features of the Diene Chromophore

We give here only a brief summary of the electronic absorption spectrum of the diene chromophore which has been extensively treated by Gross and Schnepp[5] with reference to α- and β-phellandrene.



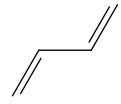
SCHEME 1



SCHEME 2

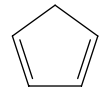
The possibility of delocalization of the π electrons of the diene system across the formally σ bond between carbon atoms 2 and 3 forces the molecule to be planar, thus we have two limiting conformations[6]:

(1) The planar *s-trans* (e.g. 1,3-butadiene).



This is the most populated form of 1,3-butadiene, which at room temperature is present in about 99% abundance[5,6]. The characteristic absorption feature of this chromophore is the intense band at about 210 nm showing ε_{max} larger than 20000. It has been unanimously[6] assigned to the $\pi_- \rightarrow \pi^*_-$ ($^1A_g \rightarrow {}^1B_u$) transition of the C_{2h} chromophore (see Appendix, Section V).

(2) The *s-cis* conformation (e.g. cyclopentadiene).



In this molecule the diene moiety assumes the C_{2v} symmetry and the prominent feature of its near-UV absorption spectrum is the 240 nm band (ε_{max} 3500), assigned[6] to the same transition $\pi_- \rightarrow \pi^*_-$, now characterized by $^1A_1 \rightarrow {}^1B_2$ symmetry in the C_{2v} point group (see Appendix, Section V).

Actually, as demonstrated by Gross and Schnepp[5], both the *s-cis* and the *s-trans* chromophores possess many other electronic transitions down to 140 nm. However, the near-UV part of the spectrum has been the most studied and only the lowest energy transition has been used as a structural probe to solve conformational and configurational

problems. The present work will therefore be limited to the discussion of this band alone.

Both theoretical calculations and experimental investigations[6] on model compounds indicate that the wavelength of the $\pi_- \rightarrow \pi^*_-$ (also indicated as $N \rightarrow V_1$) transition is longest (around 250 nm) in the *s-cis* conformation, reaches a minimum for skewed forms (190 nm when $\theta \approx 90°$), where conjugation is inhibited, and again increases (to 220 nm) for the *s-trans* structure. The oscillator strength, f, is highest in the *s-trans* and becomes much smaller in the *s-cis* and skewed conformations[7].

Increasing the number of conjugated double bonds leads to a marked bathochromic shift and to a hyperchromic effect, as predicted by Woodward's and Fieser's rules[8].

C. Chiral Dienes and the Origin of Optical Activity

The planar C_{2h} and C_{2v} geometries of the 1,3-butadiene moiety are achiral structures and obviously they cannot show optical activity (i.e. ORD and CD). This has, of course, a spectroscopic origin. The optical activity of a transition $\Psi_0 \rightarrow \Psi_i$ is determined by its Rotational Strength (R)[1] defined as the scalar product

$$R = \mathrm{Im}\{\boldsymbol{\mu}_{0i} \cdot \mathbf{m}_{0i}\} = \mathrm{Im}\{\langle\psi_0|\mu|\psi_i\rangle \cdot \langle\psi_i|\mathbf{m}|\psi_0\rangle\} \tag{1}$$

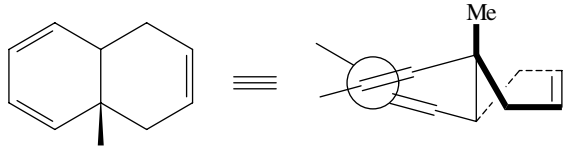
where $\boldsymbol{\mu}$ and $\mathbf{m}$ are the electric and magnetic dipole operators, respectively.

As shown in the Appendix (in Section V), in the C_{2h} point group, the $^1A_g \rightarrow {}^1B_u$ (i.e. the monoelectronic $\pi_- \rightarrow \pi^*_-$ excitation) possesses only an electric dipole moment, while in the C_{2v} structure the electric and magnetic dipole moments, both non-vanishing, are orthogonal. In both cases the product in equation 1 leads to zero rotational strength.

Optical activity can arise only on reducing the molecular symmetry. This can be achieved in the following three ways.

1. Static distortion of the chromophore

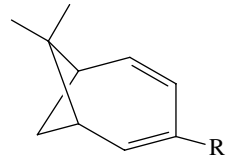
In the tetrahydronaphthalene derivative **1**, whose ORD spectrum is shown in Figure 1, the two conjugated double bonds are not coplanar[9] and define a twist angle of about 17°. The point group is now C_2 and the lowest $\pi \rightarrow \pi^*$ transition is $^1A \rightarrow {}^1B$, which is both electrically and magnetically allowed. The two moments are collinear and the transition acquires a non-vanishing rotational strength. This distortion, caused by a chemical constraint (e.g. the cycle in **1**), is present in the molecule in its equilibrium configuration and can therefore be defined as *static*.



(1)

2. Dynamic distortion of the chromophore

In molecules like **2**, or **3**, the 1,3-diene chromophore is planar. Formally, the presence of R differentiates the two vertical halves of the molecule, which becomes chiral[10]. The physical meaning of this differentiation is that it induces dissymmetric vibrations, which determine, in turn, a *dynamic* twist of the chromophore.



(2) R = Me
(3) R = D

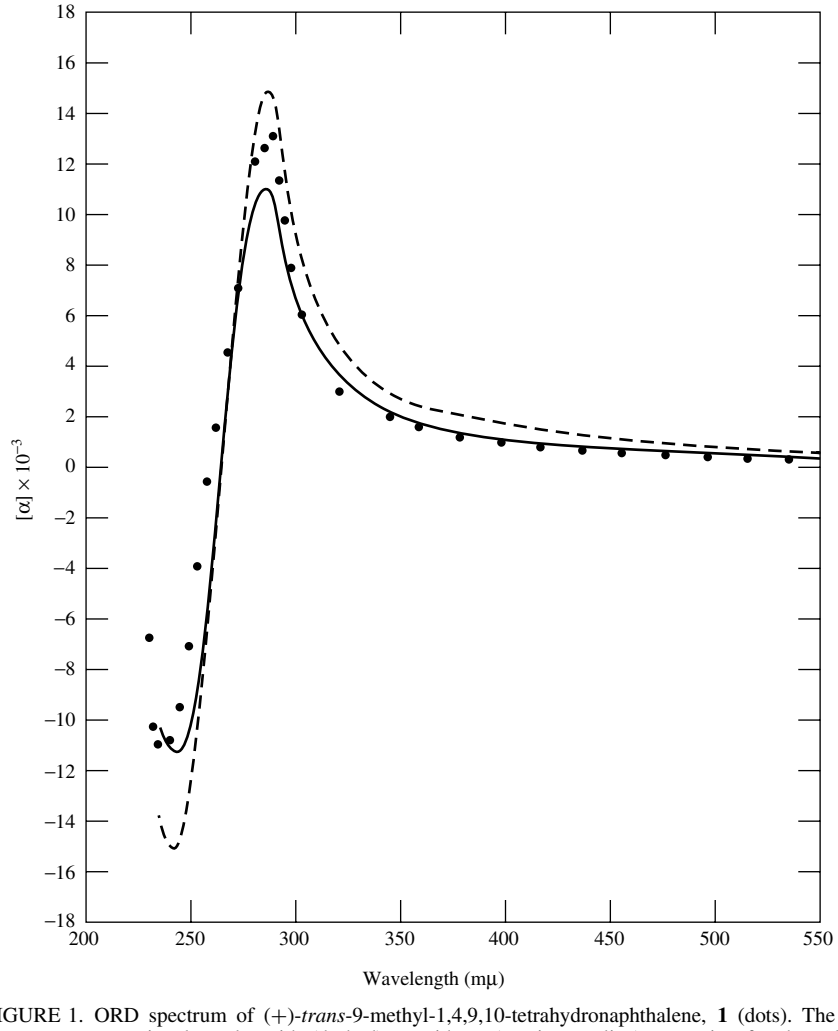


FIGURE 1. ORD spectrum of (+)-*trans*-9-methyl-1,4,9,10-tetrahydronaphthalene, **1** (dots). The two lines are computational results with (dashed) or without (continuous line) correction for the solvent refractive index. Reprinted with permission from Reference 9. Copyright 1961 American Chemical Society

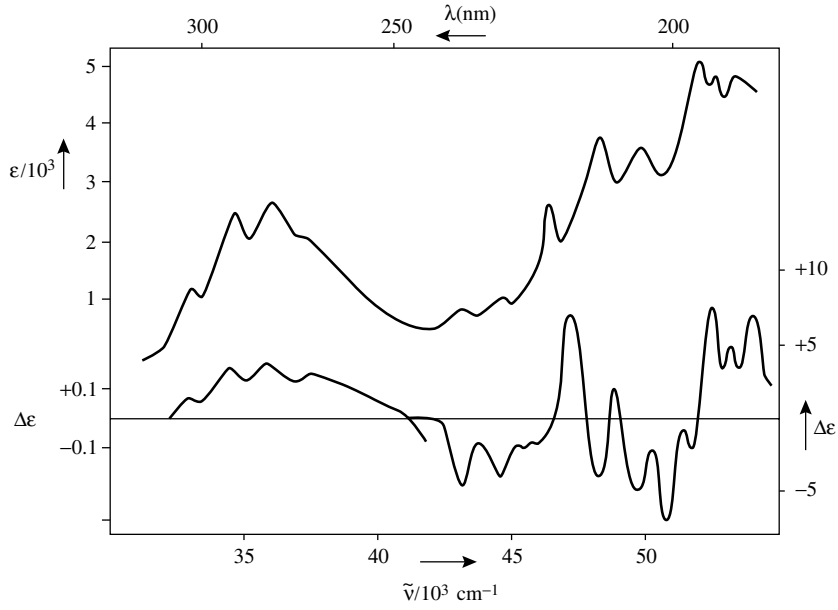


FIGURE 2. UV (upper curve) and CD (lower curve) spectra of **2**. Reprinted with permission from Reference 10. Copyright 1983 American Chemical Society

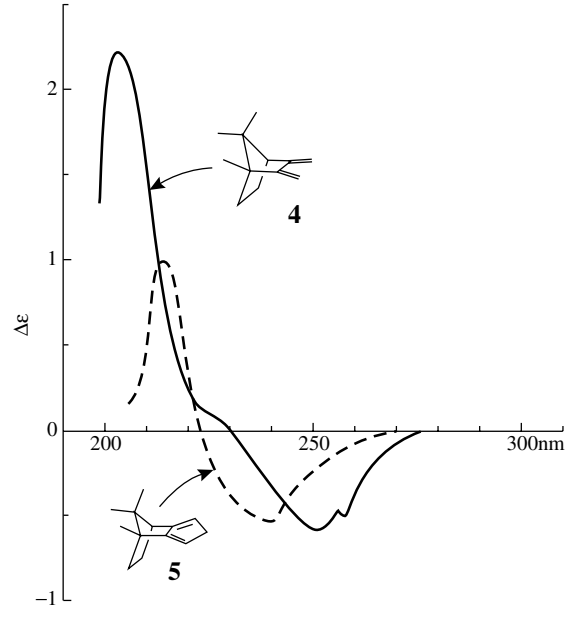
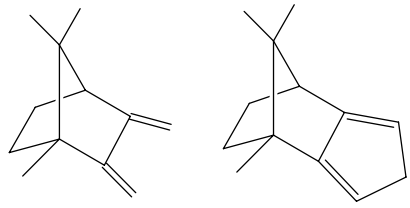


FIGURE 3. CD spectra of compounds **4** and **5**. Reprinted from Reference 11, with kind permission from Elsevier Science Ltd, The Boulevard, Langford Lane, Kidlington 0X5 1 GB, UK

The UV and CD spectra of **2** are reported in Figure 2.

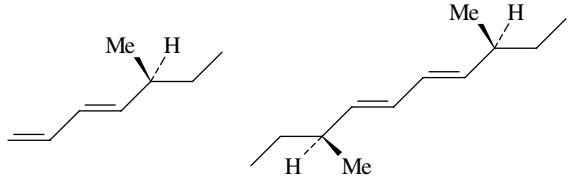
3. External dissymmetric perturbation

In **4** and **5** the chromophore is planar and the optical activity arises from the lack of a vertical symmetry plane (i.e. that bisecting the diene moiety), owing to the presence of the C_1-CH_3 bond, which has no counterpart in the other half of the molecule[11].



(4) **(5)**

Furthermore, whenever the 1,3-diene group is not embedded in a rigid structure, e.g. in **6**[12] and **7**[13], it assumes the most stable *s-trans* conformation, just as in the case of 1,3-butadiene. Again dissymmetrically disposed substituents perturb the $\pi \rightarrow \pi^*$ transition, which acquires some magnetic moment parallel to the electric one.



(6) **(7)**

Figure 3 shows the CD spectrum of **4** and **5**, while Figure 4 reports absorption and CD spectra of **7**.

D. Intrinsically Chiral Dienes

As discussed above, the distortion of the 1,3-diene determines the lowering of symmetry of the chromophore from C_{2v} to C_2. The low-energy $\pi \rightarrow \pi^*$ transition thus acquires non-vanishing rotational strength and becomes optically active[1,14]. The methods proposed for interpreting the CD of intrinsically chiral dienes tend to attribute the most relevant role either to the distortion of the chromophore or to the perturbation arising from its environment. The two effects add up, sometimes acting in the same sense, sometimes conflicting. This makes it rather difficult to find a definite, general and simple relation between stereochemistry and optical activity for these compounds.

1. The diene chirality rule

The first correlation between the sign of the CD band allied to the $^1A \rightarrow {}^1B$ transition and the molecular chirality was formulated just taking into account the lowering of symmetry of distorted dienes only[9,15].

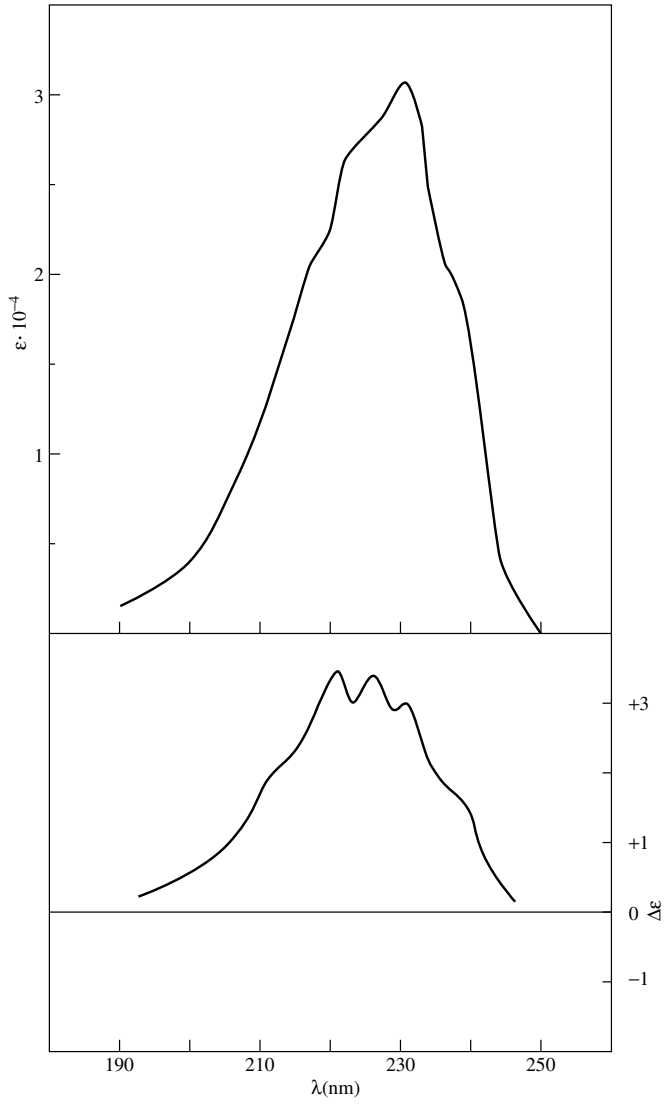
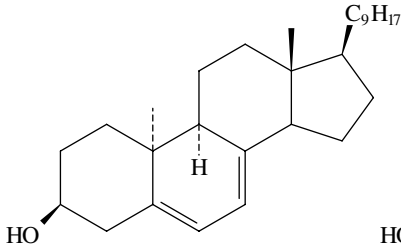


FIGURE 4. UV (upper curve) and CD (lower curve) spectra of **7** (continuous line). Reprinted from Reference 13, with kind permission from Elsevier Science Ltd, The Boulevard, Langford Lane, Kidlington OX5 1 GB, UK

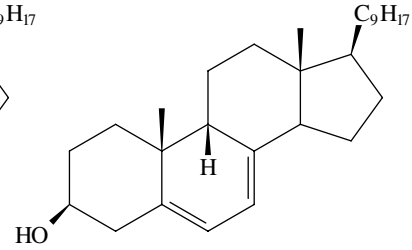
The diene chirality rule (hereafter referred to as DR) constitutes a simple tool for correlating the sign of the lowest energy $\pi \rightarrow \pi^*$ transition ($^1A \rightarrow {}^1B$ in C_2 symmetry) of the distorted diene to the chirality (left or right-handed) of the chromophore. The validity of this rule is based on the assumption that the CD of the distorted chromophore is determined by its intrinsic helicity alone and that external dissymmetric perturbations have only minor effects on the optical activity.

This point of view finds its justification in the following observations. Compounds **8** (pyrocalciferol) and **9** (isopyrocalciferol), having *opposite* absolute configurations of the stereogenic centres near the dienes, show $^1A \rightarrow {}^1B$ Cotton effects at about 275 nm of the *same* sign and intensity. The reason for this is that only the twist of the chromophore determines the optical activity; in fact the diene moieties are distorted in the same sense in **8** and **9**, as found by X-ray diffraction[16].



(8)

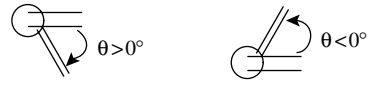
$\Delta\varepsilon = +20$ (275 nm)



(9)

$\Delta\varepsilon = +23$ (272 nm)

The correlation shown in Scheme 3 has been formulated between the sense of twist and the sign of the $^1A \rightarrow {}^1B$ Cotton effect.

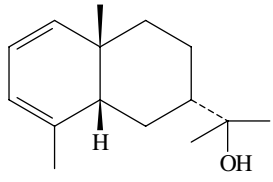


P chirality
positive Cotton effect

M chirality
negative Cotton effect

SCHEME 3

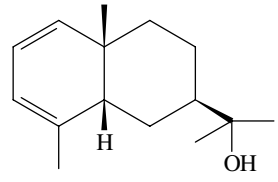
The diene rule has had much importance in the interpretation of the optical activity of distorted dienes, as in the case of occidentalol, *epi*-occidentalol and *trans*-occidentalol, **10**, **11** and **12**, respectively[17].



(10)

$\Delta\varepsilon = -2.2$

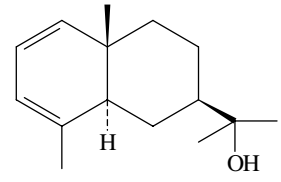
M



(11)

$\Delta\varepsilon = +8.4$

P



(12)

$\Delta\varepsilon = -6.4$

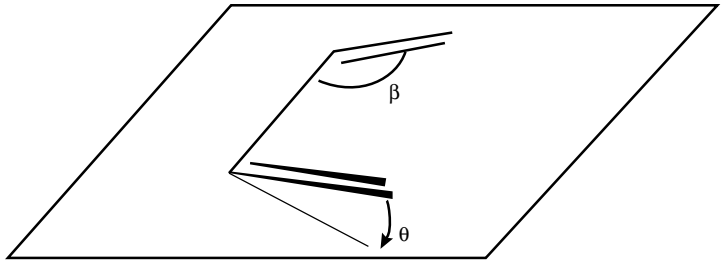
M

It has been successfully based on various calculations at different degrees of sophistication[7,18–26].

a. Theoretical models justifying the diene rule. The rotational strength (R) allied to the longest-wavelength $\pi \rightarrow \pi^*$ transition in twisted butadiene can be calculated according to two simple models: the former uses a molecular orbital approach[1a,1c,22], the latter treats the diene as a pair of interacting double bonds, in a coupled-oscillator framework[14]. A schematic derivation of the relevant equations is given in the Appendix (Section V). It is interesting to note that these totally independent approaches yield the same result:

$$R_{\pi_-\pi^*_-} \propto \sin^2 \beta \sin \theta \tag{2}$$

according to the definition of the internal angles given in Scheme 4.



SCHEME 4

This means that R is proportional to the sine of the dihedral angle between the two double bonds, with the positive sense defined in Scheme 2. Such a dependence confirms the diene rule because positive angles define positive helicity and imply positive R.

We note that this result is confirmed by the derivation of the rotational strength for a general C_2 chromophore, due to Hug and Wagnière[27]. They showed, using a pure symmetry token, that the longer-wavelength B transition follows the DR, whereas the higher-energy A transition has opposite sign. This will be shown to have relevant consequences in the case of carotenoids.

The $\sin\theta$ proportionality of $R_{\pi_-\pi^*_-}$ obtained here with two independent, however simplistic, approaches allows us to extend the DR, originally formulated for the cisoid dienes, even to the transoid chromophores, as shown in Scheme 5.

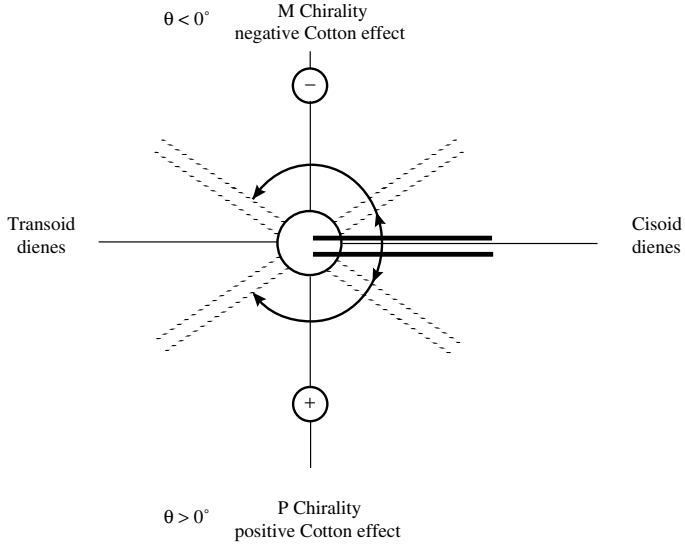
Actually, it is very important to note that this 'general diene rule', covering *s-cis* and *s-trans* systems, has been formulated on the basis of a coupled oscillator model and by means of a simple Hückel MO calculation. More sophisticated MO treatments of the 1,3-butadiene moiety afford contrasting results: while the largest part of the calculations gives positive rotational strengths for all the positive values of θ, in some cases (e.g. CNDO/S[23] and CNDO/2 calculations[23,28]) anti-DR behaviours (negative R for positive θ) have been reported. The accuracy of the wavefunctions obtained for twist angles around 90° is however questionable, which suggests that reliable results are only for $0^\circ < \theta < 45^\circ$ and $135^\circ < \theta < 180^\circ$[29].

The problem of interpreting the chiroptical properties of highly distorted dienes remains, however, a different question (see Section II.D.3 below).

2. Allylic axial chirality rule

About 10 years after the first formulation of DR and 5 years after its theoretical justification by Charney, some contradictory results emerged which make its validity questionable.

One of the major problems was the case of the *cisoid* heteroannular dienes[30,31], which present a CD band at about 240 nm with a sign opposite to that predicted on the basis of the diene helicity by means of the DR.



SCHEME 5

To account for these cases as well, Burgstahler and Barkhurst developed[30] an alternative model for the interpretation of the diene $^1A \rightarrow {}^1B$ transition optical activity, focusing their attention on the surroundings of the chromophore. They stated that: '... asymmetric perturbations of the double bond components of the chromophore through excited states interactions with their allylic axial or pseudoaxial bonds (act) as primary factors controlling the sign of the Cotton effect.' This sign should be predictable through analysis of the contributions of the allylic substituents, with the rule (henceforth called AAR) depicted in Figure 5.

With this approach, it is possible to justify the behaviour of a series of compounds, with particular reference to heteroannular *cisoid* dienes, as shown in Figure 6, which exhibit an anti-DR Cotton effect.

Hence, assuming that the axial allylic contribution outweighs that due to the internal twist, the 'anomalous' behaviour of *s-cis* heteroannular dienes is explained.

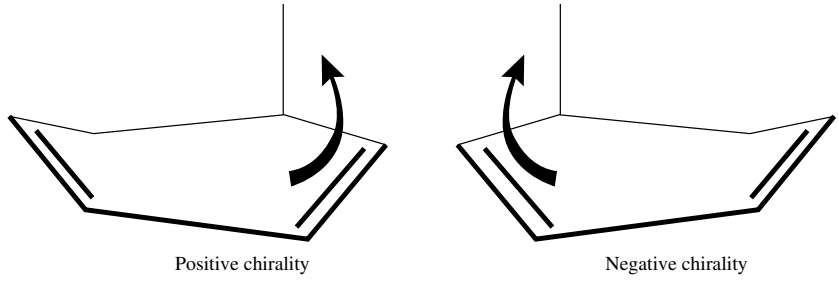
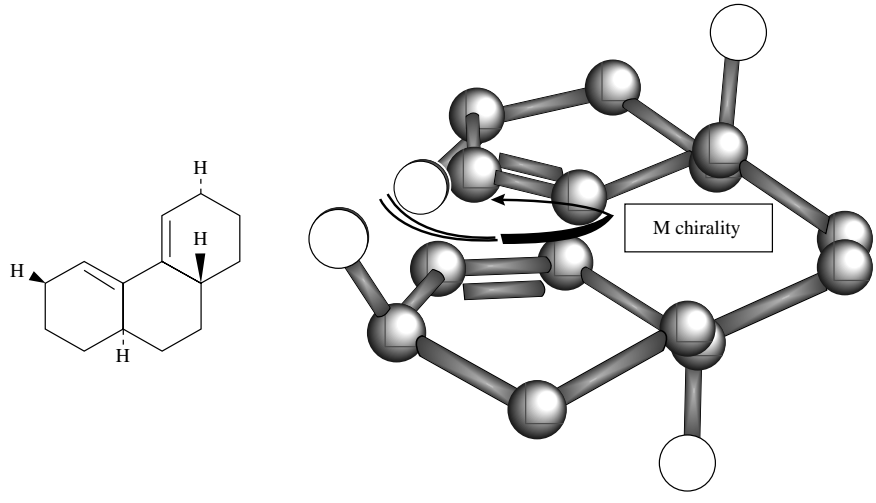


FIGURE 5. On a cyclohexadiene ring, one allylic axial bond has been put in evidence. On the left, it defines a *positive chirality* (right-handed). The reverse holds for the case on the right. This representation is discussed in Section II.D.2.b



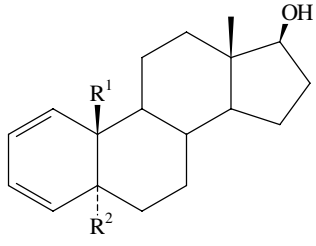
(a) (b)

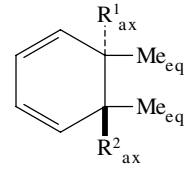
FIGURE 6. A model for heteroannular dienes. In (b) the three-dimensional structure of the molecule shown in (a) is given as an example. The figure indicates that a negative distortion of the conjugated system is allied to a distribution of pseudoaxial substituents (white balls) defining *positive* chiralities according to Figure 5, i.e. positive contributions to the rotational strength of the system

However, an important difficulty is still present: in fact, while for heteroannular *cisoid* dienes the allylic axial contributions are *opposite* in sign to the intrinsic, as depicted in Figure 6, in the case of the homoannular *cisoid* compounds, the two contributions have the same sign, as pointed out already by Burgstahler.

Bearing this in mind, however, it is not possible to interpret the three cases of **13–15**, all characterized by negative diene chirality. If diene chirality and allylic axial contributions act in the same sense, how can we explain a positive $\Delta\varepsilon$ for **15**, having M chirality? This question opens the problem of a more thorough evaluation of all the contributions to the diene optical activity.

The relative importance of the intrinsic (twist-related) and external contributions (e.g. stemming from the axial allylic groups) was evaluated for the first time by Rosenfield and Charney[23] who carried out CNDO/S calculations on the model compounds **16–18**.



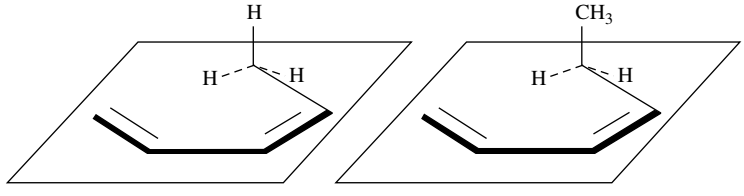


(13) $R^1 = R^2 = Me$ $\Delta\varepsilon < 0$
(14) $R^1 = H; R^2 = Me$ $\Delta\varepsilon < 0$
(15) $R^1 = R^2 = H$ $\Delta\varepsilon > 0$

(16) $R^1 = R^2 = Me$
(17) $R^1 = H; R^2 = Me$
(18) $R^1 = R^2 = H$

These molecules are used as models for the steroidal dienes **13**, **14** and **15**. The aim was to clarify the reasons why **15** does not follow the expectations of the DR and the AAR. Geometrical input parameters were taken from X-ray data of a related steroid which represents an exception to the DR. The skew angle for this geometry is 14.4°. The CNDO/S (without CI) calculations successfully predicted the signs and the absolute values of the different rotational strengths. An attempt to rationalize the physical reason of the sign change on passing from **16** and **17** to **18** (and correspondingly from **13** and **14** to **15** for the real compounds) was also made, as summarized below.

In a planar *s-cis*-butadiene the lowest lying $\pi \rightarrow \pi^*$ excited state belongs to a B_2 representation and the related transition from the ground state possesses orthogonal electric and magnetic dipole moments, along y and x directions, respectively. In a chiral *cisoid* diene, R arises from a 'borrowed' magnetic dipole transition moment in the x direction and a 'borrowed' electric moment along y. In these calculations the x and y components of the $\boldsymbol{\mu}\cdot\mathbf{m}$ scalar product are of comparable magnitudes and, in the model compounds **16**, **17** and **18**, they have opposite signs. Replacing an allylic axial hydrogen by a methyl, the x component of the dipole velocity operator $\langle\pi|\nabla_x|\pi^*\rangle$ increases and becomes dominant over the y component. This causes the change in sign of R. As this effect arises from an *induced* electric moment, it can be ascribed to the larger polarizability of the C−C compared to the C−H bond. Another important aspect of this investigation is a quantitative evaluation of the allylic axial effect. Calculations were carried out on a *planar* butadiene, bearing either a hydrogen, **I**, or a methyl, **II**, in pseudoaxial position.



(I) **(II)**

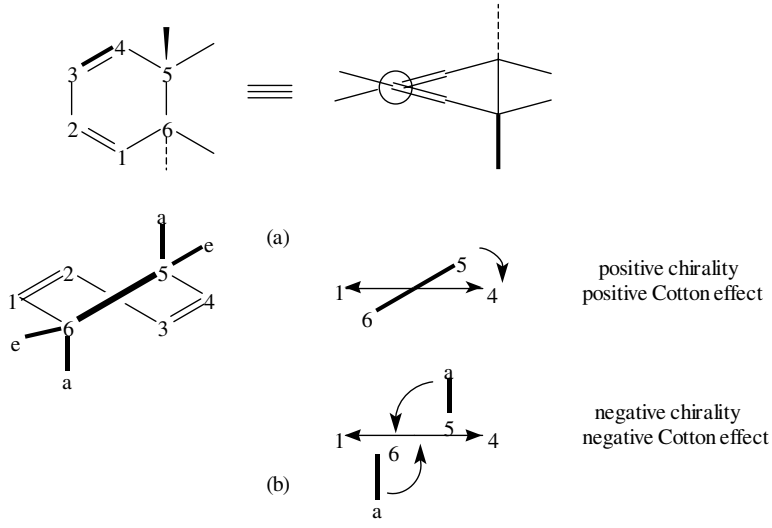
The rotational strength calculated for **I** is as large as that of a butadiene twisted by 20°. In **II**, with an out-of-plane methyl, R increases by a factor of about 2. This shows that the contributions to R of dissymmetric substituents of chiral *cisoid* dienes may be comparable to and even outweigh the contributions arising from the intrinsic dissymmetry of the chromophore.

a. Models in support of the allylic axial chirality rule. Several approaches have been followed to justify the AAR; the most recent, due to Nishio and collaborators, involves CH/π interactions between the *homoallylic* substituents and the π orbital[32]. It should be observed that it can be considered in support of the AAR only insofar as in many geometries a substituent in *allylic* relation to a double bond is *homoallylic* to the other. Furthermore, it does not account for non-alkylic substituents, whose effect has been demonstrated.

We shall consider here in more detail two models: first a dynamic coupling approach, due to Weigang[33], who considered optical activity deriving from the coupling of electric dipoles (the diene chromophore and the polarizable bonds around it); and second, a localized orbital investigation, which permits one to separate the contributions from the intrinsic diene optical activity and from the axial substituents.

We have tried to express the results of Weigang's treatment in pictorial form (Scheme 6), applying the language of the exciton chirality rules[1d] to the coupling of the chromophore transition dipole moments with those induced in the nearby bonds. These are regarded

as strongly anisotropic polarizable units, i.e. we assume that the C−C bonds can be described using only a dipole directed along the bond. A substituted cyclohexadiene having M intrinsic chirality has been considered.



SCHEME 6

Inspection of Scheme 6 reveals that:

(a) The dipole of the diene $^1A \rightarrow {}^1B$ transition at 260 nm (polarized along C_1-C_4) and the polarizable C_5-C_6 bond define a positive chirality and thus give rise to a positive contribution to CD, as shown in Scheme 6(a). This effect is *opposite* to the intrinsic (dissignate[34]) contribution.

(b) Two polarizable allylic bonds oriented as shown in Scheme 6(b) define negative chirality with respect to the diene chromophore, so when they couple with the diene transition dipole, they provide a contribution having the same sign as the intrinsic one (consignate[34] contribution).

(c) The allylic equatorial bonds give only negligible contributions, since they are almost parallel to the diene transition dipole.

This approach has the merit of providing a reasonably simple explanation of the signs of the different contributions, and also makes it clear that the observed optical activity arises from a balance of several factors. In order to make reliable predictions, it would be necessary to assess quantitatively with the same technique all the contributions, whilst Weigang's approach can only give an evaluation of the external perturbations.

The problem of the quantitative and homogeneous evaluation of the contributions to the CD intensity in a complex diene (i.e. intrinsic chirality, allylic substituents and other perturbers) has been approached by Lightner and coworkers[26], from a completely different standpoint: *ab initio* calculations in the localized random-phase approximation (LORPA) for twisted butadiene and several methyl-substituted 1,3-cyclohexadienes — all compounds distorted with P-chirality and a twist angle of 17°. The use of localized orbitals makes it possible to attribute to each group a signed contribution to the total calculated rotational strength for the $^1A \rightarrow {}^1B$ transition. The results are summarized in Table 1 and lend themselves to the following observations:

TABLE 1. Bond contributions (estimated by LORPA[26]) to the Cotton effect of the $\pi_- \rightarrow \pi^*_-$ transition in substituted 1,3-cyclohexadiene[a]

Contribution	[R]	
Diene	−13	
Bond (5,6)	−52	
	if R = H	if R = CH_3
Bond (5,a)	+60	+97
Bond (5,e)	−3.5	−13.5

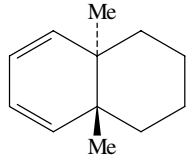
[a]The numbering is that of Scheme 6; R is the substituent occupying the positions a or e.

(a) The intrinsic diene contribution, which is calculated positive (i.e. following the DR) for 1,3-butadiene, becomes negative (anti-DR) in cyclic systems.

(b) The bond *opposite* to the diene gives a large anti-DR contribution.

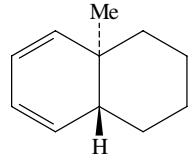
(c) Allylic axial C−H bonds give smaller contributions than C−C, but both are pro-DR.These conclusions agree with those previously indicated and possibly solve the problem of how to predict the rotational strength, at least for homoannular *cisoid* dienes. In fact, using the values reported in Table 1, Lightner and coworkers calculated *R* for some alkyl substituted 1,3-cyclohexadienes, like **19** and **20**, all with P-chirality, in substantial agreement with the experiments.

In spite of these successes, however, the problem is still open because, using the same group contributions, the wrong sign is calculated for **21**, as already observed by Lightner and coworkers[26]. Apparently, even such sophisticated calculations cannot give the correct weight to single contributions, over- or underestimating some of them, which makes it impossible to make the right assessment in all cases.



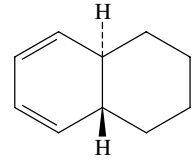
(19)

$R_{exp} = +45$
$R_{calc} = +102$



(20)

$R_{exp} = +40$
$R_{calc} = +65$



(21)

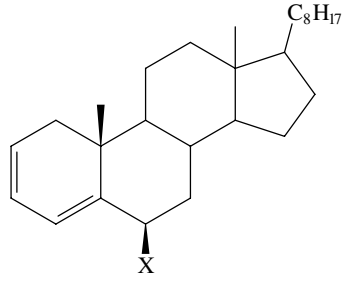
$R_{exp} = -16$
$R_{calc} = +28$

b. Problems in the definition of the allylic axial rule. In the original formulation of the allylic axial rule by Burgstahler and Barkhurst[30], the contribution of a substituent to the diene CD is due to the 'asymmetric perturbations of the double bond components', i.e. the helicity of the system is defined according to the relative disposition of the perturber and the nearest double bond.

On the other hand, from a spectroscopic point of view it is more correct to consider the diene moiety as a whole. Therefore, it seems that the allylic contribution can be evaluated using two different points of view: the 'olefin-picture' (the former) and the 'diene-picture' (the latter). This difference has important consequences. In fact, in a vast majority of cases these two pictures lead to the same result, whilst in some instances the two predictions can be opposite. Let us consider the three possible different geometries of

allylic axial substitution, as indicated in Figure 7, where, for each case, the olefin-picture is put above and the diene-picture below. In Figure 7(a) the molecular geometry is such that the two points of view provide the same result: positive allylic helicity and positive CD is predicted. In Figure 7(b) and (c), on the contrary, the olefin-picture should lead to a negative CD, the diene-picture to a positive CD.

Gawrońsky and Gawrońska[35] observed this ambiguity and studied the case represented in Figure 7(b), analysing the following compounds, all characterized by P diene helicity.



X	Δε	λ
H	+12.6	(265)
OH	+17.5	(264)
NHAc	+26.3	(264)

It is apparent that on increasing the polarizability of the allylic axial substituent, the Cotton effect becomes stronger. If we refer to the nearest double bond, however, the chirality defined by the C−X bond is *negative*, thus we should expect a *decrease* of $\Delta\varepsilon$. Only by considering the diene as a whole (diene-picture), as depicted in the lower part of Figure 7(b), can one justify the reported trend.

Another, very notable, case where the two definitions are in conflict is that of heteroannular *cisoid* dienes. As we have mentioned, this was just the class of molecules that stimulated the introduction of the AAR. Here, in order to have the correct results one should refer the chirality of the axial substituent to the individual double bonds (olefin-picture), as depicted in Figure 6 and in the upper parts of Figure 7(b) and (c). The case of heteroannular dienes is anyway peculiar, because in these compounds the chromophore is unusually distorted. This case is treated in the following section.

3. Strongly distorted dienes

We can collect here two classes of molecules, characterized by very large skew angles, between 40° and 90°. Such a situation is found in the first instance in heteroannular dienes.

a. Heteroannular s-cis-dienes. These compounds (e.g. **22** and **23**) are usually reported to have skew angles around 40–50°.

As anticipated in Section II.D.2, for these molecules anti-DR optical activity is generally found, in agreement with the 'olefin-picture' of AAR. Charney and coworkers[36] proposed an inverse rule: the inversion of sign was attributed to some change in the electronic properties of the diene when the angle θ becomes large. Indeed, as pointed out at the end of Section II.D.1, there is no general agreement within the computational results, neither on the magnitude nor on the sign of the Cotton effect allied to the longest π–π^* transition of dienes with skew angles larger than 40°. Furthermore, the strong distortion

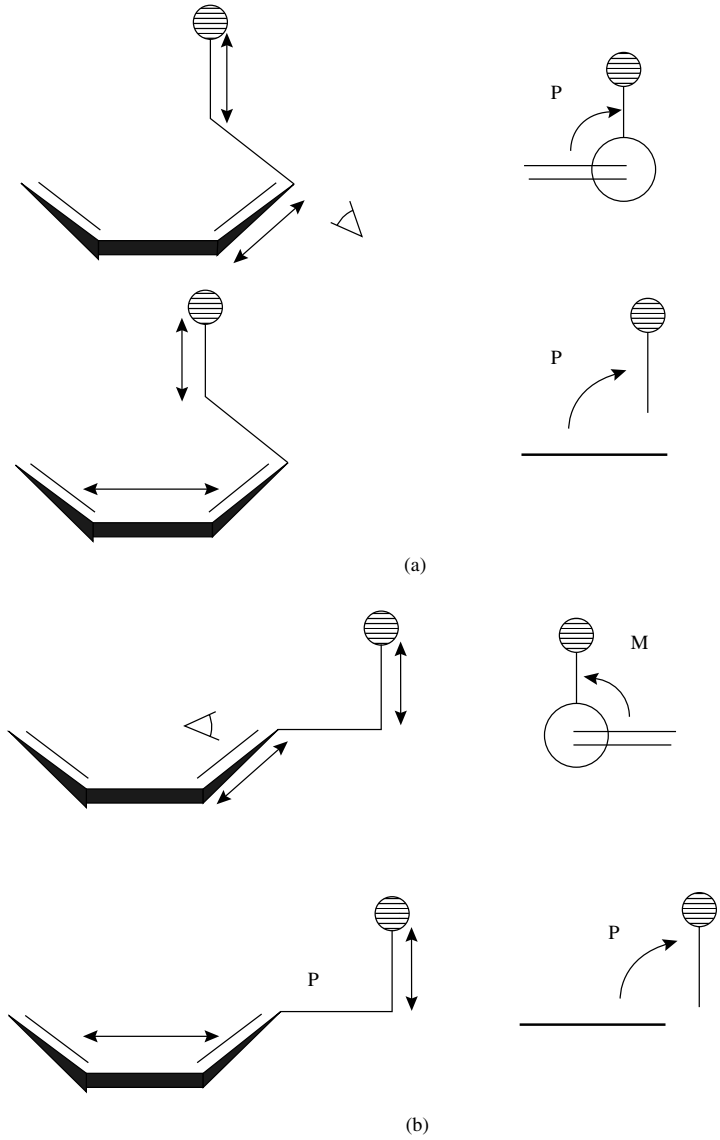
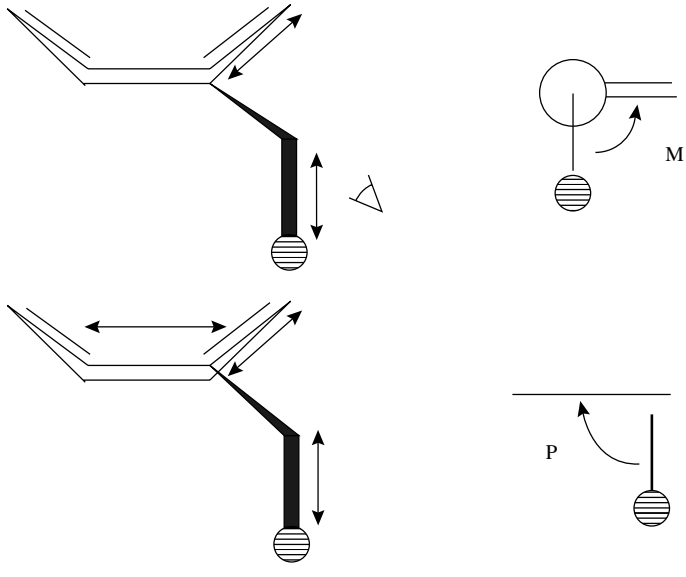
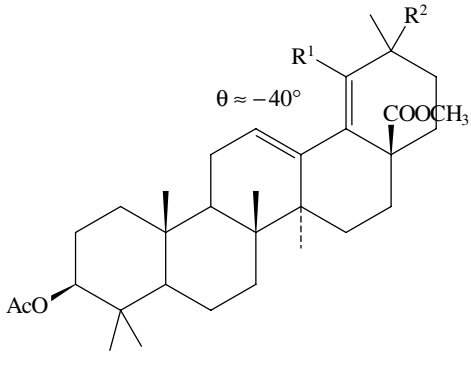


FIGURE 7. The two definitions of the allylic axial chirality rule for the three possible positions of the substituent represented by the shaded circle. For each case the upper part of the Figure represents the original proposal (olefin-picture) and refers to the orientation of the substituent with respect to the nearest double bond; the lower part indicates the 'diene-picture', which takes into account the actual location of the transition dipole. To make the drawings clearer, a planar diene has been considered and, on the right, the projections have been shown. In (a) is shown the case where the two definitions give the same result (P-chirality in this case). This is, for example, the case of a homoannular allylic axial substituent. In (b) and (c), the two definitions lead to different conclusions: M-chirality for the olefin picture, P-chirality, again, for the diene picture. The latter two instances can only be found when the axial substituent is on a different ring from the diene. It should furthermore be noted that knowledge of the exact location of the transition dipole is essential in case (b) for the 'diene-picture'

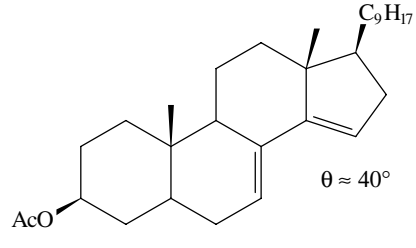


(c)

FIGURE 7. (*continued*)



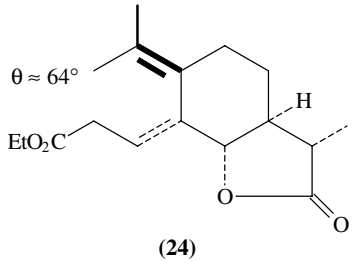
(22a) $R^1 = CH_3$; $R^2 = H$
(22b) $R^1 = H$; $R^2 = CH_3$ $\Delta\varepsilon$ (230 nm) > 0



(23) $\Delta\varepsilon$ (243 nm) < 0

could imply a substantial reduction of conjugation in the π-system, which might become better represented by the individual olefins than by a whole chromophore. It should be pointed out, however, that the experimental evidence (in terms of absorption wavelength) for such an interpretation is rather weak (see below).

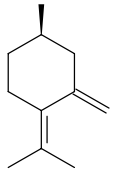
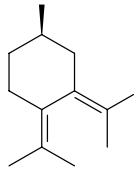
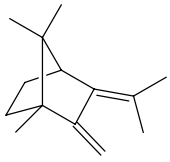
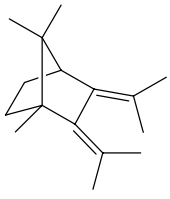
b. Highly twisted s-cis-dienes. A typical example of a very distorted diene is photosantonin[37] **(24)**, which presents a twist angle of 64° in the solid state as determined by X-ray diffraction.



(24)

UV: ε 8700, λ 210 nm (sh)
CD Δε − 12.4 (λ 210 nm, sh); Δε −25 (195 nm)

TABLE 2. Structural (molecular mechanics) and spectral parameters of selected distorted dienes[a]

Compound	Chirality	θ (deg)	UV CD	Double bond torsion angle (deg)
 **(25)**	P	+3.7	ε 4300 (sh), 224 nm [R] −3.9, 246 nm	6.8
 **(26)**	P	+22.7	ε 8300 (infl), 220 nm [R] −9.6, 224 nm	18.9 19.0
 **(27)**	M	−1.5	ε 13100, 249 nm [R] 1.98, 250 nm	4.0
 **(28)**	M	−16.3	ε 10100, 249 nm [R] 3.3, 257 nm	−15.4 −14.9

[a]The angle θ is defined according to Scheme 2, the exact definitions of the angles in the last column, describing the double bond torsion, being given in Reference 38. Here we note only that 0° torsion means a planar olefin. The values are reported only for dimethyl-substituted double bonds.

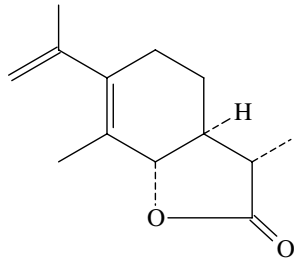
The most striking spectroscopic characteristics of this compound are: (i) there is only a shoulder at about 210 nm in the UV spectrum, which implies a substantial lack of conjugation and brings about further experimental evidence of the large skew angle; (ii) a strongly negative Cotton effect is associated with the P-chirality of the chromophore. The latter observation has been considered an experimental support for an anti-DR behaviour of highly twisted *cisoid* dienes. More recently, Lightner and coworkers[38] prepared and studied the CD spectra of a series of distorted dienes, the most relevant of which are reported in Table 2.

The authors pointed out that for M-distorted dienes a positive CD is found, while the P-distorted dienes show a negative CD, supporting the above correlation.

These results deserve comment. First of all, the chemical structure of photosantonin, **24**, is really complex, in particular the lactone chromophore (which, examining the molecular model, appears quite distorted) could contribute strongly to CD, making very difficult the correct assignment of the true CD of the highly distorted diene chromophore. In addition, as far as Lightner's dienes are concerned, it must be observed that in general the molecular mechanics (MM) results reported do not provide high values of the twist angle θ (the maximum is about 23°), nor do the compounds derived from camphor show the spectroscopic behaviour typical of a highly twisted diene. An examination of the conformational analysis carried out by Lightner reveals other interesting aspects. In the case of diene **28**, there are two almost degenerate minimum energy conformations (separated by about 0.4 kcal mol^{-1}) which must both be significantly populated but *show opposite intrinsic chirality*.

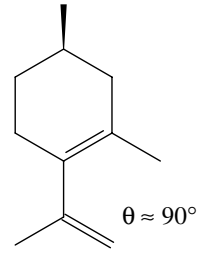
Furthermore, for both **28** and for **26**, MM calculations indicate that even the individual double bonds are highly twisted (15–20°). This could be (*vide infra*) a further mechanism giving rise to optical activity of the $\pi-\pi^*$ transition of the diene chromophore.

Other interesting examples of highly distorted dienes are **29** and **30**. In these cases there is a further difficulty. For **30**[39], for instance, two low-energy conformations in equilibrium are possible: These two conformations are differentiated essentially by the interaction between the methylidene groups and the equatorial and axial hydrogens on the ring.



(29)

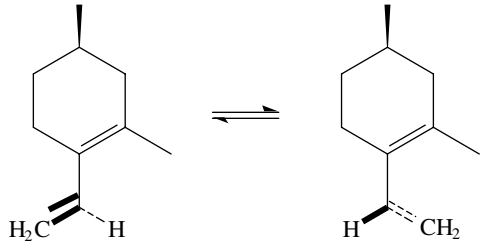
ε 7300 sh (205 nm)
Δε + 4.4 (210 nm)[37]



(30)

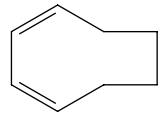
ε 3300 sh (217 nm)
Δε + 1.77 (217 nm)[39]

It is apparent that the π systems in **30a** and **30b** are distorted in opposite senses. The measured rotational strength is thus the weighted average over these two conformations, which depends on the relative populations as well as on the individual rotational strengths.



(30a) **(30b)**

A peculiar case of a strongly distorted diene is represented by *cis,trans*-1,3-cycloctadiene[40]:



The main interest of this molecule resides in the fact that the principal source of rotational strength of the $\pi \rightarrow \pi^*$ lowest energy transition has been attributed[40] to the twist of one of the two double bonds ($\alpha = -136^\circ$, as in *trans*-cyclooctene) rather than to the twist of the 1,3-butadiene moiety ($\theta = +50.2^\circ$)

4. Transoid dienes[21,35]

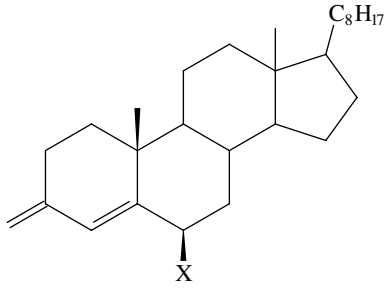
Dienes in quasi-*s-trans* conformation are found only in cyclic structures where perfect planarity is hindered. The DR also holds valid for this kind of conformation, as demonstrated by the considerations of Section II.D.1.a and also confirmed by all the reported calculations. Indeed, contrary to what is sometimes found for *cisoid* systems, the rotational strength evaluated by many types of calculation is invariably found to follow the diene rule for *transoid* systems. However, very small skew angles are usually found in real molecules and this implies that the main contribution to the observed optical activity cannot come from the weak intrinsic distortion, but is more likely to stem from the dissymmetric perturbations, notably of the allylic axial substituents.

A few examples will illustrate the case. The parent *trans*-diene derivatives **31a** and **32**[35] have nearly planar chromophores, but the Cotton effects are quite strong and opposite in sign (+15 and −27.9, respectively). This can be attributed mainly to the allylic axial C−CH_3 bonds, which provide a positive contribution for compounds **31** and a negative for **32**. Furthermore, the $\Delta\varepsilon$ values of P-chiral *s-trans*-**31** are strongly dependent on the polarizability of the allylic C−X bond.

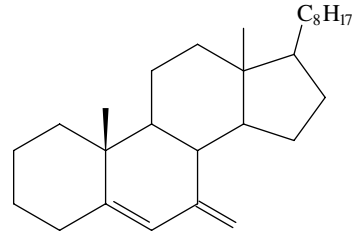
5. Conclusions on skewed dienes

The interpretation of the optical activity of these compounds is rather debatable and no single theory seems to effectively accommodate the whole variety of cases.

The intrinsic contribution, accounted for by the diene rule, seems to be easily outweighed by the perturbations arising from the allylic axial substituents, which in turn define the allylic axial chirality rule. This latter can be formulated in two ways: The 'olefin-picture', where chirality is referred to the nearest double bond, and the 'diene-picture',



	X	Δε	λ (nm)
31a	H	+15.0	(237)
31b	OH	+7.85	(239)
31c	NHAc	+0.8	(253)



(32)

Δε = −27.9 (238 nm)

which considers the electric-dipole transition moment of the diene chromophore as a whole.

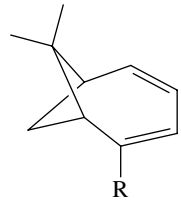
The two representations lead to the same result in the majority of the cases studied so far, where agreement with experiment is rather good and there are only few exceptions. The cases in which the two pictures are in conflict can be divided into two classes: strongly versus 'normally' distorted dienes ($\theta \gtrsim 30^\circ$). The former is typified by the heteroannular dienes, which seem to obey the 'olefin-picture'. The latter, much less well characterized, seems to be better interpreted in terms of the 'diene-picture'.

We consider it rather reasonable to suppose that when the distortion is small the π-electron system is delocalized, justifying the diene-picture; whereas in the presence of large skew angles the contribution of localized double bonds can be much more important, supporting the olefin-picture.

A further mechanism, based on the distortion of the individual olefin plane, has also been proposed[40], but has received rather little attention. It is possible that its role has been unjustifiedly neglected in many cases.

E. Dienes Owing Their Chirality to a Dynamic Twist[10]

Mason and coworkers[10] studied the chiral bicyclic derivatives **2, 3, 33** and **34**, having known absolute configuration. These molecules possess a planar *s-cis* diene chromophore and formally their chirality is due to the presence of the D or CH_3 substituents, which rule out all the symmetry planes. However, it is interesting to point out a peculiar structural



(33) R = D
(34) R = CH_3

feature of these compounds with respect to analogous molecules also having a planar *s-cis* diene, like **4** and **5**. While in the latter molecules the C-10 methyl group (i.e. the substituent responsible for the molecular chirality) is displaced from the chromophore at equilibrium, the methyl group bonded to the diene moiety of **2** and **34** lies *in the plane* of the diene, at least in the equilibrium conformation. In this case, therefore, the origin of optical activity of the planar diene chromophore cannot be found in a simple interaction between the chromophore itself and the substituent responsible for the overall molecular chirality. The detailed analysis of the absorption and CD data carried out by Mason and coworkers reveals that there is a chiral distortion of the diene chromophore in **2, 3, 33** and **34** of dynamic origin[10], i.e. it arises from a vibrational mode (or modes) with inequivalent turning points, resulting from the mass difference between the groups occupying the 2- and 3-positions in each of these dienes. The out-of-plane bending modes of the groups in the 2-position of **33** and **34** could be the most effective. As far as **2** and **3** are concerned, it has been observed that the rotatory strength of the $\pi \rightarrow \pi^*_-$ in **2** is some 7 times larger than that of the deuterio derivative **3**, a factor close to the mass ratio of the substituents replacing hydrogen in the parent diene. This relation suggests a common vibronic perturbation of the symmetric diene chromophore in **2** and **3**.

F. External Dissymmetric Perturbation

1. Planar s-cis-dienes

When there is no intrinsic chirality, because the internal distortion is completely absent, as for example in **4** and **5**[11], optical activity can only arise from the perturbation of the $^1A_1 \rightarrow {}^1B_2$ transition, due to the presence around the chromophore of chirally distributed substituents. The origin of optical activity can be found in a dynamic coupling mechanism and in such cases a coupled oscillator treatment (like that of DeVoe[1,47]) can be used to evaluate R[1,41]. In this approach, a chiral molecule is regarded as a set of suitable subsystems (the chromophore and the perturbers that make it chiral), which are polarized by the external electromagnetic field and are coupled together by their own local fields. The optical properties (absorption, refraction and circular dichroism) can be calculated by taking into account the above interactions among the subsystems. Of course, for this purpose, each subsystem has to be fully characterized in terms of one (or several) oscillators, representing an electric-dipole-allowed transition defined by the polarization direction $\mathbf{e}_i$ and the complex polarizability $\alpha_i(\tilde{\nu}) = R_i(\tilde{\nu}) + iI_i(\tilde{\nu})$. Here, $I_i(\tilde{\nu})$ can be obtained from experiment, i.e. from the absorption spectrum of compounds which can be considered good models of the subsystem; $R_i(\tilde{\nu})$ can be calculated from $I_i(\tilde{\nu})$ by means of a Kronig–Kramers transform. A molecule like **4** (or **5**) can be considered as the aggregate of only two subsystems: the chromophore (i.e. the *cis*-diene moiety) and a perturber, which, for symmetry reasons, can be found in the C−C bond linking the methyl group to the bicyclic skeleton. Each of these groups can be represented by a single oscillator: the former is polarized along the line joining the midpoints of the double bonds and the latter along the C−CH_3 axis. As for the values of $I_i(\tilde{\nu})$ and $R_i(\tilde{\nu})$, a Lorentzian polarizability of 25 D^2 centred at 250 nm gives a satisfactory representation of the absorption band of the *cis*-diene chromophore, while to describe the polarizability of the C−CH_3 bond a Lorentzian polarizability of 2 D^2 at 134 nm is known to be reasonable[41b].

At this point we have the geometrical and spectroscopic parameters necessary to calculate $\Delta\varepsilon(\tilde{\nu})$ from the general DeVoe equations[41a]. In the present case of two different oscillators we have

$$\Delta\varepsilon(\tilde{\nu}) = 0.014\pi^2 N \mathbf{e}_1 \times \mathbf{e}_2 \cdot \mathbf{R}_{12} G_{12} \tilde{\nu}^2 [I_1(\tilde{\nu}) R_2(\tilde{\nu}) + I_2(\tilde{\nu}) R_1(\tilde{\nu})] \qquad (3a)$$

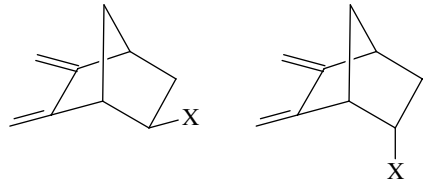
$$G_{12} = \left(\frac{1}{r_{12}}\right)^3 [\mathbf{e}_1 \cdot \mathbf{e}_2 - 3(\mathbf{e}_1 \cdot \mathbf{e}_{12})(\mathbf{e}_2 \cdot \mathbf{e}_{12})] \tag{3b}$$

Here $\mathbf{e}_1$ and $\mathbf{e}_2$ are the unit vectors of oscillator 1 (the diene chromophore) and 2 (the C−CH_3 dipole), respectively; $\mathbf{R}_{12}$ is the vector joining their midpoints, G_{12} is the point-dipole interaction term and N is the Avogadro number; all quantities are expressed in c.g.s. units. In the absorption region of the chromophore, where the perturber does not show a significant absorption, the above formula reduces to the simpler equation[41c]

$$\Delta\varepsilon(\tilde{\nu}) = 0.014\pi^2 N \mathbf{e}_1 \times \mathbf{e}_2 \cdot \mathbf{R}_{12} G_{12} \tilde{\nu}^2 I_1(\tilde{\nu}) R_2(\tilde{\nu}) \tag{4}$$

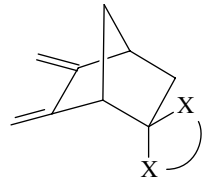
In this way, a $\Delta\varepsilon$ value of −0.57 is calculated at 250 nm, as compared with an experimental value of −0.63. This excellent agreement between the experimental and calculated values is a strong indication that a dynamic coupling mechanism is the major source of optical activity in these molecules.

Another group of chiral dienes where a planar *s-cis*-1,3-butadiene chromophore is present, is that of the compounds **35–40** prepared by Sonney and Vogel[42]. These compounds have the general structures indicated below.



	exo-series	*endo*-series
X = OH	**35**	**38**
OAc	**36**	**39**
OBs	**37**	**40**

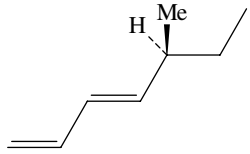
The CD spectra of the dextrorotatory isomers of **35–39** show a weak positive band corresponding to the lowest π–π^* transition ($^1A_1 \rightarrow {}^1B_2$) of the *s-cis*-butadiene. Their behaviour is strictly analogous to that of **4** and **5**. The sign of the CD band can be predicted by taking into account the interaction of the diene dipole with that on C−X. The spectrum of **40** is complicated by the presence of a couplet-like feature, probably resulting from the coupling of the diene and the brosylate (OBs) chromophore. In a more recent paper, Vogel and coworkers[43] describe the CD data of several 5,6-dimethylidenebicyclo[2.2.1]hept-2-yl derivatives, having the general formula



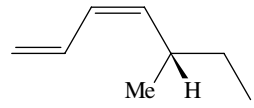
Unfortunately, no general rule can be proposed for interpreting the experimental data. In particular, if the substituent at C(2) is a π-system, different from $\rangle$=O, the Cotton effect associated with the $^1A_1 \rightarrow {}^1B_2$ transition of the *cis*-diene is opposite in sign to that of the exciton chirality of the two homoconjugated π-chromophores.

2. Planar s-trans-dienes

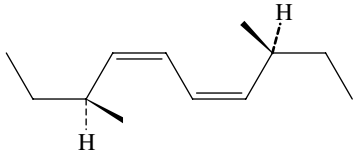
The first report of the chiroptical properties of a planar *s-trans*-diene chromophore is due to Di Corato[12], who described the CD data of (+)-(*S*)-**6**, which shows a positive weak ($\Delta\varepsilon \approx +0.2$) Cotton effect at about 220 nm, in both the *E* and *Z* isomers. Lardicci and coworkers[13] described in 1978 the absorption and CD spectra of the planar *s-trans*-diene derivatives **7** and **41**.



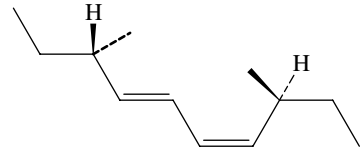
(*E*)-(**6**)



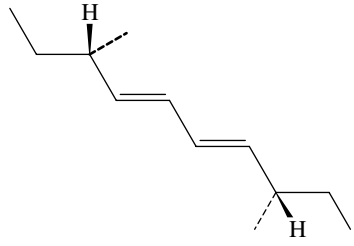
(*Z*)-(**6**)



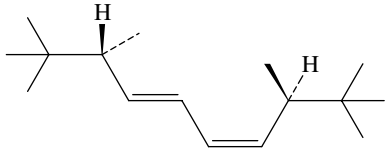
(*Z*, *Z*)-(3*S*, 8*S*)-(**7**)



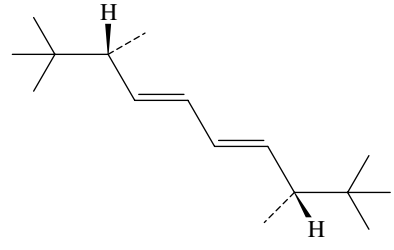
(*E*, *Z*)-(3*S*, 8*S*)-(**7**)



(*E*, *E*)-(3*S*, 8*S*)-(**7**)



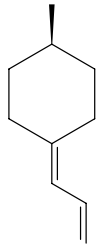
(*E*, *Z*)-(3*S*, 8*S*)-(**41**)

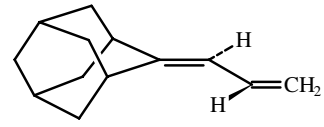


(*E*, *E*)-(3*S*, 8*S*)-(**41**)

These compounds show typical *s-trans*-1,3-butadiene absorption bands between 230 and 235 nm, with $\varepsilon_{max} \approx 30000$. In correspondence, the CD spectra show an intense ($\Delta\varepsilon \approx 3-5$) Cotton effect, positive for the (*S*) absolute configuration of the chiral centres. It is noteworthy that if one considered (*E*)-(*S*)-**6** as a 'half' of (*E*, *E*)-(3S,8S)-**7** a value of $\Delta\varepsilon$ of about 0.4 would be predicted: the actual $\Delta\varepsilon$ of +3 is one order of magnitude larger!

An interesting series of *s-trans* planar dienes is that due to Walborsky and coworkers[44,45]. They prepared and studied the chiroptical properties of several compounds where the diene moiety is linked to a chirally substituted ring, such as **42** and **43**.





(42): (*aR*)-(+)-(4-methylcyclohexylidene)propene
$\varepsilon_{237.5} = 24300$
$\Delta\varepsilon_{237.5} = +3.7$

(43): (*aS*)-(−)-(5-methyladamantylidene)propene
$\varepsilon_{240} = 30600$
$\Delta\varepsilon_{236} = -0.45$

Walborsky and coworkers[44] proposed a sector rule, the planar diene rule, to correlate the sign of the $^1A_g \rightarrow {}^1B_u$ transition Cotton effect of these derivatives with the absolute configuration and, in addition, they provided a qualitative interpretation of the CD data of the molecules by means of the two-group electric-dipole mechanism[44c]. Later on, in

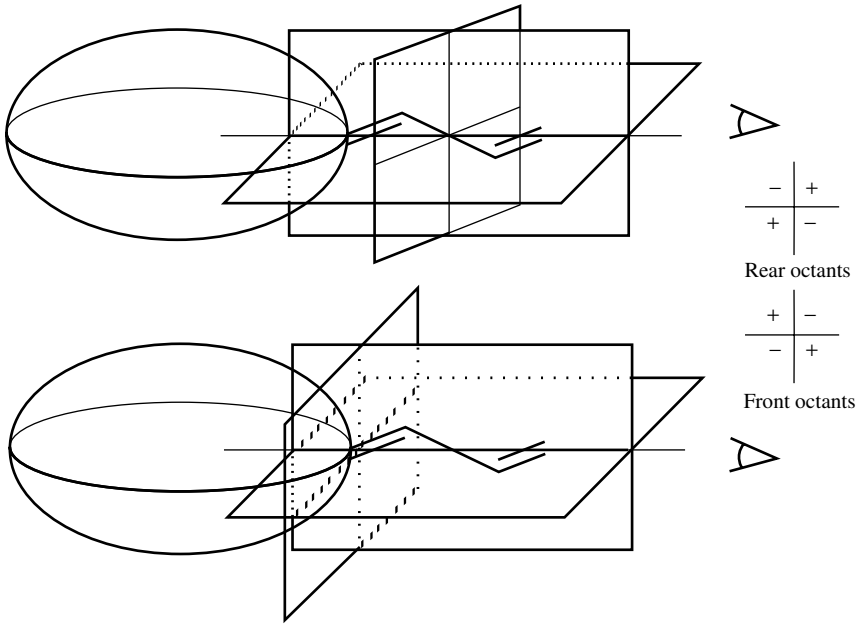


FIGURE 8. Sector rules for exocyclic *s-trans* dienes. Top: 'bond-centred', bottom: 'atom-centred' rule. The ellipsoid represents the rest of the molecule and also defines the direction opposite to the observer. In both cases two planes are defined by the transition dipole and the plane containing the diene; only the third plane is located differently. The 'bond-centred' rule holds for cyclohexylidene compounds, while the 'atom-centred' rule should apply to adamantylidene derivatives

1988, Walborsky, Reddy and Brewster[45] introduced a more complex empirical rule, which replaced the first one. The space around the chromophore is divided into sectors by the plane of the diene, the plane perpendicular to it and containing the transition moment (usually directed along the line C_1-C_4) and a third plane. The latter has been placed either in the middle of the diene (the so-called bond-centred model) or on the end atom of the chromophore, the one inserted in the ring (atom-centred model). The signs of the contributions to CD of the various substituents are given in Figure 8.

In spite of the practical usefulness of such empirical sector rules, the physical origin of the optical activity in these molecules remains an open question. In fact, polarizability calculations[41c] (both by means of the Weigang amplified sector rule for allowed transitions and the DeVoe dynamic coupling model), taking full account of the interaction between the $^1A_g \rightarrow {}^1B_u$ transition dipole and the polarizable matter around it, give the wrong sign. The correct sign and order of magnitude for this Cotton effect can be reproduced only by assuming the existence of a very small (less than 5°) distortion of the chromophore; this is in conflict with the results of MM and *ab initio* calculations, which clearly indicate the presence of a planar *s-trans* chromophore[41c].

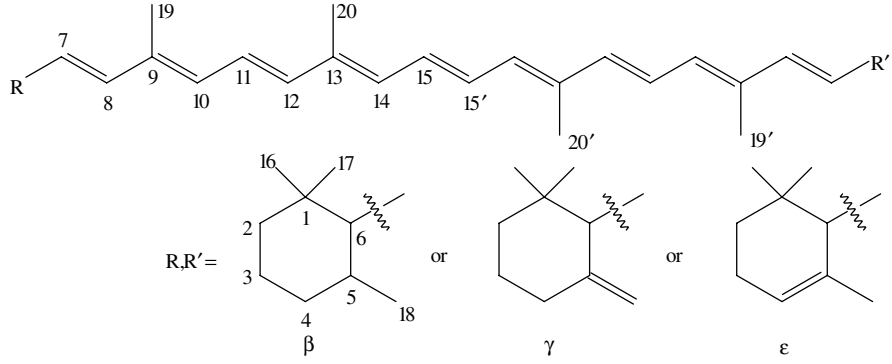
These observations suggest an interesting question: can CD spectroscopy be so sensitive to minute conformational details as to challenge apparently sophisticated computational methods?

III. POLYENES

A. Carotenoids

1. General aspects

Carotenoids are natural compounds characterized by a conjugated polyenic chain connecting two terminal groups, as represented in Scheme 7. Terminal groups can be of different natures; they often contain a cyclic double bond and allow one to classify carotenoids.



SCHEME 7

The two terminal groups, R and R′, are in most cases totally responsible for the chirality of carotenoids, which can thus be further classified into the three categories: *homodichiral*, with two identical end groups, of symmetry C_2; *heterodichiral*, with two different end groups; or *monochiral*, with one chiral and one achiral terminal group. Naturally, the chiral terminal groups are responsible for the CD of these molecules, a subject which

has been recently thoroughly reviewed by Buchecker and Noack[4], Liaaen-Jensen[46a] and Noack[46b]. A few general statements have been found true for the CD of carotenoids:

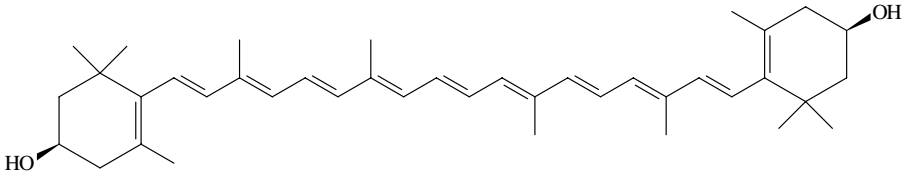
1. Carotenoids with one or two terminal groups containing a double bond formally conjugated with the polyenic chain have conservative CD spectra, i.e. in the region of $\pi-\pi^*$ transitions (220–500 nm) there are 5 or 6 maxima of opposite signs, whose intensities add up to zero.
2. The signs of the bands in conservative spectra of *all-trans* forms are opposite to those of the corresponding derivatives containing one *cis* double bond (the spectra of di-*Z* compounds are analogous to the *all-trans*).
3. Molecules having terminal groups with non-conjugated double bonds feature non-conservative spectra.
4. The effects of terminal groups are additive.
5. The CD spectra are strongly temperature-dependent.

2. Origins of the optical activity[47]

Carotenoid spectra are characterized by several absorptions in the normally accessible range of UV-Vis spectrometers. In fact, the large number of conjugated double bonds creates a manifold of easily accessible excited states. Fortunately, some features of the diene spectroscopy are retained, which allows one to correlate, at least in some cases, the CD to conformation and configuration by simple symmetry tokens. As long as we can recognize a C_2 symmetry of the chromophoric system, the lowest-lying excited state belongs to a *B* representation, just as in 1,3-dienes. The other $\pi-\pi^*$ excitations are often alternately *A* and *B*. The A-type transitions are electrically polarized along the C_2 axis, the B-type are polarized parallel to the chain. They have opposite rotational strengths and thus give rise to the typical feature of CD of carotenoids with alternating signs.

In order to deal with one transition of a specific symmetry, that of longest wavelength $^1A \rightarrow {}^1B$ is usually chosen.

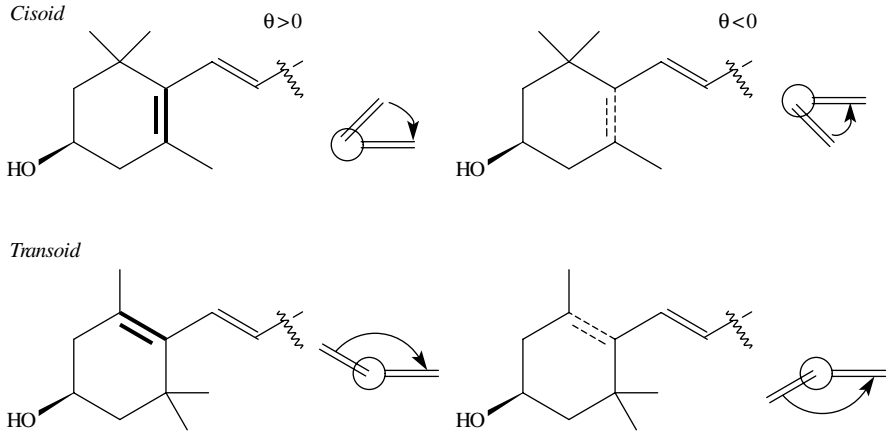
Let us consider a carotenoid system having a β end group, i.e. a molecule with the possibility of conjugation between the terminal double bond of the polyenic chain and the ring double bond, for example zeaxanthin, **44**.



(44)

The planar conformations *s-cis* and *s-trans* cannot be appreciably populated owing to the repulsive steric interaction between the C_8-H and C_5-methyl (in the *s-cis*) or between the same C_8-H and the methyl group on (C_1 in the *s-trans*). This repulsion is minimized by introducing a twist around the C_6-C_7 bond. Limiting conformations, with skew angles of about $\pm 40^\circ$ and $\pm 140^\circ$, can be assumed, as shown in Scheme 8. In this way, an intrinsically dissymmetric chromophore is created.

Owing to the presence of the substituent in position 3 of the cycle, this assumes the more stable chair conformation with the substituent in the equatorial position: the other one, with the substituent axial, is about 1 kcal mol^{-1} less stable.



SCHEME 8

The two twisted conformations discussed above are thus in a diastereoisomeric relationship, one being more populated than the other. Molecular mechanics calculations show that in the case of zeaxanthin the most stable conformation by about 0.3–0.4 kcal mol^{-1} is that depicted in Figure 9.

The optical activity of such a molecule has been interpreted using a model that stresses the similarity with a twisted butadiene. The long and planar polyenic chain formally acts as the bond (2,3) in a 1,3-butadiene, as long as it allows conjugation between the two terminal double bonds. The same considerations regarding the distortion of the chromophore and the sign of the rotational strength of the longest-wavelength transition should therefore apply. This means that the optical activity is expected to follow the diene rule, presented in Section II.D, with reference to the helicity defined by the two terminal double bonds.

The CD spectrum of such a structure can be predicted as follows, once we represent this conformation as in Figure 10.

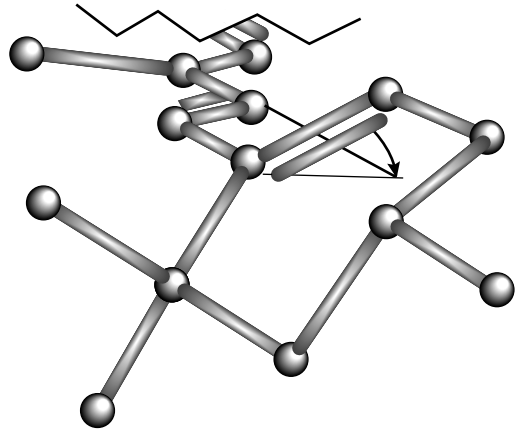


FIGURE 9. Molecular mechanics most stable conformation for zeaxanthin **(44)** showing a positive twist of about 40° between the first two double bonds

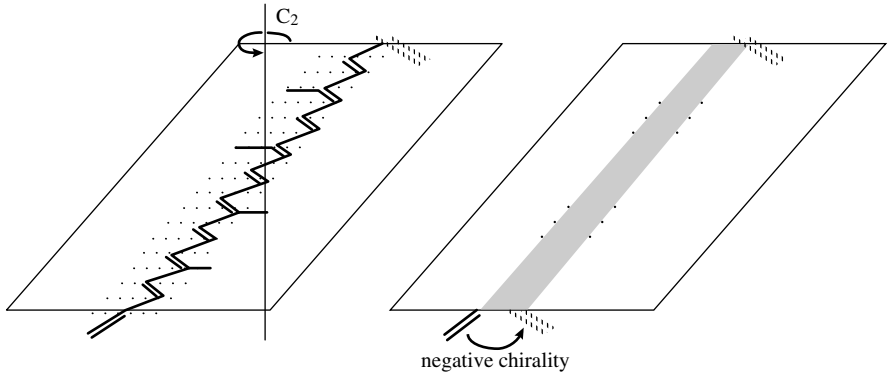


FIGURE 10. On the left is shown the conjugated system of *all-trans* zeaxanthin **(44)** in its most stable conformation. On the right, the planar part of the system is represented as a grey band to make clearer the similarity with a 1,3-butadiene

The terminal double bonds define a *trans*-butadiene with negative helicity, for which the $^1A \rightarrow {}^1B$ transition (the lowest-energy $\pi \rightarrow \pi^*$ excitation) is predicted to have a negative rotational strength on the basis of the twisted diene rule. This is indeed what is found experimentally. The same considerations explain the change in sign of the CD bands on passing from the *all-trans* to the mono-*cis* systems. The case of 15-*cis*-zeaxanthin is revealing. In Figure 11 we show the relative positions of the double bonds in the most stable conformation of the molecule.

In this situation the two end-ring double bonds define a positive chirality. Application of the twisted diene rule gives a positive sign for the lowest-energy $^1A \rightarrow {}^1B$ transition, and in the case of 15-*cis*-(3*R*,3′*R*)-zeaxanthin this is confirmed by experiment.

The behaviour of the CD of (3*R*,3′*R*)-zeaxanthin at low temperature can also be explained on the basis of simple conformational considerations. On lowering the temperature, the most stable form becomes more populated and gives a predominant contribution to the spectrum. Obviously there may be instances where the CD as a function of temperature is much more complicated than that just discussed, one example being (3*S*, 3′*S*)-astaxanthin. However, the low-temperature spectra can be interpreted even here by

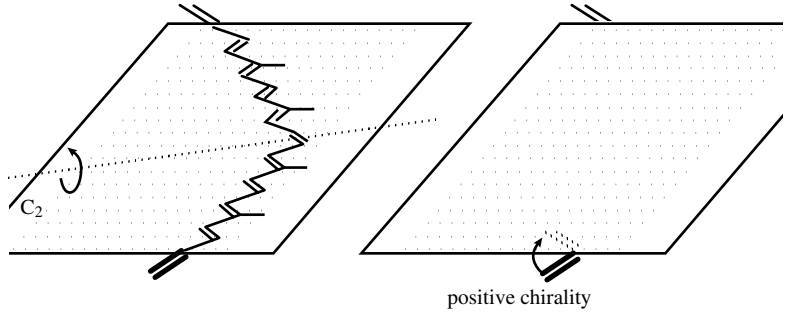


FIGURE 11. In analogy with Figure 10, the conjugated system in the most stable conformation of 15-*cis*-zeaxanthin is depicted, demonstrating the helicity defined by the terminal double bonds of the conjugated chain

means of MM calculations, which show that the most stable conformer again obeys the diene helicity rule. The CD spectra of compounds featuring non-conservative behaviour, i.e. of molecules where a twist of the conjugated system is not present, have not been studied so much and a theoretical interpretation of the spectroscopic data has not been provided so far[4].

3. Polymers[48]

Polyacetylenes are the most important class of synthetic polymers containing conjugated carbon–carbon double bonds. Some optically active monomers have been used with the following conclusions. Polymers of 1-alkynes having a branched side-chain assume in solution a helical conformation. A chiral side-chain induces a predominant screw sense in these helices. In particular, for alkyl branching, it has been shown that (*S*) monomers lead to a left-handed screw sense.

The CD spectra of polymers of a series of homologue chiral terminal acetylenes[48] shows a marked dependence on the distance of the asymmetric centre from the triple bond. The relation between the two facts is however unclear, even because the UV spectrum results from the superposition of several bands, owing to the extended conjugation.

IV. OLIGOENES

We have considered so far two extreme cases: the simplest diene chromophore and a long chain of conjugated double bonds, trying to find out a few keys to interpret the relation between structure and chiroptical properties. Intermediate systems, i.e. molecules with a limited number ($2 < n < 10$) of double bonds, have received much less attention in this respect. In fact, they do not constitute a homogeneous class of compounds and any extrapolation would have limited scope. Nevertheless, considerable attention has been devoted to some oligoenes of biological importance, such as the members of the vitamin D and vitamin A families. These molecules often undergo important photochemical reactions and CD spectroscopy has been used to reveal labile intermediates. An example is provided by an unstable rotamer of tachisterol$_3$, which occurs during the irradiation of previtamin D$_3$ at 92 K[49].

The analysis of CD and absorption data has been used since 1974, mainly by Nakanishi and his coworkers, to study the structure of the rhodopsins, pigments involved in the mechanism of vision, and of their chromophores[50].

A special field of application of CD to oligoenes is that of some antibiotics, like filipin[51] and amphotericin B[52]. These molecules are characterized by a strong tendency to autoaggregation, which causes the CD spectra to be strongly solvent, temperature and concentration dependent. In fact, in the presence of dimers, the CD is dominated by the appearance of a strong exciton couplet between the polyenic chains of neighbouring molecules.

V. APPENDIX

A. 1,3-Butadiene MOs, Symmetry and Electronic Transitions

Butadiene can exist in two planar conformations, *s-trans* and *s-cis*. They belong to the C_{2h} and C_{2v} symmetry point group, respectively. Obviously, both forms have symmetry planes. A skewed conformation, instead, has only a C_2 axis. We can choose the reference frames depicted in Figure 12, characterized by z as the symmetry axis and x directed along the single bond.

Treating the π-system butadiene molecule with a HMO (Hückel molecular orbital) approach, we get four MOs, which are linear combinations of the four atomic p orbitals

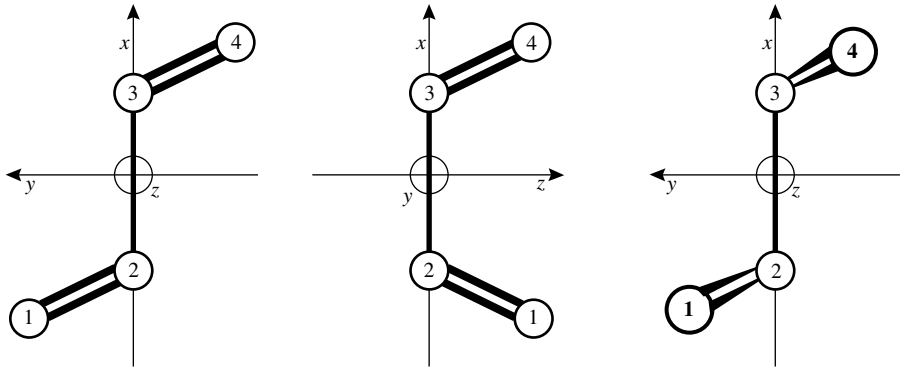


FIGURE 12. Reference axes and numbering of *s-trans*, *s-cis* and skewed butadiene

and are given by the equations

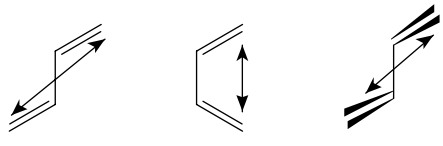
$$\pi_{\pm} = c_1 p_1 \pm c_2 p_2 + c_2 p_3 \pm c_1 p_4 \tag{5a}$$

and

$$\pi^*_{\pm} = c_2 p_1 \pm c_1 p_2 - c_1 p_3 \mp c_2 p_4 \tag{5b}$$

where c_1 and c_2 represent the two distinct coefficients in the linear combinations of AOs and depend on Hückel's parameters α and β.

Inspecting the character tables of Figure 13, we notice that the first (lowest-energy) excited state, corresponding to the electronic transition $\pi_- \rightarrow \pi^*_-$, is, for the *s-trans* isomer, B_u, for the *s-cis*, B_2 and finally for the skewed form, B. This transition is therefore electrically allowed in all three cases, being in-plane polarized for the former two cases as shown in Scheme 9.



SCHEME 9

The long-wavelength, $\pi_- \rightarrow \pi^*_-$, transition is also magnetically allowed for the skewed and for the *s-cis* conformations, as seen by inspection of the character tables. It is therefore apparent that for the planar isomers, *s-trans* and *s-cis*, there is no optical activity allied to the $\pi_- \rightarrow \pi^*_-$ transition (as obviously expected). In fact, for the *s-trans* form $\mathbf{m}_{B_u} = 0$, while for the *s-cis* μ and $\mathbf{m}$ are orthogonal. In both cases the scalar product in equation 1 vanishes.

In the skewed form, instead, the transition is allowed both electrically and magnetically, with parallel transition moments. The product in equation 1 is hence non-vanishing, implying that this transition has finite rotational strength. This observation leads to the conclusion that skewed 1,3-butadiene is an *intrinsically dissymmetric* chromophore.

C_{2v}	E	C_2	σ_1	σ_2		
A_1	1	1	1	1	μ_z	
A_2	1	1	−1	−1	m_z	π_+, π_-^*
B_1	1	−1	1	−1	μ_x, m_y	π_-, π_-^*
B_2	1	−1	−1	1	μ_y, m_x	

C_{2h}	E	C_2	i	σ		
A_g	1	1	1	1	m_z	
A_u	1	1	−1	−1	μ_z	π_+, π_-^*
B_g	1	−1	1	−1	m_x, m_y	π_-, π_-^*
B_u	1	−1	−1	1	μ_x, μ_y	

C_2	E	C_2		
A	1	1	μ_z, m_z	π_+, π_-^*
B	1	−1	m_x, m_y	π_-, π_+^*

FIGURE 13. Character tables for symmetry point groups C_{2h}, C_2 and C_{2v}

B. MO Calculation of the Rotational Strength

In order to calculate R from equation 3, we have to evaluate the integrals $\mu_{\pi_-^*\pi_-}$ and $\mathbf{m}_{\pi_-^*\pi_-}$, with the MO π_- and π_-^* given in equations 5a and 5b. We assume only nearest-neighbour interactions and equal β-integrals in all the integrals for the pairs (1,2) and (3,4), as justified by symmetry. The electric dipole will be described by the velocity operator ∇, in order to ensure origin-independent results, and equation 6 follows:

$$\begin{aligned}\langle\pi_-^*|\boldsymbol{\mu}|\pi_-\rangle &= \langle\pi_-^*|\boldsymbol{\nabla}|\pi_-\rangle \\ &= c_1c_2[-\boldsymbol{\nabla}_{12} + \boldsymbol{\nabla}_{21} - \boldsymbol{\nabla}_{34} + \boldsymbol{\nabla}_{43}] - c_1^2[\boldsymbol{\nabla}_{23} - \boldsymbol{\nabla}_{32}] \\ &= -2c_1c_2[\boldsymbol{\nabla}_{12} + \boldsymbol{\nabla}_{34}] - 2c_1^2\boldsymbol{\nabla}_{23} \end{aligned} \tag{6}$$

where $\boldsymbol{\nabla}_{ij} = \langle p_i|\boldsymbol{\nabla}|p_j\rangle$.

We can simplify this expression by decomposing the vectors along the three axes, with unit vectors $\hat{\mathbf{i}}$, $\hat{\mathbf{j}}$ and $\hat{\mathbf{k}}$ and introducing the direction cosines of the bond (1,2), namely $\cos x_{12}$, $\cos y_{12}$ and $\cos z_{12}$. The z-components of ∇_{12} and ∇_{34}, cancel, while ∇_{23} is directed along x. This yields the equation

$$\langle\pi_-^*|\boldsymbol{\mu}|\pi_-\rangle = -4c_1c_2\boldsymbol{\nabla}_{12}(\hat{\mathbf{i}}\cos x_{12} + \hat{\mathbf{j}}\cos y_{12}) - 2c_1^2\boldsymbol{\nabla}_{23}\,\hat{\mathbf{i}} \tag{7}$$

The calculation of the magnetic moment

$$\langle\pi_-^*|\mathbf{m}|\pi_-\rangle = \langle\pi_-^*|\mathbf{r}\times\boldsymbol{\nabla}|\pi_-\rangle \tag{8}$$

seems more involved, owing to the presence of the vector product. However, following Charney[22], the expression can be decomposed into the product of the individual integrals:

$$\langle P_i|\mathbf{m}|p_j\rangle = \boldsymbol{\rho_{ij}} \times \boldsymbol{\nabla_{ij}} \tag{9}$$

where $\boldsymbol{\rho_{ij}}$ is the polar vector from the origin to the midpoint of the bond (i, j). We observe that $\boldsymbol{\rho_{23}}$ is trivially vanishing, in our coordinate system, thus $\mathbf{m}_{23} = 0$. This reduces the preceding expression to

$$\langle \pi^*_-|\mathbf{m}|\pi_-\rangle = -2c_1c_2(\mathbf{m}_{12} + \mathbf{m}_{34}) = -2c_1c_2(\boldsymbol{\rho_{12}} \times \boldsymbol{\nabla_{12}} + \boldsymbol{\rho_{34}} \times \boldsymbol{\nabla_{34}}) \tag{10}$$

Again, using the direction cosines and the coordinates of the midpoint of the bond, $\bar{x}_{ij}$, $\bar{y}_{ij}$ and $\bar{z}_{ij}$, and observing that $(\bar{y}_{12}\cos z_{12} - \bar{z}_{12}\cos \bar{y}_{12} = 0$, we obtain the equation

$$\langle \pi^*_-|\mathbf{m}|\pi_-\rangle = -4c_1c_2\nabla_{12}\hat{\mathbf{j}}(\bar{z}_{12}\cos x_{12} - \bar{x}_{12}\cos z_{12}) \tag{11}$$

We are now able to calculate the rotational strength according to equation 3:

$$R_{\pi^*_-\pi_-} = 16c_1^2c_2^2\nabla_{12}^2(\bar{z}_{12}\cos x_{12}\cos y_{12} - \bar{x}_{12}\cos z_{12}\cos y_{12}) \tag{12}$$

On using $\bar{x}_{12} = (x_1 + x_2)/2$ and $\cos x_{12} = (x_2 - x_1)/r_{12}$, with r_{12} the internuclear distance between 1 and 2, and similar expressions for the other components, we obtain

$$R_{\pi^*_-\pi_-} = 16c_1^2c_2^2\nabla_{12}^2\left(\frac{x_2y_1z_1}{r_{12}^2}\right) \tag{13}$$

We note that y_1 and z_1 are functions of the skew angle θ and of the bend angle β (see Scheme 4):

$$y_1 = a\sin\beta\sin\frac{\theta}{2} \quad \text{and} \quad z_1 = a\sin\beta\cos\frac{\theta}{2} \tag{14}$$

a being the length of bond (1,2). This leads to the final result

$$R_{\pi^*_-\pi_-} \propto \sin^2\beta\sin\theta \tag{15}$$

C. Charge-displacement Calculation of *R*

We shall now assume a classical picture to describe the transition $\pi_- \rightarrow \pi^*_-$.

On the basis of the analysis of Figure 14 we deduce that the $\pi_- \rightarrow \pi^*_-$ transition can be seen as the sum of two electric dipoles, $\mathbf{e}_1 + \mathbf{e}_2$. We notice that this transition has B character and is therefore antisymmetric. Hence, even from the classical point of view, we may conclude that this will be the lowest-energy transition.

The sum of the two vectors is given by

$$\boldsymbol{\mu} = \mathbf{e}_1 + \mathbf{e}_2 \tag{16}$$

and the same vectors serve to describe a rotation of charge, yielding a magnetic moment $\mathbf{m}$ given by

$$\mathbf{m} = (\mathbf{r}_1 \times \mathbf{e}_1) + (\mathbf{r}_2 \times \mathbf{e}_2) \tag{17}$$

where $\mathbf{r}_1$ and $\mathbf{r}_2$ are the vectors joining the origin to the midpoints of $\mathbf{e}_1$ and $\mathbf{e}_2$, respectively.

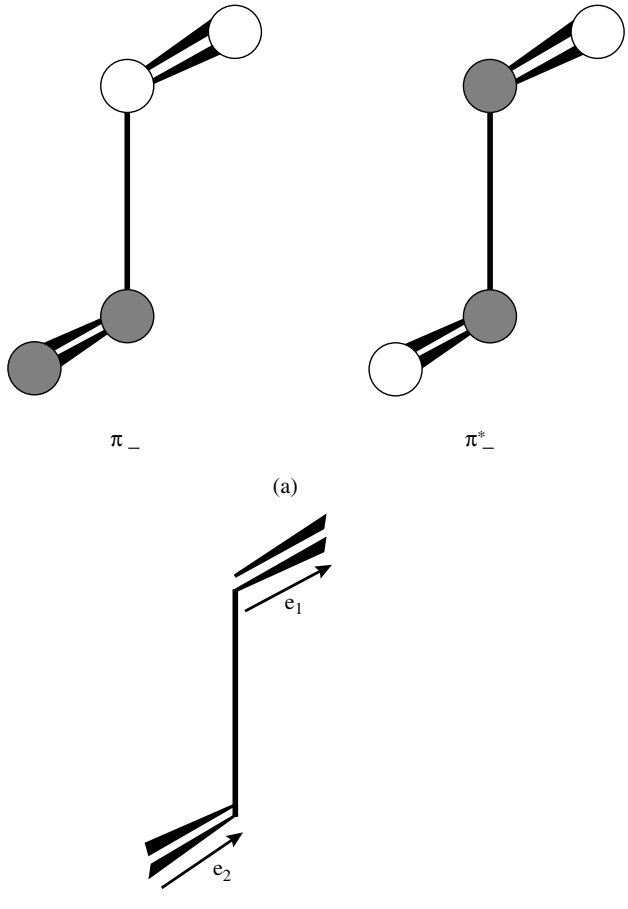


FIGURE 14. (a) Representation of charge excess, ●, and defect, ○, on the four carbon atoms for the two orbitals π_- (left) and π^*_- (right) for 1,3-butadiene. (b) Electric transition moments arising from the $\pi_- \rightarrow \pi^*_-$ transition

The rotational strength is then easily calculated by the equation

$$\begin{aligned} R &= \boldsymbol{\mu} \cdot \mathbf{m} \\ &= (\mathbf{e}_1 + \mathbf{e}_2) \cdot [(\mathbf{r}_1 \times \mathbf{e}_1) + (\mathbf{r}_2 \times \mathbf{e}_2)] \\ &= \mathbf{e}_1 \cdot [(\mathbf{r}_1 \times \mathbf{e}_1) + (\mathbf{r}_2 \times \mathbf{e}_2)] + \mathbf{e}_2 \cdot [(\mathbf{r}_1 \times \mathbf{e}_1) + (\mathbf{r}_2 \times \mathbf{e}_2)] \\ &= \mathbf{e}_1 \cdot (\mathbf{r}_2 \times \mathbf{e}_2) + \mathbf{e}_2 \cdot (\mathbf{r}_1 \times \mathbf{e}_1) \end{aligned} \tag{18}$$

Remembering that for any three vectors $\mathbf{a} \cdot \mathbf{b} \times \mathbf{c} = \mathbf{a} \times \mathbf{b} \cdot \mathbf{c}$, and defining $\mathbf{r} = \mathbf{r}_1 - \mathbf{r}_2$, we obtain

$$R = \mathbf{r} \cdot (\mathbf{e}_1 \times \mathbf{e}_2) \tag{19}$$

where

$$\mathbf{r} \equiv (x_1 + x_2,\, y_1,\, 0) \tag{20}$$

The x- and y-components of the vector product in equation 19 are given by

$$(\mathbf{e}_1 \times \mathbf{e}_2)_x = 2y_1z_1 \qquad (\mathbf{e}_1 \times \mathbf{e}_2)_y = 2z_1(x_2 - x_1) \tag{21}$$

On combining the latter two equations in equation 19, we obtain

$$R = 4x_2y_1z_1 \tag{22}$$

which, just like equation 16, contains the product (y_1z_1). Therefore we obtain again

$$R_{\pi^*_-\pi_-} \propto \sin^2\beta \sin\theta \tag{23}$$

This result is in agreement with that reported by Norden[53] in a context only formally different.

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CHAPTER **5**

Ultraviolet/visible, infrared and Raman spectra

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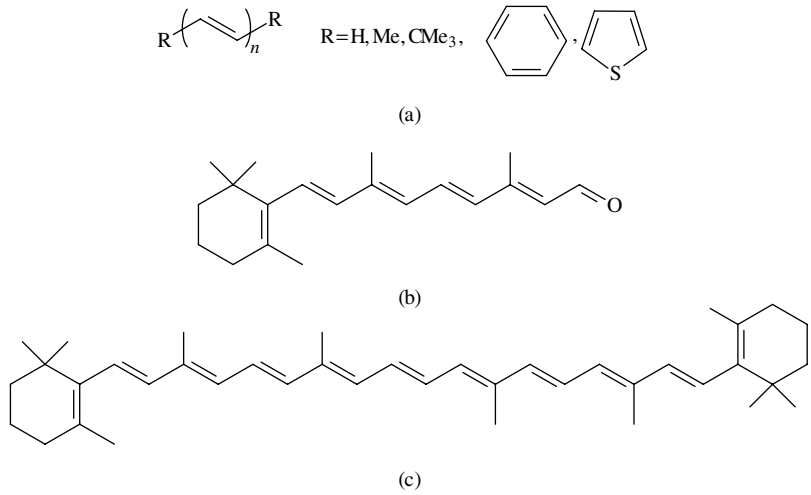
I. INTRODUCTION

Ultraviolet/visible absorption, fluorescence, infrared and Raman spectroscopies are useful for studying structures (configuration, conformation, symmetry etc.) of electronically ground and excited states of linear polyenes, which have attracted much attention of



(a)

(b)

(c)

FIGURE 1. Chemical structures of various polyenes: (a) unsubstituted and α,ω-disubstituted polyenes; (b) retinal; (c) β-carotene

researchers in quantum chemistry, solid-state physics, biophysics etc. Linear polyenes exhibit interesting chemical and physical properties originating from π-electrons. Firstly, these compounds show novel spectroscopic properties due to electron correlation[1–3]. Hudson and coworkers[1] and Kohler[2] have reviewed the electronic states of unsubstituted polyenes and α,ω-diphenylpolyenes (Figure 1a), emphasizing the ordering of the electronically excited states, $1\,^1B_u$ and $2\,^1A_g$. Orlandi and coworkers[3] have reviewed vibrational analyses based on quantum chemical calculations for the electronically ground and excited states of unsubstituted polyenes, and have explained the frequency increase of the in-phase C=C stretch upon excitation to the $2\,^1A_g$ state. Secondly, polyenes are model compounds of polyacetylene $[(CH{=}CH)_n]$ which is the prototype of conducting polymers. Polyacetylene shows new electrical, magnetic and optical properties; for example, it shows high electrical conductivities when doped with electron acceptors (iodine, AsF_5 etc.) or electron donors (Na, K etc.)[4]. The application of vibrational spectroscopy to polyacetylene is described in previous reviews[5–7]. Lastly, retinal (Figure 1b) and its Schiff base play important roles in retinal proteins[8], and so do carotenoids in photosynthetic bacteria[9]. The chemical structure of β-carotene, which is one of the carotenoids, is shown in Figure 1c. Several reviews[10–14] have described the application of vibrational spectroscopy to polyenes in biological systems. There exist geometrical isomers around C=C double bonds and rotamers around C–C single bonds for polyenes. Vibrational studies on the conformers of polyenes may lead us to a better understanding of the functions of polyacetylene and biological systems. In this chapter, we mainly present the spectroscopic properties of various conformers of unsubstituted polyenes. We focus our attention on the structures (configuration, conformation etc.) of the ground states of polyenes and the relation between the number of conjugated C=C bonds and spectroscopic properties. In Section II, we mention experimental techniques and outlines of normal coordinate calculations and resonance Raman spectroscopy. In Section III, we describe the electronic absorption spectra of polyenes. In Section IV, we describe vibrational spectra of polyenes from 1,3-butadiene to polyacetylene.

II. ELECTRONIC AND VIBRATIONAL SPECTROSCOPIES

A. Infrared and Raman Spectroscopies

Vibrational spectra of polyenes can be obtained by infrared and Raman spectroscopies. Infrared and Raman spectra are measured by means of dispersive-type or Fourier transform spectrophotometers. The combination of matrix-isolation infrared spectroscopy and a high-temperature nozzle technique (or photoexcitation) is useful for studying the ground states of unstable conformers of polyenes[15]. A sample is diluted with an inert gas, such as argon, xenon and nitrogen. This mixture is passed through a pipe (or a cell) at a high temperature and immediately sprayed onto a cold CsI plate maintained at a low temperature (e.g. 10 K). Then, unstable conformers can be trapped in the matrices. Biological systems have been studied by resonance Raman spectroscopy[10,12,13] and Fourier transform infrared spectroscopy[14]. These systems consist of various components, such as proteins, membranes and pigments; resonance Raman spectroscopy can give us information about a pigment, when the excitation wavelength for Raman scattering is within the electronic absorption of the pigment. On the other hand, very small absorbance changes associated with external stimuli such as light irradiation can be detected by Fourier transform infrared spectroscopy. Thus, short-lived polyene conformers which are reaction intermediates in biological systems have been studied by the use of steady-state and time-resolved resonance Raman spectroscopy[10,12] and Fourier transform infrared spectroscopy[14]. Strong fluorescence often prevents us from observing Raman spectra. This is the major obstacle in Raman measurements. Coherent anti-Stokes Raman spectroscopy (CARS)[16] can partly solve this fluorescence problem. Since fluorescence appears in the Stokes region, anti-Stokes Raman spectra are not disturbed by fluorescence in principle. It is difficult to measure spontaneous anti-Stokes Raman scattering with high signal-to-noise ratios, because their intensities are very weak. However, coherent anti-Stokes scatterings are strong enough to be measured with high signal-to-noise ratios.

B. Absorption and Fluorescence Spectroscopies

Absorption and fluorescence spectra of polyenes in the region from ultraviolet to visible in the condensed phases (liquid, solid, solutions etc.) are very broad in most cases. Thus, bands arising from distinct vibronic transitions are not resolved. However, the spectra of polyenes in hydrocarbon environments at very low temperatures or in supersonic expansions show fine structures originating from vibrational transitions[1,2]. Absorption and fluorescence excitation spectra provide us with the vibrational frequencies of electronically excited states, whereas fluorescence spectra provide us with those of ground states. Two-photon absorption spectroscopy is complementary to one-photon absorption spectroscopy. Let us consider a molecule with a centre of inversion. The transitions between the ground state and electronically excited states with ungerade symmetry are allowed for one-photon processes, but forbidden for two-photon processes. On the other hand, the selection rules are just reversed for the transitions between the ground state and excited states with gerade symmetry. The electronically excited states labelled with $1\,^1B_u$ and $2\,^1A_g$ of polyenes have been studied by means of one- and two-photon absorption (fluorescence excitation) experiments[1,2].

C. Normal Coordinate Calculations

The frequencies of some vibrational bands are sensitive to molecular conformation. Normal coordinate calculations are useful for assigning observed vibrational spectra and deducing from them precise structural information. Normal coordinate calculations were

previously performed by means of empirical methods[17,18]. It has recently been demonstrated that *ab initio* molecular orbital (MO) methods are useful for evaluating vibrational spectra[19]. The frequencies calculated at the Hartree–Fock (HF) level are usually higher than those obtained from experiments. Then, the calculated force constants are fitted by the use of parameters, which are called scale factors, to the observed frequencies. In most cases, the scale factor for an off-diagonal force constant is the geometric mean of the scale factors for the corresponding diagonal force constants. The force field thus obtained is called a scaled quantum mechanical (SQM) force field[19]. It is noted that electron correlation is not taken into account explicitly under the HF approximation. Electron correlation is usually introduced by adding the Moller–Plesset (MP) perturbation correction to the HF result. The second-order MP perturbation method is abbreviated to MP2.

D. Vibronic Theory of Resonance Raman Scattering

Resonance Raman spectroscopy has been applied to studies of polyenes for the following reasons. The Raman spectrum of a sample can be obtained even at a dilute concentration by the enhancement of scattering intensity, when the excitation laser wavelength is within an electronic absorption band of the sample. Raman spectra can give information about the location of dipole forbidden transitions, vibronic activity and structures of electronically excited states. A brief summary of vibronic theory of resonance Raman scattering is described here.

The intensity of a Raman transition from the initial vibrational level i of the ground electronic state g to the final vibrational level j of the g state is given by equation 1:

$$I_{gi,gj} = CI_0\nu_0\nu_S^3 \sum_{\rho\sigma} \left|(\alpha_{\rho\sigma})_{gi,gj}\right|^2 \tag{1}$$

where C is a constant, I_0 and ν_0 are the intensity and the frequency of the incident laser light, ν_S is the frequency of the scattered light and $(\alpha_{\rho\sigma})_{gi,gj}$ is the Raman polarizability tensor element, with ρ and σ being labels for the Cartesian coordinates in the molecular frame. Second-order perturbation theory gives equation 2 for the Raman polarizability tensor[20,21].

$$(\alpha_{\rho\sigma})_{gi,gj} = \sum_{ev} \left[\frac{\langle ig|M_\sigma|ev\rangle\langle ve|M_\rho|gj\rangle}{E_{ev} - E_{gi} - E_0 - i\Gamma_{ev}} + \frac{\langle ig|M_\rho|ev\rangle\langle ve|M_\sigma|gj\rangle}{E_{ev} - E_{gj} + E_0 - i\Gamma_{ev}} \right] \tag{2}$$

Here $|gi\rangle$, $|gj\rangle$ and $|ev\rangle$ are the vibronic wavefunctions of the initial, final and intermediate states, respectively; M_σ and M_ρ are the electronic dipole operators of σ and ρ polarizations, respectively; E_0 is the energy of the incident laser photon; E_{gi}, E_{gj} and E_{ev} are the energies of the initial, final and intermediate vibronic levels, respectively; and Γ_{ev} is a damping factor which defines the linewidth of the $|ev\rangle$ vibronic state. When the wavelength of the incident laser light coincides with the electronic absorption band (i.e. $E_{ev} - E_{gi} \approx E_0$), the first term is dominant, and the second term can be neglected because it is much smaller than the first term. In the following discussion the second non-resonant term is neglected.

If Born–Oppenheimer wavefunctions are used to describe the vibronic wavefunctions, the electronic and vibrational portions of the wavefunctions can be separable:

$$\langle ig|M_\sigma|ev\rangle = \langle i|\langle g|M_\sigma|e\rangle|v\rangle = \langle i|M_{ge}^\sigma|v\rangle \tag{3}$$

This integral of the electronic dipole moment operator is a function of a nuclear coordinate Q. The integral may be expanded in a Taylor series with respect to Q (equation 4) and

evaluated at the equilibrium position of the potential surface.

$$M_{ge}^{\sigma} = (M_{ge}^{\sigma})^0 + \sum_a \frac{\partial M_{ge}^{\sigma}}{\partial Q_a} Q_a + \cdots \equiv (M_{ge}^{\sigma})^0 + \sum_a (M_{ge}^{\sigma})'_a Q_a + \cdots \tag{4}$$

Substitution of the first two terms into the Raman polarizability tensor gives the following three terms[22–24]:

$$(\alpha_{\rho\sigma})_{gi,gf} = \alpha^{\mathrm{I}} + \alpha^{\mathrm{II}} + \alpha^{\mathrm{III}} \tag{5}$$

where

$$\alpha^{\mathrm{I}} = \sum_e \sum_v \frac{(M_{ge}^{\sigma})^0 (M_{eg}^{\rho})^0}{E_{ev} - E_{gi} - E_0 - i\Gamma_{ev}} \langle i|v\rangle\langle v|j\rangle \tag{6}$$

$$\alpha^{\mathrm{II}} = \sum_e \sum_v \sum_a \frac{(M_{ge}^{\sigma})'_a (M_{eg}^{\rho})^0 \langle i|Q_a|v\rangle\langle v|j\rangle}{E_{ev} - E_{gi} - E_0 - i\Gamma_{ev}} + \sum_e \sum_v \sum_b \frac{(M_{ge}^{\sigma})^0 (M_{eg}^{\rho})'_b \langle i|v\rangle\langle v|Q_b|j\rangle}{E_{ev} - E_{gi} - E_0 - i\Gamma_{ev}} \tag{7}$$

$$\alpha^{\mathrm{III}} = \sum_e \sum_v \sum_{ab} \frac{(M_{ge}^{\sigma})'_a (M_{eg}^{\rho})'_b \langle i|Q_a|v\rangle\langle v|Q_b|j\rangle}{E_{ev} - E_{gi} - E_0 - i\Gamma_{ev}} \tag{8}$$

In these terms, the electronic integrals such as $(M_{ge}^{\sigma})^0$ and $(M_{ge}^{\sigma})'_a$ are constrained by the symmetry of the electronic states. While term I involves Frank–Condon overlap integrals, terms II and III involve integrals of the form $\langle i|Q_a|v\rangle$; in the harmonic approximation, the integrals of this type obey the selection rule $v = i + 1$. Keeping these considerations in mind, we will next discuss how terms I, II and III contribute to distinct vibrational transitions.

(1) The term I scattering (equation 6) is dominant when the excitation laser wavelength is resonant with an allowed electronic transition ($M^0 \neq 0$, $|M^0| \gg |M'|$). The term I scattering becomes significant if the Frank–Condon overlap integrals $\langle i|v\rangle$ and $\langle v|j\rangle$ have non-zero values simultaneously; it usually provides the enhancement of a series of fundamental, overtone and combination transitions of totally symmetric modes. When the displacement between the adiabatic potential minima of the g and e states is large, the intensities of overtone and combination transitions are greatly enhanced. This term corresponds to the A term of the Albrecht theory[25].

(2) The term II scattering (equation 7) from vibronic activity in allowed electronic transitions mainly results in fundamental transitions of non-totally symmetric vibrations. This term corresponds to the B and C terms of the Albrecht theory[25].

(3) The term III scattering (equation 8) is the weakest in the three scattering mechanisms, as shown by two derivative terms (M') in the electronic transition integrals. Clearly, for a dipole forbidden transition ($M^0 = 0$) the only non-zero term is term III. The term III scattering results in binary overtone and combination transitions of vibronically active modes. It is noted that no fundamental transition survives.

In the case of polyenes, the term I scattering is dominant in the Raman spectra resonant with the $1\,{}^1B_{\mathrm{u}}$ excited states[22,26]; the contribution of the term III scattering is important in the Raman spectra resonant with the $2\,{}^1A_{\mathrm{g}}$ excited states[27]. In addition, an interference effect between the $1\,{}^1B_{\mathrm{u}}$ and $2\,{}^1A_{\mathrm{g}}$ states in a Raman-intensity vs excitation-photon-energy plot (which is called an excitation profile) of the in-phase C=C stretch has been suggested[28].

III. ELECTRONIC SPECTRA

A. Electronic Structure

Let us consider an unsubstituted linear polyene with N C=C double bonds, i.e. $2N\pi$-electrons. The number of molecular orbitals equals the number of π-electrons. These molecular orbitals can be classified into two types: N bonding orbitals and N antibonding orbitals. It has been shown[1,2] that three low-lying singlet states of linear polyenes are described in terms of the configurations shown in Figure 2. The ground state S_0 is well described by the single configuration in which the N bonding orbitals are doubly occupied (Figure 2a). For a normal π-system, the first excited state S_1 is described by the single configuration which is derived from the ground state by promoting one electron from the highest occupied molecular orbital (HOMO) to the lowest unoccupied molecular orbital (LUMO), as shown in Figure 2b. However, in linear polyenes this state is the second excited state S_2. The S_1 state is a correlated state that cannot be written in terms of a single configuration because of electron correlation, but is approximately described by a linear combination of the doubly excited configuration in which two electrons are promoted from the HOMO to the LUMO (Figure 2c) and the double jump configuration in which one electron is promoted from the HOMO to the LUMO + 1 (Figure 2d). Electron correlation is essential for a correct description of the electronic state ordering for linear polyenes[1,2]. In the all-*trans* planar structure (C_{2h} symmetry), S_0 and S_1 have A_g symmetry and are called $1\,^1A_g$ and $2\,^1A_g$, respectively; S_2 has B_u symmetry and is called $1\,^1B_u$. As a result, the transition between S_0 and S_1 is dipole forbidden, whereas the transition between S_0 and S_2 is dipole allowed.

The ultraviolet/visible absorption spectrum of a polyene shows an intense absorption band and an extremely weak absorption band which is located below the strong absorption band, as described in the following section. This spectral pattern is a general property of linear polyenes of all chain lengths independent of local symmetry and/or the presence of *cis* bonds. This is the reason why in the literature on polyenes the labels $1\,^1A_g$ for S_0, $2\,^1A_g$ for S_1 and $1\,^1B_u$ for S_2 are used even in cases where C_{2h} symmetry is not realized. The ordering that the $2\,^1A_g$ excited state is located below the $1\,^1B_u$ excited state is peculiar to linear polyenes.

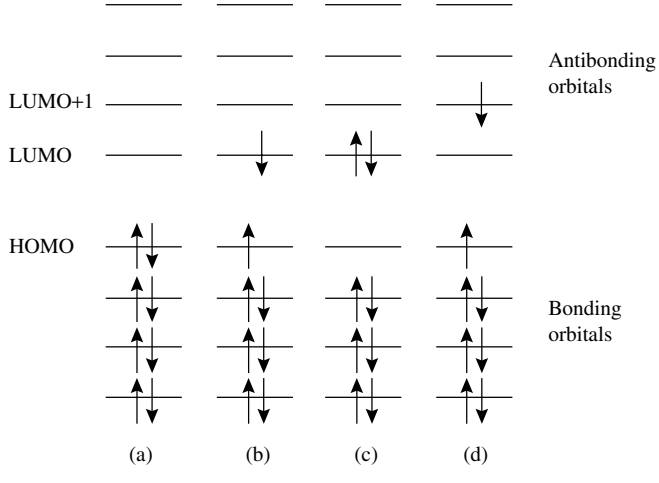


FIGURE 2. Some configurations describing the low-energy singlet states of linear polyenes

TABLE 1. Observed absorption maxima (λ_{max}) and molar absorption coefficients (ε) of unsubstituted all-*trans*-polyenes

$N_{C=C}$	λ_{max}/nm ($\varepsilon/10^3$ $l\,mol^{-1}\,cm^{-1}$)	Solvent	Reference
2	218.5 (23.0)	cyclohexane	30
3	268 (34.6), 257 (42.7), 248 (30.5)	iso-octane	29
4	303 (53), 289 (54.3), 276 (37), 264 (19.9)	95% ethanol	31
5	334 (121), 317 (115), 303 (71.2), 290 (37.1)	iso-octane	29
6	364 (138), 344 (127), 328 (73.2), 313 (37.3)	iso-octane	29
8	410 (108), 386 (112), 367 (72.8), 349 (35.8)	iso-octane	29
10	447, 420, 397, 376	iso-octane	29

TABLE 2. Observed absorption maxima (λ_{max}) and molar absorption coefficients (ε) of all-*trans*-α,ω-dimethylpolyenes

$N_{C=C}$	λ_{max}/nm ($\varepsilon/10^3$ $l\,mol^{-1}\,cm^{-1}$)	Solvent	Reference
2	226.5 (24.0)	cyclohexane	30
3	274.5 (30.2)	hexane	32
4	310 (76.5)	hexane	32
5	341 (122)	hexane	32
6	380 (146.5)	chloroform	32
7	398 (52.5), 375 (56.2), 355 (33.9)	dichloromethane	33
8	420 (53.7), 395 (56.2), 375 (36.3)	dichloromethane	33
9	443 (58.9), 416 (63.1), 393 (43.7)	dichloromethane	33
10	460 (39.8), 431 (60.3), 406 (36.3)	dichloromethane	33

TABLE 3. Observed absorption maxima (λ_{max}) and molar absorption coefficients (ε) of all-*trans*-α,ω-dibutylpolyenes[34]

$N_{C=C}$	λ_{max}/nm ($\varepsilon/10^3$ $l\,mol^{-1}\,cm^{-1}$)	Solvent
2	237.2, 227.8, 219.8	*n*-pentane
3	275.6, 264.8, 255.6	*n*-pentane
4	311.4, 297.4, 284.8, 274.6	*n*-pentane
5	343.0, 325.8, 311.0, 297.8	*n*-pentane
6	371.2, 351.0, 334.2, 319.0	*n*-pentane
7	396.2, 373.6, 355.6, 338.0	*n*-pentane
8	418.8, 394.0, 374.0, 354.2	*n*-pentane
	432 (111), 406 (103), 384 (643)	dichloromethane
9	438.8, 411.2, 390.2, 371.8	*n*-pentane
	452 (114), 424 (101), 402 (65)	dichloromethane
10	456.4, 427.8, 405.2, 382.6	*n*-pentane
11	468.8, 439.4, 414.4, 393.4	*n*-pentane
13	494, 462, 438, 412	*n*-pentane

B. Ultraviolet/Visible Absorption Spectra

The absorption bands or peaks reported for the all-*trans* conformers of unsubstituted polyenes[29–31], α,ω-dimethylpolyenes[30,32,33], α,ω-di-*tert*-butylpolyenes[34], α,ω-diphenylpolyenes[35,36] and α,ω-dithienylpolyenes[37] are complied in Tables 1–5, respectively. The data for carotenoids are described in a previous review[38]. These absorptions are attributed to the $1\,^1B_u \leftarrow 1\,^1A_g$ transitions ($\pi-\pi^*$ transitions).

TABLE 4. Observed absorption maxima (λ_{max}) and molar absorption coefficients (ε) of all-*trans*-α,ω-diphenylpolyenes in benzene[36]

$N_{C=C}$	λ_{max}/nm ($\varepsilon/10^3$ $l\,mol^{-1}\,cm^{-1}$)
1	319 (21.7), 306 (24.3), 294 (23.5)
2	352 (26.1), 334 (40.0), 316 (30.4)
3	377 (52.1), 358 (74.7), 343 (54.3)
4	404 (76.9), 384 (86.0), 363 (58.2)
5	424 (88.6), 403 (93.8), 387 (60.8)
6	445 (109), 420 (113), 400 (76.4)
7	465 (122), 435 (135), 413 (86.9)

TABLE 5. Observed absorption maxima (λ_{max}) of all-*trans*-α,ω-dithienylpolyenes in dichloromethane[37]

$N_{C=C}$	λ_{max}(nm)
3	404, 382, 364
4	426, 402, 380
5	443, 416, 395
6	461, 432, 409

As a typical example of polyene spectroscopy, absorption and fluorescence spectra[39] of *trans*,*trans*-1,3,5,7-octatetraene in hexane at 23 °C are shown in Figure 3. An absorption band with several peaks is observed in Figure 3a. It should be noted that the positions of electronic absorption bands strongly depend on solvents[1,2]. This absorption band is dipole allowed, because the molar absorption coefficient of this band is very large (Table 1). This band is attributed to the transition from the $1\,^1A_g$ ground state to the $1\,^1B_u$ excited state ($\pi-\pi^*$ transition). Although the absorption peaks are due to vibrational transitions, a precise vibrational analysis cannot be made because of the broad band widths. The position of the observed emission spectrum (Figure 3b) shows a considerable red shift in

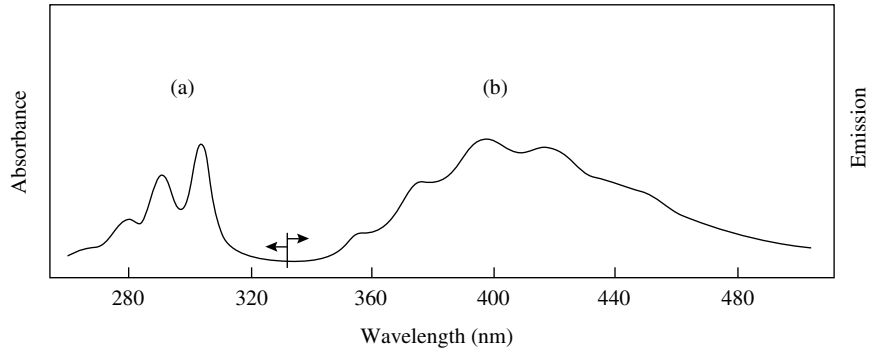


FIGURE 3. (a) Absorption and (b) fluorescence spectra of *trans*,*trans*-1,3,5,7-octatetraene in hexane at 23 °C. Reproduced by permission of American Institute of Physics from Reference 39

comparison with the position of the absorption spectrum. In other words, a large Stokes shift is observed. This emission band is due to the transition from the $2\,^1A_g$ excited state to the $1\,^1A_g$ ground state. The absorption band associated with the $2\,^1A_g \leftarrow {}^1A_g$ transition is not observed, because this absorption is expected to be extremely weak. These assignments of the absorption and emission spectra have been confirmed by the following experiments. In one- and two-photon excitation spectra of *trans*,*trans*-1,3,5,7-octatetraene in *n*-octane at 4.2 K (not shown), fine structures are observed, and these vibronic bands have been analysed[40]. As a result, it has been shown that the 0–0 transition between the $2\,^1A_g$ and $1\,^1A_g$ states is observed at 28561 cm^{-1} (350 nm) and the 0–0 transition between the $1\,^1B_u$ and $1\,^1A_g$ states is observed at 32100 cm^{-1} (312 nm).

The reported[2,41,42] 0–0 transition energies associated with the $2\,^1A_g$ and $1\,^1B_u$ excited states are plotted against $N_{C=C}$ in Figure 4. The transition energy for the $2\,^1A_g$ excited state is always lower than that for the $1\,^1B_u$ state for each polyene. The transition energy for a series of excited states decreases with increasing number of C=C bonds ($N_{C=C}$). The observed $1\,^1B_u \leftarrow 1\,^1A_g$ (0–0) transition energy, E_n, has been fitted by equation 9[34,43]:

$$E_n(\text{eV}) = E_\infty + \frac{k}{N_{C=C}} \tag{9}$$

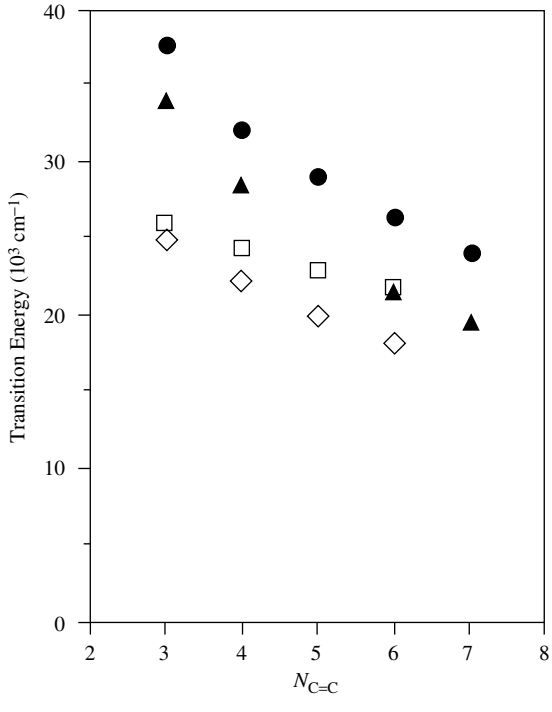


FIGURE 4. Observed 0–0 electronic transition energies (cm^{-1}) of linear polyenes[2,41,42]: ●, $1\,^1B_u \leftarrow 1\,^1A_g$ and ▲, $2\,^1A_g \leftarrow 1\,^1A_g$ for unsubstituted polyenes; □, $1\,^1B_u \leftarrow 1\,^1A_g$ and ◇, $2\,^1A_g \leftarrow 1\,^1A_g$ for *α*,*ω*-diphenylpolyenes

where E_∞ and k are constants. From observed transition energies of α,ω-dibutylpolyenes (Table 3), E_∞ and k are determined to be about 1.56 and 9.5 eV in carbon disulphide, respectively, and about 1.79 and 9.4 eV in pentane, respectively[34]. The differences between these estimated values come from the fact that the observed transition energies are sensitive to solvents. Equation 9 suggests that the $1\,^1B_u$ transition energy approaches a finite limit (E_∞) at infinite chain length. A *trans*-polyacetylene film prepared from the polymerization of acetylene shows a very broad absorption band in the visible region; the peak of the absorption is 1.95 eV and the edge of the absorption is 1.4 eV[44]. The E_∞ values, 1.56 and 1.79 eV, estimated from the data of α,ω-dibutylpolyenes are not in good agreement with the absorption edge, 1.4 eV, of *trans*-polyacetylene.

IV. VIBRATIONAL SPECTRA

A. Butadiene

1. s-Trans conformer

1,3-Butadiene ($CH_2{=}CH{-}CH{=}CH_2$) has two C=C bonds and one C−C bond. It has been shown experimentally that the most stable rotamer has the planar s-*trans* structure[45−47]. The lengths of the C=C and C−C bonds are 1.341 and 1.463 Å, respectively[47]. The infrared and Raman spectra of 1,3-butadiene in the vapour, liquid and solid phases have been studied[48−51]. The spectra of deuterated[51−55] and ^{13}C-substituted[56] analogs have been studied for the purpose of the assignments of vibrational spectra. On the basis of these vibrational spectra, normal coordinate calculations have been performed by the use of empirical force fields[54−60]. The structure and vibrational frequencies of the s-*trans* conformer have been calculated by *ab initio* MO methods[61−65]. The assignments of all the fundamental bands have been established.

The s-*trans* conformer of 1,3-butadiene belongs to C_{2h} symmetry. There are 24 normal modes: $9a_g + 4a_u + 3b_g + 8b_u$. The a_g and b_u modes are the in-plane vibrations, while the a_u and b_g modes are the out-of-plane vibrations; the vibrations of a_g and b_g are Raman active and the vibrations of a_u and b_u are infrared active. The observed and calculated vibrational frequencies of s-*trans*-1,3-butadiene are listed in Table 6. Most of the frequencies calculated even at the MP2/6-311G* level[64] (column 6) are higher than those observed (column 3); most of the frequencies calculated at the MP2/6-31G* level[64] (not shown) are also higher than those observed. However, the frequencies obtained by a scaled MP2/6-31G* calculation[65] (column 7) are in good agreement with those observed. Vibrational modes of some strong Raman and infrared bands are as follows. The 1644-cm^{-1} Raman band (ν_4) is assigned to the vibrational mode in which two C=C bonds stretch in phase. The 1279-cm^{-1} Raman band (ν_6) is assigned to the CH in-plane bending, and the 1206-cm^{-1} Raman band (ν_7) to the C−C stretch. The infrared bands observed at 1022 and 905 cm^{-1} (ν_{10} and ν_{11}, respectively) are assigned to the CH out-of-plane bending and CH_2 wagging, respectively.

The group-coordinate force constants (not shown) obtained by an empirical method[60] are in good agreement with those obtained by a scaled *ab initio* MO calculation at MP2/6-31G* level[65]. Guo and Karplus[64] have calculated group-coordinate force constants at the HF and MP2 levels with various basis sets (6-31G, 6-31G*, 6-311G and 6-311G*). In most cases in-plane diagonal force constants decrease by 5%–15% from the corresponding HF values when electron correlation is included via the MP2 method; the C=C stretch force constant shows an especially larger decrease (20%) with all the basis sets, whereas the C−C stretch force constant shows a smaller decrease (3%) with the 6-31G* and 6-311G* basis sets. It is noted that the C=C/C−C off-diagonal force constant increases by 15%–20% with all the basis sets in going from the HF to the MP2 method.

TABLE 6. Observed and calculated vibrational frequencies (cm^{-1}) of s-*trans*-1,3-butadiene

Sym	No.	Obsd[a]		Calcd			Description
				Empirical[c]	MP2/6-311G*[d]	Scaled MP2/6-31G*[e]	
a_g	ν_1	3105	R, w	3102	3284	3107.0	CH_2 a-stretch
	ν_2	3025	R, m	3039	3178	3020.4	CH stretch
	ν_3	3014	R, m	2997	3189	3005.9	CH_2 s-stretch
	ν_4	1644	R, vs	1645	1719	1643.5	C=C stretch
	ν_5	1441	R, s	1446	1495	1444.8	CH_2 scis
	ν_6	1279	R, s	1296	1325	1285.8	CH ip-bend
	ν_7	1206	R, s	1203	1248	1209.7	C−C stretch
	ν_8	887	R, w	901	914	892.0	CH_2 rock
	ν_9	513	R, m	510	521	511.3	CCC deform
a_u	ν_{10}	1022	IR, vs	1019	1038	1016.4	CH op-bend
	ν_{11}	905	IR, vs	908	891	909.6	CH_2 wag
	ν_{12}	535	IR, m	527	525	526.6	CH_2 twist
	ν_{13}	163[b]	IR, vw	162	156	163.3	C−C torsion
b_g	ν_{14}	974	R, vw	969	980	969.8	CH op-bend
	ν_{15}	908	R, m	910	891	910.6	CH_2 wag
	ν_{16}	754	R, w	751	764	751.4	CH_2 twist
b_u	ν_{17}	3103	IR, m	3101	3284	3115.7	CH_2 a-stretch
	ν_{18}	3062	IR, m	3029	3192	3042.6	CH stretch
	ν_{19}	2986	IR, m	2997	3182	3026.0	CH_2 s-stretch
	ν_{20}	1597	IR, vs	1601	1651	1601.3	C=C stretch
	ν_{21}	1381	IR, s	1387	1429	1387.7	CH_2 scis
	ν_{22}	1297	IR, w	1293	1335	1293.9	CH ip-bend
	ν_{23}	988	IR, w	995	1016	987.2	CH_2 rock
	ν_{24}	301[b]	IR, vw	300	298	299.8	CCC deform

[a]Reference 60. In an Ar matrix. R, Raman; IR, infrared; vs, very strong; s, strong; m, medium; w, weak; vw, very weak.
[b]Reference 51.
[c]Reference 60.
[d]Reference 64.
[e]Reference 65.

Resonance Raman spectra of 1,3-butadiene vapour have been observed with several laser lines between 239.5 and 165.7 nm[27,66,67]. A broad absorption spectrum due to the $1\,^1B_u \leftarrow 1\,^1A_g$ transition is observed in the region from 230 to 190 nm; the peak which is attributed to the 0–0 transition is observed at 215.2 nm[27]. Figure 5 shows the Raman spectra taken with excitation wavelengths between 239.5 and 199.8 nm. The intensities of fundamental, combination and overtone transitions of totally symmetric modes are prominent in the spectra taken with the 212.8- and 199.8-nm laser lines (Figures 5e and 5f); these features appear because of the resonance enhancement with the allowed $1\,^1B_u$ state through the term I (Frank–Condon) scattering mechanism. The ν_4 (the C=C stretch) and ν_7 (the C−C stretch) transitions and their overtone and combination transitions are especially enhanced, because the ν_4 and ν_7 modes suffer the largest displacement in equilibrium position in going from the ground electronic state to the $1\,^1B_u$ excited state. Since the $1\,^1B_u$ state results from a π–π^* excitation, one would expect the C=C double bond distances to become longer and the C−C single bond distance to become shorter. On the other hand, a Raman spectrum resonant with the $1\,^1B_u$ excited state has been calculated from the quantum chemical force field (QCFF/PI) method[22]; the results

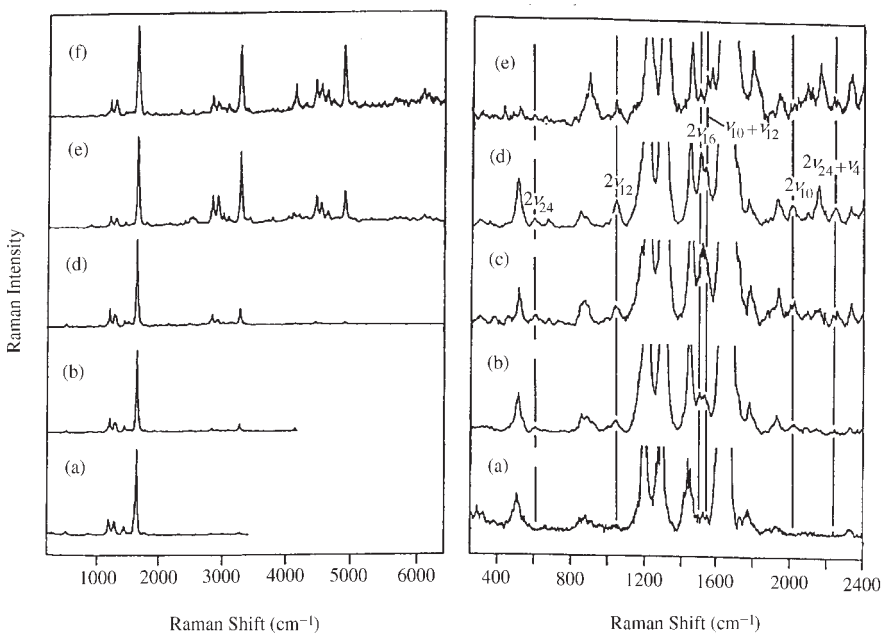


FIGURE 5. Raman spectra of s-*trans*-1,3-butadiene vapour. Excitation wavelengths: (a) 239.5 nm; (b) 228.7 nm; (c) 223.1 nm; (d) 217.9 nm; (e) 212.8 nm; (f) 199.8 nm. The spectra shown on the right are expansions. Reproduced by permission of American Institute of Physics from Reference 27

obtained have shown that the term I contributions to the a_g modes are much larger than the corresponding term II contributions.

In the case of the forbidden $2\,^1A_g \leftarrow 1\,^1A_g$ transition, the contribution of the term III scattering to Raman intensities is important, as described in Section II.D. In the Raman spectra taken with the 228.7-, 223.1- and 217.9-nm laser lines (Figures 5b–5d), the intensity of the 600-cm^{-1} band due to the binary overtone of $\nu_{24}(b_u)$ is enhanced; the ν_{24} band is assigned to the in-plane CCC deform (Table 6). It has been shown[27,66] that $2\nu_{24}$ is enhanced by resonance with the $2\,^1A_g$ state through the $\langle 0_{24}|Q_{24}|1_{24}\rangle\langle 1_{24}|Q_{24}|2_{24}\rangle$ term. It should be noted that the ν_{24} fundamental band is not enhanced through the term III scattering mechanism. The vibronic coupling matrix elements between the $2\,^1A_g$ and $1\,^1B_u$ excited states are non-zero for promoting modes with b_u symmetry; calculations of these matrix elements for the eight b_u modes have shown that ν_{24} is expected to be the most active mode[27]. In the case of *trans*,*trans*-1,3,5,7-octatetraene, a similar b_u CCC deform is a promoting mode which is active in vibronic coupling between the $1\,^1B_u$ and $2\,^1A_g$ excited states[1]. From the Raman results of 1,3-butadiene, the $2\,^1A_g$ electronic state has been estimated to be about 2000 cm^{-1} below the $1\,^1B_u$ state.

The Raman spectra of 1,3-butadiene have also been taken with the excitation wavelengths in the range between 425 and 270 nm (pre-resonance conditions)[68]. The pre-resonance Raman excitation profiles have been analysed by the term I scattering mechanism associated with the $1\,^1B_u$ state, and the bond lengths and bond angles of this state have been estimated; for example, the estimated lengths of the C_1C_2 and C_2C_3 bonds are 1.418 and 1.403 Å, respectively. The term II contributions to the b_g

(non-totally symmetric) modes in a non-resonant condition are clearly shown in the spectrum calculated at the QCFF/PI method[22].

2. Gauche conformer

The potential energy function around the C−C bond of 1,3-butadiene has been studied by measuring the fundamental and overtones of the C−C torsional vibration[69]. The structure of the second stable conformer (planar s-*cis* or *gauche*), however, was not determined, because few bands due to the second stable conformer were observed. The second stable conformer has been detected by means of the combination of matrix-isolation infrared spectroscopy and a high-temperature nozzle technique[56,60,70]. The structure of the second stable conformer has been proposed to be planar s-*cis*, on the basis of the following reasons[71]. The position of the observed electronic absorption maximum of the second stable conformer is lower in energy than that of the s-*trans* conformer; this red shift has been attributed to the s-*cis* conformer on the basis of the results of molecular orbital calculations[71]. On the other hand, a *gauche* structure is proposed from a vibrational study[60]. A polarized infrared study has supported the s-*cis* conformation (maximum dihedral angle, 10–15°)[72]. However, Bock and Panchenko[73] have argued that there is no direct correlation between the shift of the electronic absorption maximum and the conformation of 1,3-butadiene, and the polarization measurements can be interpreted in terms of a *gauche* structure. *Ab initio* MO calculations at high levels[63,64,74–76] have been performed, and all the results have indicated that the second stable conformer has *gauche* structures. High-level *ab initio* MO calculations[63,64,74–76] indicate that CCCC dihedral angles are in the range between 35° and 40° and barriers to the s-*cis* transition state are in the range between 0.5 and 1.0 kcal mol^{-1}.

Vibrational spectroscopy has given us evidence that the second stable conformer has a *gauche* structure. A *gauche* structure has C_2 symmetry. There are 24 normal modes: $13a + 11b$. The *a* and *b* modes are both Raman and infrared active. On the other hand, the s-*cis* conformer has C_{2v} symmetry. There are 24 normal modes: $9a_1 + 4a_2 + 8b_1 + 3b_2$. The a_1 and b_1 modes are the in-plane vibrations whilst the a_2 and b_2 modes are the out-of-plane vibrations. The vibrations of a_1, b_1 and b_2 species are infrared active, whereas all the vibrations are Raman active. It is noted that the infrared inactive a_2 vibrations of the s-*cis* conformer are correlated with the infrared active *a* vibrations of a *gauche* conformer. The observed infrared bands have been reasonably assigned to a *gauche* conformer, on the basis of the results of empirical normal coordinate calculations[60] and high-level *ab initio* MO calculations[63,64,75,76]. The observed and calculated vibrational frequencies of *gauche*-1,3-butadiene are listed in Table 7. What is important is that the 727-cm^{-1} band is reasonably assigned to $\nu_{11}(a)$. The corresponding bands are observed at 594, 587 and 731 cm^{-1} for 1,3-butadiene-1,1,4,4-d_4,-d_6 and -1,4-$^{13}C_2$, respectively[56,60]. These observations support the assignment of $\nu_{11}(a)$. The 1087-cm^{-1} band has been attributed to ν_{20} in Reference 56 and 64, but to ν_7 in Reference 60. A scaled MP2/6-31G* calculation[63] indicates that the infrared intensity of ν_{20} is much larger than that of ν_7. The 1087-cm^{-1} band is thus assigned to ν_{20}.

The second stable conformer of isoprene ($H_2C{=}C(CH_3)CH{=}CH_2$) has also been studied experimentally[77,78] and theoretically[79–81]. It has been concluded that the second stable conformer has a *gauche* structure[78–81].

B. Hexatriene

1,3,5-Hexatriene ($CH_2{=}CH{-}CH{=}CH{-}CH{=}CH_2$) has three C=C bonds and two C−C bonds. There exist geometrical isomers around the central C=C bond and rotamers around

TABLE 7. Observed and calculated vibrational frequencies (cm^{-1}) of *gauche*-1,3-butadiene

Sym	Sym[a]	No.	Obsd[b]		Calcd			Description
					Empirical[f]	MP2/6-311G*[g]	Scaled MP2/6-31G*[h]	
a	a_1	ν_1	3103[c]	IR, m	3098	3286	3110	CH_2 a-stretch
	a_1	ν_2	3014[c]	IR, w	3032	3197	3035	CH stretch
	a_1	ν_3	2986[c]	IR, m	3000	3183	3024	CH_2 s-stretch
	a_1	ν_4	1633	IR, w	1629	1687	1641	C=C stretch
	a_1	ν_5	1425	IR, m	1432	1487	1464	CH_2 scis
	a_1	ν_6	—	—	1328	1350	1313	CH ip-bend
	a_1	ν_7	—	—	1081	1086	1057	CH_2 rock
	a_2	ν_8	983	IR, vw	982	1001	1004	CH op-bend
	a_2	ν_9	915[d]	IR, vs	915	914	943	CH_2 wag
	a_1	ν_{10}	—	—	872	905	859	C−C stretch
	a_2	ν_{11}	727	IR, w	731	754	733	CH_2 twist
	a_1	ν_{12}	—	—	256	277	281	CCC deform
	a_2	ν_{13}	136[e]		137	190	151	C−C torsion
b	b_1	ν_{14}	3103[c]	IR, m	3098	3284	3108	CH_2 a-stretch
	b_1	ν_{15}	3014[c]	IR, w	3032	3179	3028	CH stretch
	b_1	ν_{16}	2986[c]	IR, m	3001	3188	3014	CH_2 s-stretch
	b_1	ν_{17}	1612	IR, vw	1619	1688	1645	C=C stretch
	b_1	ν_{18}	1403	IR, w	1413	1453	1431	CH_2 scis
	b_1	ν_{19}	—	—	1278	1317	1284	CH ip-bend
	b_1	ν_{20}	1087	IR, w	1040	1112	1101	CH_2 rock
	b_2	ν_{21}	996	IR, vs	996	1024	1017	CH op-bend
	b_2	ν_{22}	914	IR, vs	907	910	946	CH_2 wag
	b_1	ν_{23}	596	IR, w	597	632	619	CCC deform
	b_2	ν_{24}	470	IR, m	465	462	455	CH_2 twist

[a]Corresponding symmetry species of the s-*cis* conformer with C_{2v} symmetry.
[b]Reference 60. In an Ar matrix. R, Raman; IR, infrared; vs, very strong; s, strong; m, medium; w, weak; vw, very weak.
[c]Double assignments.
[d]Estimated from the observed 1829 cm^{-1} band ($\nu_9 + \nu_{22}$).
[e]Reference 69.
[f]Reference 60.
[g]Reference 64.
[h]Reference 63.

the C−C bonds (Figure 6). The *trans* and *cis* structures around the central C=C bond are denoted as T and C, respectively, and the *trans*, *gauche* and *cis* structures around the C−C bonds as t, g and c, respectively. The two stable conformers, tTt (Figure 6a) and tCt (Figure 6d), exist at room temperature; the tTt and tCt conformers are called *trans*- and *cis*-1,3,5-hexatriene, respectively.

1. Trans conformer

A gas-phase electron diffraction study[82] has shown that *trans*-hexatriene has a planar structure and the lengths of the terminal C=C, central C=C and C−C bonds are 1.337, 1.368 and 1.458 Å, respectively. The infrared and Raman spectra of *trans*-hexatriene[83−86] and its deuterated analogs[87−89] have been reported. Normal coordinate calculations have been performed by the extended Pariser–Parr–Pople CI method[90], the QCFF/PI method[88] and *ab initio* MO methods[62,91−94]. There are 36 normal modes: $13a_g + 6a_u + 12b_u + 5b_g$.

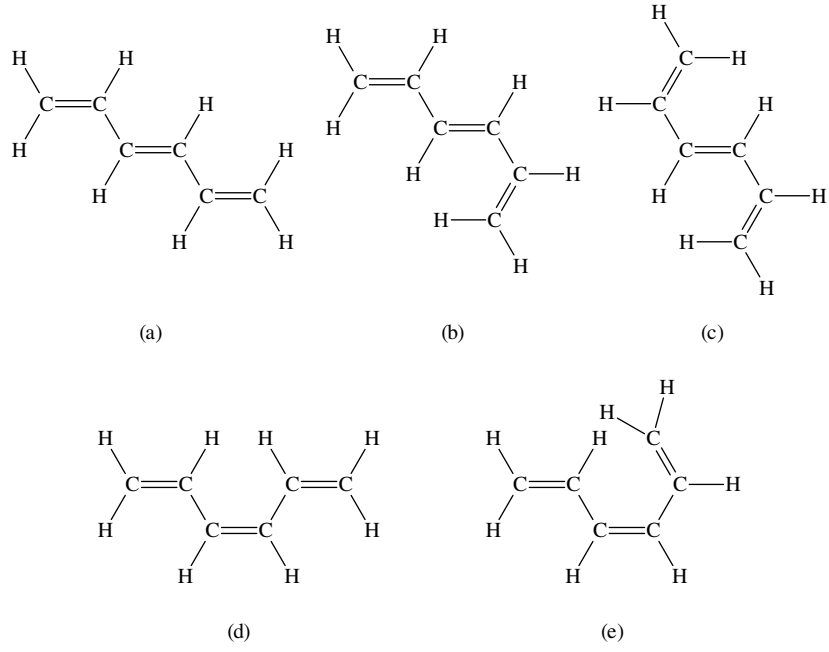


FIGURE 6. Conformers of 1,3,5-hexatriene: (a) tTt (*trans*); (b) gTt; (c) gTg; (d) tCt (*cis*); (e) gCt

The a_g and b_u modes are the in-plane vibrations whilst the a_u and b_g modes are the out-of-plane vibrations. The observed vibrational spectra and calculated frequencies are shown in Table 8. The assignments of the fundamental bands except ν_2, ν_8 and ν_{23} have been established. The 3017-cm^{-1} Raman band reported in Reference 89 is tentatively assigned to ν_2, although this band is not observed in References 85, 86 and 93. The medium-intensity Raman band observed at 1288 cm^{-1} in Reference 85 probably corresponds to the 1283-cm^{-1} band in Reference 86; this band is assigned to ν_9. The very weak Raman band at 1320 cm^{-1} has been assigned to ν_9 in Reference 85, whereas the Raman band observed at 1288 cm^{-1} as a shoulder in a carbon disulphide solution has been assigned to ν_9 in Reference 86. According to the assignments in Reference 93, the Raman band observed at 651 cm^{-1} in the solid state has been tentatively assigned to ν_{23}. Vibrational modes of some strong Raman and infrared bands are as follows. The 1626-cm^{-1} Raman band (ν_5) is assigned to the vibrational mode in which three C=C bonds stretch in-phase. The 1288-cm^{-1} band (ν_9) is assigned to the CH in-plane bend. The 1191-cm^{-1} Raman band (ν_{10}) is assigned to the in-phase C−C stretch. The 1009-cm^{-1} infrared band (ν_{14}) is assigned to the in-phase CH out-of-plane bending of *trans* −CH=CH−. The 900-cm^{-1} infrared band (ν_{16}) is assigned to the CH_2 wagging.

2. Cis conformer

A gas-phase electron diffraction study[95] has shown that *cis*-hexatriene has a slightly twisted structure (torsional angle of 10° around the central C=C bond) and the lengths of the terminal C=C, central C=C and C−C bonds are 1.336, 1.362 and

TABLE 8. Observed and calculated vibrational frequencies (cm^{-1}) of *trans*-1,3,5-hexatriene

Sym	No.	Obsd[a]		Calcd		Description
				Scaled HF/6-31G[g]	Scaled MP2/ 6-31G*[h]	
a_g	ν_1	3089	R, m	3097	3106	CH_2 a-stretch
	ν_2	3017[b]	R, w	3022	3019	CH_2 s-stretch
	ν_3	3000	R, m	3012	3005	CH stretch
	ν_4	2992	R, m	3008	2992	CH stretch
	ν_5	1626	R, vs	1649	1637	C=C stretch
	ν_6	1576	R, w	1558	1571	C=C stretch
	ν_7	1399	R, m	1405	1397	CH_2 scis
	ν_8	1288[c]; 1320[d]	R, w, sh; R, vw	1298	1296	CH ip-bend
	ν_9	1288[d]	R, m	1275	1288	CH ip-bend
	ν_{10}	1191	R, s	1197	1195	C−C stretch
	ν_{11}	932	R, w	930	938	CH_2 rock
	ν_{12}	443	R, w	429	436	CCC deform
	ν_{13}	353	R, w	344	349	CCC deform
a_u	ν_{14}	1009	IR, vs	1018	1020	CH op-bend
	ν_{15}	941	IR, m	939	942	CH op-bend
	ν_{16}	900	IR, vs	903	901	CH_2 wag
	ν_{17}	682	IR, m	672	680	CH_2 twist
	ν_{18}	248[e]	IR, vw	246	245	C=C torsion
	ν_{19}	94[e]	IR, vw	98	98	C−C torsion
b_g	ν_{20}	986	R, vw	991	988	CH op-bend
	ν_{21}	903	R, w	913	901	CH_2 wag
	ν_{22}	868	R, vw	858	866	CH op-bend
	ν_{23}	615[f]	R, vw	589	600	C=C torsion
	ν_{24}	215[e]	R, vw	221	215	C−C torsion
b_u	ν_{25}	3091	IR, m	3097	3106	CH_2 a-stretch
	ν_{26}	3039	IR, m	3022	3018	CH stretch
	ν_{27}	3008	IR, m	3017	3006	CH_2 s-stretch
	ν_{28}	2969	IR, w	3006	2994	CH stretch
	ν_{29}	1624	IR, s	1618	1624	C=C stretch
	ν_{30}	1429	IR, m	1444	1431	CH_2 scis
	ν_{31}	1294	IR, w	1293	1287	CH ip-bend
	ν_{32}	1255	IR, w	1251	1254	CH ip-bend
	ν_{33}	1128	IR, w	1125	1123	C−C stretch
	ν_{34}	964	IR, vw	955	960	CH_2 rock
	ν_{35}	541	IR, w	533	544	CCC deform
	ν_{36}	152[e]	IR, w	145	148	CCC deform

[a] Reference 93. Observed in liquid.
[b] Reference 89.
[c] Reference 86. Observed in CS_2 solution.
[d] Reference 85. Observed in liquid.
[e] Reference 86. Observed in vapour.
[f] Observed in solid at low temperature.
[g] Reference 93.
[h] Reference 94.

1.462 Å, respectively. The infrared and Raman spectra of *cis*-hexatriene[84−86,96] and its deuterated analogs[87,88] have been reported. The structures and vibrational frequencies have been calculated by means of MO methods[87,88,91,93,94]. According to *ab initio* MO calculations[91,93,94] (HF/6-31G, HF/6-31G* and MP2/6-31G* levels), *cis*-hexatriene has a planar structure. The observed vibrational spectra have been reasonably explained by the

TABLE 9. Observed and calculated vibrational frequencies (cm^{-1}) of *cis*-1,3,5-hexatriene

Sym	No.	Obsd[a]		Calcd		Description
				Scaled HF/631G[c]	Scaled MP2/ 6-31G*[d]	
a_1	ν_1	3090	R, w	3097	3105	CH_2 a-stretch
	ν_2	—	—	3051	3038	CH stretch
	ν_3	3011	R, m	3032	3016	CH stretch
	ν_4	2995	R, m	3014	3012	CH_2 s-stretch
	ν_5	1626	R, vs	1649	1637	C=C stretch
	ν_6	1580	R, vw	1548	1558	C=C stretch
	ν_7	1397	R, m; IR, vw	1405	1397	CH_2 scis
	ν_8	1318	R, m; IR, w	1317	1314	CH ip-bend
	ν_9	1247	R, s	1254	1249	CH ip-bend
	ν_{10}	1084	R, w; IR, vw	1080	1085	C−C stretch
	ν_{11}	883	R, w	862	875	CH_2 rock
	ν_{12}	392	R, m	383	390	CCC deform
	ν_{13}	166	R, w	164	173	CCC deform
a_2	ν_{14}	990; 1032[b]	R, vw; R, vw	1007	985	CH op-bend
	ν_{15}	953	R, w	962	918	CH op-bend
	ν_{16}	905	R, w	908	901	CH_2 wag
	ν_{17}	705	R, w	701	689	CH_2 twist
	ν_{18}	331	R, w	324	312	C=C torsion
b_1	ν_{19}	155[b]	R, vw	148	140	C−C torsion
	ν_{20}	3089	IR, s	3096	3105	CH_2 a-stretch
	ν_{21}	3045	IR, m	3033	3025	CH stretch
	ν_{22}	3014	IR, m	3015	3013	CH_2 s-stretch
	ν_{23}	2979	IR, w	3007	2994	CH stretch
	ν_{24}	1616	IR, s	1611	1617	C=C stretch
	ν_{25}	1449	IR, s; R, vw	1456	1448	CH_2 scis
	ν_{26}	1355	IR, vw	1347	1350	CH ip-bend
	ν_{27}	1279	IR, w	1284	1274	CH ip-bend
	ν_{28}	1185	IR, w; R, w	1189	1192	C−C stretch
	ν_{29}	950	IR, m; R, w	944	950	CH_2 rock
	ν_{30}	675	IR, vw	675	679	CCC deform
	ν_{31}	356	IR, w; R, vw	346	352	CCC deform
b_2	ν_{32}	989	IR, s	994	988	CH op-bend
	ν_{33}	906	IR, vs	915	904	CH_2 wag
	ν_{34}	815	IR, m	789	838	CH op-bend
	ν_{35}	590	IR, s	576	587	CH_2 twist
	ν_{36}	100[b]	IR	101	101	C−C torsion

[a]Reference 93. Observed in liquid.
[b]Reference 86.
[c]Reference 93.
[d]Reference 94.

planar structure (C_{2v} symmetry). There are 36 normal modes: $13a_1 + 6a_2 + 12b_1 + 5b_2$. The a_1 and b_1 modes are the in-plane vibrations and the a_2 and b_2 modes are the out-of-plane vibrations. The a_1, b_1 and b_2 vibrations are infrared active and all the vibrations are Raman active. The observed and calculated vibrational frequencies are shown in Table 9. The assignments of the fundamental bands except ν_2, ν_{14} and ν_{26} have been established. Vibrational modes of some strong Raman and infrared bands are as follows. The 1626-cm^{-1} Raman band (ν_5) is assigned to the in-phase C=C stretch. The frequency of this mode is almost equal to that of *trans*-1,3,5-hexatriene. The 1247-cm^{-1} Raman band (ν_9) is assigned to the CH in-plane bending. The 883-cm^{-1} Raman band (ν_{11}) is

assigned to the C−C stretch. The 906-cm^{-1} infrared band (ν_{33}) is assigned to the CH_2 wagging. The 815-cm^{-1} infrared band (ν_{34}) is assigned to the CH out-of-plane bending of *cis* −CH=CH−.

3. Other conformers

Unstable conformers of *trans*- and *cis*-hexatriene have been detected by means of the combination of matrix-isolation infrared spectroscopy and photoexcitation (or the high-temperature nozzle technique)[84]. *Ab initio* MO calculations at the HF/6-31G level have been performed for several conformers of 1,3,5-hexatriene[93]. The observed infrared bands of unstable conformers have been attributed to the gTt (major species) and gTg (minor species) conformers of *trans*-hexatriene and the gCt conformer of *cis*-hexatriene[93]. It is noted that, in the previous paper[93], the notation c is used for twisted structures for the sake of simplicity. The calculated torsional angles around C−C bonds for the gTt, gTg and gCt conformers are in the range between 32° and 45°. The observed and calculated vibrational frequencies of gTt and gCt are reported in Reference 93.

C. Long Chain Polyenes

1. All-trans conformers

The Raman spectra of all-*trans*-α,ω-dibutylpolyenes have been studied[97] systematically as a function of $N_{C=C}$ from 3 to 12. The observed Raman spectra of α,ω-dibutylpolyenes are shown in Figure 7. Four branches which are called ν_1, ν_2, ν_3 and ν_4 are observed. Figure 8 shows the plots of observed Raman frequencies against $N_{C=C}$ for unsubstituted polyenes[60,93,98,99], α,ω-dibutylpolyenes[97] and carotenoids [β-carotene[100] (Figure 1c), rhodovibrin[101], spirilloxanthin[101], decapreno-β-carotene[102] ($C_{50}H_{68}$) and dodecapreno-β-carotene[102] ($C_{60}H_{80}$)]. *Trans*-polyacetylene gives rise to the Raman bands similar to those of polyenes[103−107]. A *trans*-polyacetylene film consists of all-*trans* conjugated segments with various conjugation lengths[5−7]. The all-*trans* structure is schematically shown in Figure 9a. Figure 4 and Tables 1–5 show that with increasing $N_{C=C}$, the electronic absorption maximum of the $1\,^1B_u \leftarrow 1\,^1A_g$ transition shifts to longer wavelengths. Thus, a Raman spectrum taken with a red laser line provides Raman bands arising from a long segment, whose conjugation length is not accurately determined. In the Raman spectrum taken with the 632.8-nm laser line[107], the 1457-, 1294-, 1174- and 1066-cm^{-1} Raman bands are observed. These frequencies are shown as dotted lines in Figure 8, in comparison with those of the polyenes. The 1457-, 1294- and 1066-cm^{-1} bands are assigned to optically active a_g modes under the infinite all-*trans* structure (C_{2h} symmetry), whereas the 1174-cm^{-1} band is assigned to an optically inactive mode[107]. Normal coordinate calculations have been performed for the all-*trans* conformers of unsubstituted polyenes ($N_{C=C}$ = 4–6)[59,62,98,99,108−112] and the infinite all-*trans* structure[107,111,113−121].

The frequency of the ν_1 band, which is assigned to the in-phase C=C stretch, is not affected by the substitution of hydrogen atoms with alkyl groups. The ν_1 frequency is sensitive to $N_{C=C}$[102,103]. As $N_{C=C}$ increases, the ν_1 frequency decreases drastically; the ν_1 frequency shows a downshift of about 190 cm^{-1} in going from 1,3-butadiene to *trans*-polyacetylene. *Ab initio* MO calculations[99,111,112] at the HF and MP levels have shown that electron correlation has a profound effect on the frequency of the in-phase C=C stretches (ν_1). While these unusually low frequencies of the ν_1 bands for the ground state ($1\,^1A_g$) are observed, unusually high frequencies of corresponding modes are observed for the $2\,^1A_g$ electronically excited state; these results have been explained[3] by the vibronic

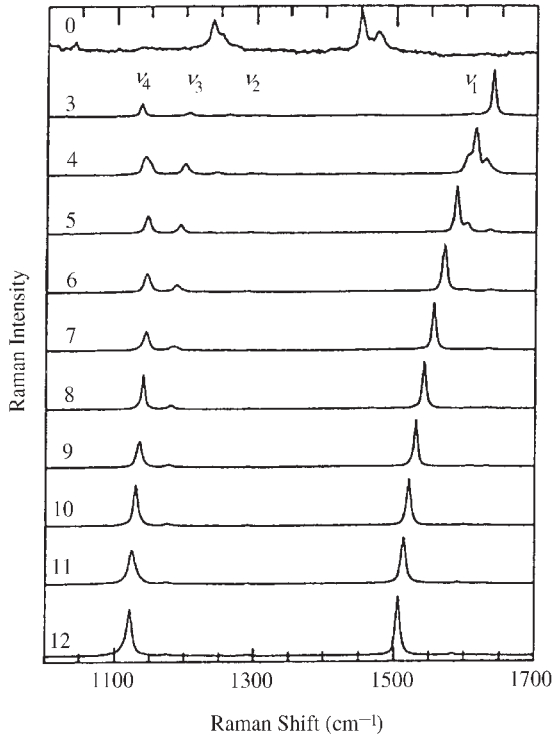


FIGURE 7. Raman spectra of α,ω-dibutylpolyenes in solid ($N_{C=C} = 3$–12). Reproduced by permission of American Institute of Physics from Reference 97

coupling between the $1\,^1A_g$ ground state and the $2\,^1A_g$ excited state. The observed ν_1 frequencies have been fitted by equation 10[122] and equation 11[97]:

$$\nu_1(\text{cm}^{-1}) = \nu_\infty + \frac{K}{N_{C=C} + 1} \tag{10}$$

where $\nu_\infty = 1454\ \text{cm}^{-1}$ (the observed ν_1 frequency of *trans*-polyacetylene) and $K = 727\ \text{cm}^{-1}$, and

$$\nu_1(\text{cm}^{-1}) = \nu'_\infty + \frac{K'}{N_{C=C}} \tag{11}$$

where $\nu'_\infty = 1438\ \text{cm}^{-1}$ and $K' = 830\ \text{cm}^{-1}$; these values have been obtained from the observed ν_1 frequencies of α,ω-dibutylpolyenes ($N_{C=C} = 7$–12). By using equation 10 or 11, it is possible to estimate $N_{C=C}$ of the all-*trans* structure from the observed ν_1 frequency. It should be noted that equation 10 or 11 gives a rough estimation of $N_{C=C}$ in the region of large $N_{C=C}$ values.

The ν_2 band is assigned to a mixture of the C−C and C=C stretches. The frequencies of the ν_2 bands are insensitive to $N_{C=C}$.

The ν_3 and ν_4 bands are assigned to mixtures of CH in-plane bend and C=C and C−C stretches. The frequencies of these bands are affected significantly by the substitution of

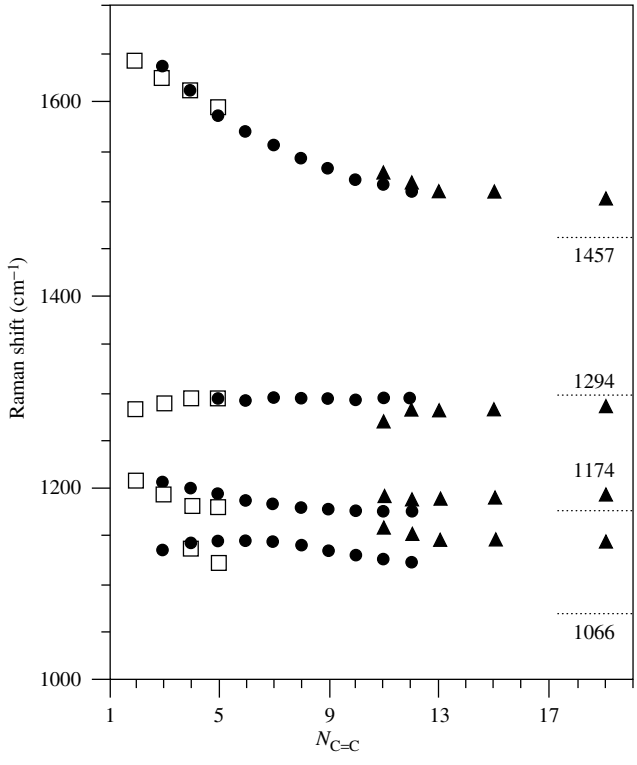
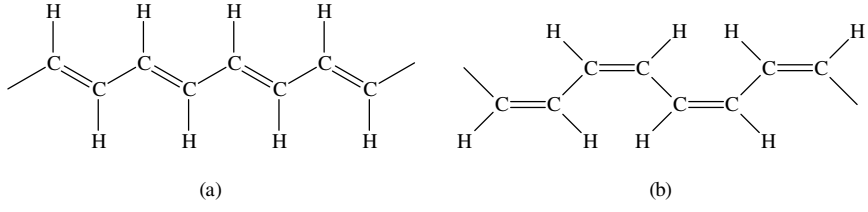


FIGURE 8. Relationship between $N_{C=C}$ and observed Raman frequencies: □, unsubstituted polyenes[60,93,98,99]; ●, α,ω-dibutylpolyenes[97]; ▲, carotenoids (β-carotene[100] [$N_{C=C} = 11$], rhodovibrin[101] [$N_{C=C} = 12$], spirilloxanthin[101] [$N_{C=C} = 13$], decapreno-β-carotene[102] [$N_{C=C} = 15$] and dodecapreno-β-carotene[102] [$N_{C=C} = 19$]). Dotted lines and figures refer to the observed Raman frequencies of *trans*-polyacetylene[107]



(a) (b)

FIGURE 9. Chemical structures of polyacetylene: (a) *trans-transoid (trans)*; (b) *cis-transoid (cis)*

hydrogen atoms with alkyl groups. In a series of unsubstituted polyenes, the intensity of the ν_3 band is much larger than that of the ν_4 band. On the other hand, for a series of α,ω-dibutylpolyenes, the intensity of the ν_4 band is much larger than that of the ν_3 band. These observations indicate that the mode mixing between ν_3 and ν_4 for α,ω-dibutylpolyenes is different from that for unsubstituted polyenes. The spectral features of α,ω-dibutylpolyenes are similar to that of *trans*-polyacetylene.

It has been reported[123] that infrared frequencies of the CH out-of-plane bending vibrations of olefins are sensitive to the number and position of hydrogen atoms attached to the C=C bond. The in-phase CH out-of-plane bending vibrations are observed in the range between 1009 and 1015 cm^{-1}: 1009, 1011, 1010 and 1015 cm^{-1}, for *trans*-hexatriene[90], *trans*,*trans*-1,3,5,7-octatetraene[98], all-*trans*-1,3,5,7,9-decapentaene[99] and *trans*-polyacetylene[124], respectively.

2. Cis conformers

In addition to the vibrational spectra of *cis*-hexatriene, only the frequencies 1604 and 1260 cm^{-1} of *cis*,*cis*-octatetraene[125] have been reported for unsubstituted polyenes. Raman studies[13,126] of the β-carotene conformers with one or two *cis* C=C bonds have shown that frequencies and intensities of several Raman bands in the region between 1300 and 1100 cm^{-1} are sensitive to the conformation of β-carotene. The Raman and infrared spectra of all-*trans* retinal and its geometrical isomers with one or two *cis* bonds are described in a previous review[11]. A *cis*-polyacetylene film contains mainly all-*cis* conjugated segments[7,124]. The all-*cis* structure is shown schematically in Figure 9b. In the Raman spectrum[127] of a *cis*-polyacetylene film, strong bands are observed at 1540, 1250 and 910 cm^{-1}; these bands have been assigned to the a_g modes of the infinite all-*cis* structure (D_{2h} symmetry). Normal coordinate calculations have been performed for the infinite all-*cis* structure[118,128]. The 1540-, 1250- and 910-cm^{-1} bands of *cis*-polyacetylene correspond to the 1626-, 1247- and 883-cm^{-1} bands of *cis*-1,3,5-hexatriene, respectively. Since the number of the C=C bonds of all-*cis* conjugated segments in *cis*-polyacetylene is believed to be large, it is likely that the frequency dispersion of the C=C stretches for all-*cis* polyenes is smaller than that for all-*trans* polyenes. It has been reported[123] that the CH out-of-plane bending vibrations of *cis* −CH=CH− are observed between 675 and 730 cm^{-1} for olefins. The corresponding vibration is observed at 815 cm^{-1} for *cis*-hexatriene. The strong infrared band observed at 740 cm^{-1} for *cis*-polyacetylene is assigned to the CH out-of-plane bending[124]; the corresponding bands are observed at 810, 800, 760 and 748 cm^{-1} for *cis*-copoly(acetylene + acetylene-d_2), and these bands have been attributed to the *cis* CH out-of-plane bending vibrations of $(-CH=CH-)_1$, $(-CH=CH-)_2$, $(-CH=CH-)_{3-5}$ and $(-CH=CH-)_n$ ($n \geqslant 6$), respectively[124]. The CH out-of-plane bending is thus a marker for *cis* −CH=CH−.

Since there are few studies on the vibrational spectra of polyenes with *cis* C=C bonds, experimental studies of *cis* polyenes are required.

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CHAPTER **6**

Electronic structure of diene and polyene radical cations

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I. INTRODUCTION

The present review is intended as a convenient starting point for chemists interested in the electronic structure of diene and polyene radical cations, by providing leading references to publications dealing with particular molecules, and by presenting the essential ground rules governing their electronic structure. With regard to the latter we have tried to avoid — as much as possible — sophisticated treatments dear to the specialists of theoretical chemistry, by using only such concepts of molecular orbital theory that can be found in elementary introductions[1] (in particular, the Hückel HMO model[2]), or even in modern textbooks such as Atkins's *Physical Chemistry*[3]. In other words, we shall try to discuss our topic by translating the results of more complex theoretical treatments into the type of HMO formalism to which chemists have become accustomed in the wake of the Woodward–Hoffmann rules[4,5]. Whenever we need to refer to more advanced theoretical methods, we shall do so on an elementary, qualitative level.

We are aware that our review is by no means complete, the topic of diene and polyene radical cations having ramifications into such diverse fields as biology or interstellar chemistry. In the following we shall first discuss the photoelectron spectra of dienes

and polyenes, not only because of their relative simplicity, but also because the results derived from them form the basis for the detailed investigations using more sophisticated methods. In a second section we turn to other, often complementary methods which have been used for probing the electronic structure of polyene radical cations. In particular we shall discuss the relationship between the photoelectron spectra of polyenes and the electronic absorption spectra of the corresponding radical cations, as well as the necessary implementation of the simple HMO formalism needed for an adequate correlation of such data.

It should be mentioned that the present review does not cover in detail the ground-state electronic and/or molecular structure of diene and polyene radical cations as revealed, for example, by electron spin resonance (ESR) spectroscopy or variants thereof.

II. PHOTOELECTRON (PE) SPECTROSCOPY

Classical UV photoelectron (PE) spectroscopy as pioneered by D. W. Turner[6] is nowadays — like futurology — a thing of the past. Much more precise and efficient methods are available for studying the electronic states of radical cations $M^{+\bullet}$, making use of lasers, molecular beams and low-temperature matrices (see Section III). However, because of its inherent simplicity, Turner-type PE spectroscopy can still be a convenient tool for exploratory investigations of the lower electronic states of radical cations $M^{+\bullet}$, yielding the corresponding ionization energies with an accuracy of 0.1 to 0.05 eV.

A. PE Spectrum and Ionization Energies

The theoretical and experimental principles of PE spectroscopy have been reviewed extensively[7–10]. In particular, the reader is referred to the chapter *The Photoelectron Spectra of Saturated Hydrocarbons* in the volume *The Chemistry of Alkanes and Cycloalkanes* of the present series[11]. Consequently we shall limit ourselves to the essentials needed for following the arguments presented in this chapter.

The primary process taking place in a PE spectrometer is best viewed as a 'reaction' in which a closed-shell diene or polyene M in its electronic (singlet) ground state $^1\Psi_0$ reacts with a photon of energy $h\nu$ to yield a radical cation $M^{+\bullet}$ in one of its electronic doublet states $^2\tilde{\Psi}_j$, and an electron e^- which carries off the excess energy $E_{\mathrm{kin},j}$:

$$M(^1\Psi_0) + h\nu \longrightarrow M^{+\bullet}(^2\tilde{\Psi}_j) + e^-(E_{\mathrm{kin},j}) \tag{1}$$

It has become customary to characterize state functions (and also other wave functions) of the radical cation by a tilde, e.g. $^2\tilde{\Psi}_j$.

The ionization energy I_j of a closed-shell ground-state molecule M is defined as the energy needed to yield $M^{+\bullet}$ in its electronic state $^2\tilde{\Psi}_j$ according to

$$M(^1\Psi_0) \longrightarrow M^{+\bullet}(^2\tilde{\Psi}_j) + e^-(E_{\mathrm{kin}} = 0) \tag{2}$$

or, if $E(^1\Psi_0)$ and $E(^2\tilde{\Psi}_j)$ are the energies of $M(^1\Psi_0)$ and of $M^{+\bullet}(^2\tilde{\Psi}_j)$ respectively, I_j is given by

$$I_j = E(^2\tilde{\Psi}_j) - E(^1\Psi_0) \tag{3}$$

If the radical cation $M^{+\bullet}(^2\tilde{\Psi}_j)$ is created according to equation 2 in its minimum-energy geometry when in the electronic state $^2\tilde{\Psi}_j$, and if both $M(^1\Psi_0)$ and $M^{+\bullet}(^2\tilde{\Psi}_j)$ are in their

respective vibrational and rotational ground states, then the ionization energy defined by equation 3 is called the *adiabatic* ionization energy, denoted by I_j^a. If the structure of $M(^1\Psi_0)$ is conserved during the process (equation 2), i.e. if $M^{+\bullet}(^2\tilde{\Psi}_j)$ has exactly the same internal structure parameters as the closed-shell molecule $M(^1\Psi_0)$, then the ionization energy defined by equation 3 is called the *vertical* ionization energy I_j^v, which satisfies the condition $I_j^v \geqslant I_j^a$.

From equations 1–3 it follows that

$$I_j = h\nu - E_{\text{kin},j} \tag{4}$$

which requires that the photon energy $h\nu$ must be larger than the ionization energies I_j in which we are interested, i.e. $h\nu > I_j$. For the spectra discussed below the photon sources used are excited helium atoms, He(I), or helium ions, He(II), yielding photons of $h\nu = 21.2$ eV and $h\nu = 40.8$ eV, respectively.

The photoelectron spectrometer is an instrument which scans the range $0 < E_{\text{kin}} < h\nu$ of the kinetic energies E_{kin} of the ejected photoelectrons and thus — according to equation 4 — the range $0 < I < h\nu$ of ionization energies, recording for each value of I the count rate cps (cps = counts per second), i.e. the number of electrons ejected per second from a stream of molecules M in the gas phase. The plot of cps vs I is known as the photoelectron (PE) spectrum of M. Figure 1 shows the PE spectrum of a hypothetical molecule M.

Contrary to naive expectation, the PE spectrum does not consist of sharp lines, but of rather broad, sometimes fine-structured bands. Apart from some minor effects with which we shall not be concerned, this is mainly due to two facts. To begin with, not all neutral molecules $M(^1\Psi_0)$ of the gas sample are present in their vibrational and rotational ground state, but most of them in vibrationally and rotationally excited states. More importantly, the radical cations $M^{+\bullet}(^2\tilde{\Psi}_j)$ are obtained according to equation 1 in various degrees of vibrational and rotational excitation. The corresponding changes in ionization energy lead to the observed band contours, known as 'Franck–Condon envelopes'. If one vibrational mode dominates, it will lead to a resolvable vibrational fine structure of the band. With reference to Figure 1, we briefly mention how the shape of the Franck–Condon envelope can yield information about the structural changes accompanying the transition from M to $M^{+\bullet}$, Band ①, in which the first vibrational component is the most prominent, is

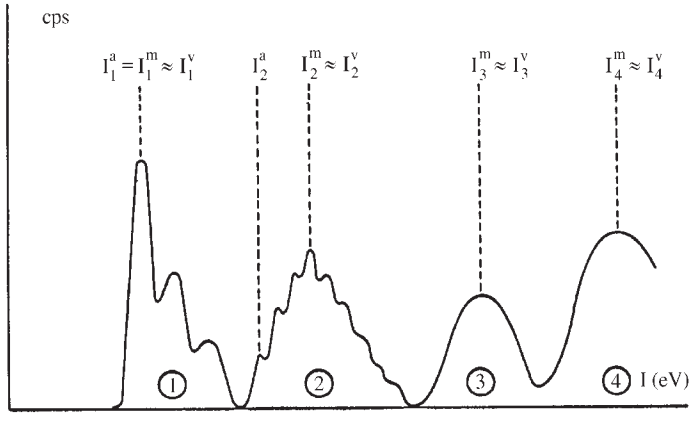


FIGURE 1. Photoelectron spectrum of a hypothetical molecule

traditionally thought to indicate that the transition $M \rightarrow M^{+\bullet}(^2\tilde{\Psi}_1)$ is accompanied by small changes in geometry, whereas the envelope of band ② is assumed to be the consequence of a significant change in the equilibrium structure accompanying the transition $M \rightarrow M^{+\bullet}(^2\tilde{\Psi}_2)$. However, these are only rules-of-thumb which suffer notable exceptions. During the transitions $M \rightarrow M^{+\bullet}(^2\tilde{\Psi}_3)$ and $M \rightarrow M^{+\bullet}(^2\tilde{\Psi}_4)$ so many vibrational (and rotational) degrees of freedom are excited that the fine structure of bands ③ and ④ remains unresolved. For this reason, it is usual to characterize the positions of the individual bands in the PE spectrum by quoting the ionization energy I_j^{m} corresponding to the band maximum. The assumption $I_j^{\mathrm{m}} \approx I_j^{\mathrm{v}}$, i.e. that the band maximum position I_j^{m} can be roughly identified with the vertical ionization energy I_j^{v}, is a sufficiently good approximation for most practical applications.

As a real example we show in Figure 2 the PE spectrum of 1,1-divinylcyclopropane (**46** in Table 1)[12], taken from the considerable number of diene and polyene PE spectra published by R. Gleiter and his coworkers. In the second column of the insert (5) are listed the I_j^{m} values in eV corresponding to the first bands of **46**.

ⓙ	Cation state	I_j^{m} (eV)	Vacated orbital φ_j
①	$\tilde{X}$	9.0	$3b_1$
②	$\tilde{A}$	9.8	$2a_2$
③	$\tilde{B}$	10.9	$8a_1$
④	$\tilde{C}$	11.7	$6b_2$
⑤	$\tilde{D}$	11.9	$2b_1$

(5)

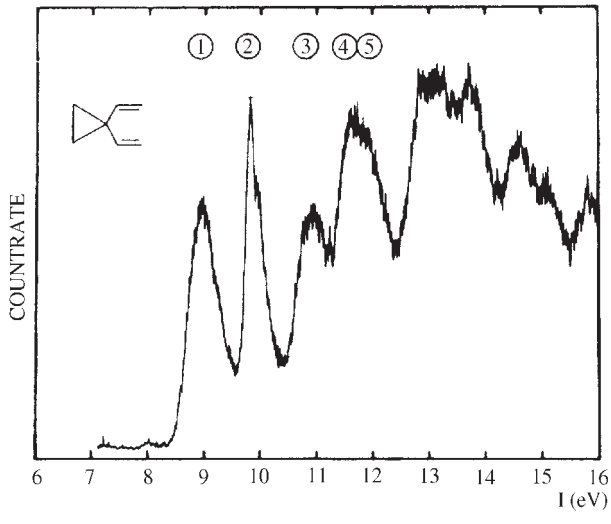


FIGURE 2. Photoelectron spectrum of 1,1-divinylcyclopropane **46**[12]

The symbols in the second column of (5) stand for the electronic doublet states of the radical cation $M^{+\bullet}$, i.e. $\tilde{X}$ for its electronic ground state $^2\tilde{\Psi}_1$, and $\tilde{A}$, $\tilde{B}$, $\tilde{C}$ . . . for its electronically excited states $^2\tilde{\Psi}_2$, $^2\tilde{\Psi}_3$, $^2\tilde{\Psi}_4$ . . .. The conventional labels presented in the fourth column of (5) (which assume that 1,1-divinylcyclopropane **46** has C_{2v} symmetry) are those of the molecular orbitals φ_j having lost the photoelectron according to the theoretical models to be discussed in Section II.C. [The lower-case orbital labels, such as a_1, b_1 etc., refer to the irreducible representations A_1, B_1 etc. of the group to which they belong. In contrast, the state labels $\tilde{A}$, $\tilde{B}$, etc. shown in the second column of (5) have no group theoretical meaning.] Such a list of labels is called the 'assignment' of the spectrum. With rare exceptions such an assignment cannot be deduced from the PE spectrum alone, but is either derived from a quantum-chemical calculation, or inferred by correlation with the assigned PE spectra of closely related molecules. With reference to the primary process (equation 2), the symmetry implied by the labels of the molecular orbitals φ_j is also that of the corresponding radical cation states $^2\tilde{\Psi}_j$, e.g. for 1,1-divinylcyclopropane: $\varphi_1 \equiv 3b_1 \rightarrow \tilde{X} \equiv {}^2\tilde{\Psi}_1(B_1)$; $\varphi_2 \equiv 2a_2 \rightarrow \tilde{A} \equiv {}^2\tilde{\Psi}_2(A_2)$; $\varphi_3 \equiv 8a_1 \rightarrow \tilde{B} \equiv {}^2\tilde{\Psi}_3(A_1)$; etc.

B. PE Spectra of Dienes and Polyenes

Table 1 lists publications containing PE spectra or PE-spectroscopic ionization energies of dienes and polyenes defined by

$$C_nH_m, \quad m = 2(n - d - r + 1) \tag{6}$$

where d is the number of double bonds and r the number of rings. For the smaller molecules the entries have been limited to leading references only. The table is largely based on a computer search, performed in March 1995, using the STN International Beilstein file. For references to work prior to 1970 the reader is referred to the fundamental treatise *Molecular Photoelectron Spectroscopy* by D. W. Turner, C. Baker, A. D. Baker and C. R. Brundle[7]. Another useful source of additional references for the period 1971 to 1981 is the compilation *Ionization Potential and Appearance Potential Measurements* edited by Rhoda D. Levin and Sharon G. Lias[13].

Concerning the contents of Table 1 the following points should be noted:

(1) Hydrocarbons containing one or more triple bonds in addition to double bonds have been excluded from the file, as have been radicals (e.g. the allyl radical $C_3H_5^{\bullet}$) and aromatic molecules, i.e. molecules for which more than one 'unexcited' resonance structure (Kekule structure) can be written. Consequently, hydrocarbons such as phenyl-substituted polyenes, or annulenes — bridged or unbridged — have not been included.

(2) A rather special case are unsaturated, cyclic hydrocarbons undergoing second-order double-bond localization[14], e.g. cyclobutadiene or pentalene. Although equivalent pairs of Kekule structures can be written for these molecules, they assume a structure with alternant single and double bonds, corresponding to only one of these structures. These molecules will be dealt with later, in a separate section.

(3) Linear and branched molecules, as well as some of the monocyclic ones, are identified only by their IUPAC names if their structure is immediately obvious. In the absence of accepted trivial or easy-to-read systematic names, larger polycyclic dienes and polyenes with rather unwieldy IUPAC names have been given numbers (4th column of the Table), which refer to the formula scheme following Table 1.

(4) Reference numbers followed by 'He(II)' refer to PE spectra recorded with He(II) radiation, which therefore show also bands in the ionization energy region above 24 eV.

TABLE 1. PE spectra of dienes and polyenes C_nH_m
[$m = 2(n - d - r + 1)$ where d = number of double bonds and r = number of rings]

C_nH_m				Name[a]	References
r	*n*	*m*	No.		
Dienes: $d = 2$					
0	3	4	**1**	Allene	15, 16 He(ll), 17
	4	6	**2**	1,3-Butadiene	15, 16 He(ll), 18–26, 27 He(ll)
			3	1,2-Butadiene (Methylallene)	16 He(ll), 17
	5	8	**4**	(3*E*)-1,3-Pentadiene (1-Methylbutadiene)	16 He(ll), 20, 21, 25, 28
			5	2-Methylbutadiene (Isoprene)	16 He(ll), 20, 25, 28
			6	3-Methylbuta-1,2-diene (1,1-Dimethylallene)	16 He(ll), 17
			7	2,3-Pentadiene (1,3-Dimethylallene)	16 He(ll), 17
			8	1,4-Pentadiene	29, 30
	6	10	**9**	4-Methyl-1,3-pentadiene (1,1-Dimethylbuta-1,3-diene)	2
			10	(2*E*, 4*E*)-Hexa-2,4-diene	16 He(ll), 20
			11	2,3-Dimethylbuta-1,3-diene	16 He(ll), 20, 25, 28
			12	(3*E*)-3-Methylpenta-1,3-diene	25
			13	(3*E*)-2-Methylpenta-1,3-diene	25, 31, 32
			14	(3*Z*)-2-Methylpenta-1,3-diene	31, 32
			15	2-Methylpenta-2,3-diene (1,1,3-Trimethylallene)	16 He(ll), 17
			16	(3*E*)-Hexa-1,3-diene	21, 25, 31, 33
			17	Hexa-1,5-diene	29, 34
	7	12	**18**	2,4-Dimethylpenta-2,3-diene (Tetramethylallene)	16 He(ll), 17
			19	2,4-Dimethylpenta-1,3-diene	25
			20	1,1-Dimethylpenta-1,4-diene	30
			21	3,3-Dimethylpenta-1,4-diene	35
			22	1,6-Heptadiene	29
	8	14	**23**	(4*E*)-2,3-Dimethylhexa-2,4-diene	36
			24	(3*E*)-Octa-1,3-diene	21
			25	2,5-Dimethylhexa-2,4-diene	16 He(ll), 20, 25
			26	(2*Z*, 4*Z*)-3,4-Dimethylhexa-2,4-diene	37
			27	(2*Z*, 4*E*)-3,4-Dimethylhexa-2,4-diene	37
			28	(2*E*,4*E*)-3,4-Dimethylhexa-2,4-diene	37
			29	(4*E*)-2,3-Dimethylhexa-2,4-diene	36
			30	(4*E*)-2,4-Dimethylhexa-2,4-diene	36
			31	(4*Z*)-2,4-Dimethylhexa-2,4-diene	36
			32	Octa-1,7-diene	29
	9	16	**33**	Nona-1,8-diene	29
	11	20	**34**	2,2,6,6-Hepta-3,4-diene (1,1-Di-*t*-butylallene)	17
	12	22	**35**	2,3-Di-*t*-butylbuta-1,3-diene	37
1	4	4	**36**	Methylidenecyclopropene	38
	5	6	**37**	Cyclopentadiene	39
	6	8	**38**	3-Vinyl-3-methylcyclopropene	40, 41
			39	1,2-Dimethylidenecyclobutane	42
			40	1,3-Dimethylidenecyclobutane	42
			41	1-Methylcyclopentadiene	43
			42	5-Methylcyclopentadiene	43
			43	3-Methylidenecyclopentene	44
			44	Cyclohexa-1,3-diene	15, 39
			45	Cyclohexa-1,4-diene	15, 45–47

(*continued overleaf*)

TABLE 1. (*continued*)

C_nH_m				Name[a]	References
r	*n*	*m*	No.		
Dienes: $d = 2$					
1	7	10	**46**	1,1-Divinylcyclopropane	12
			47	3-(2-Propenyl)-3-methylcyclopropene	40
			48	4-Methylidenecyclohexene	48
			49	Cyclohepta-1,3-diene	39, 49
			50	Cyclohepta-1,4-diene	50
	8	12	**51**	3-(1-Isobutenyl)-3-methylcyclopropene	40
			52	*cis*-1,2-Divinylcyclobutane	51
			53	*trans*-1,2-Divinylcyclobutane	51
			54	*cis*-1,3-Divinylcyclobutane	51
			55	*trans*-1,3-Divinylcyclobutane	51
			56	1,2-Dimethylidenecyclohexane	48
			57	Cycloocta-1,3-diene	39, 50
			58	Cycloocta-1,4-diene	50
			59	Cycloocta-1,5-diene	50
	9	14	**60**	(1*E*, 1*E*)-Di-(1-propenyl)cyclopropane	52
			61	(1*E*,1*Z*)-Di-(1-propenyl)cyclopropane	12
			62	(1*Z*,1*Z*)-Di-(1-propenyl)cyclopropane	16, 52
			63	Cyclonona-1,2-diene	17
	10	16	**64**	1,2,3,4,5-Pentamethylcyclopentadiene	53
			65	3,3,6,6-Tetramethylcyclohexa-1,4-diene	54
			66	(1*Z*,5*E*)-Cyclodeca-1,5-diene	39
			67	(1*Z*,6*Z*)-Cyclodeca-1,6-diene	39
			68	(1*E*,6*E*)-Cyclodeca -1,6-diene	39
	11	18	**69**	Hexamethylcyclopentadiene	53
2	6	6	**70**	(Bicyclo[2.2.0]hexa-2,5-diene)	55
			71	(Dewar benzene) Bicyclopropyl-2,2′-diene	56–59
	7	8	**72**	6-Methylidenespiro[2,3]hex-4-ene	60
			73	5-Methylidenebicyclo[2.2.0]hex-2-ene	61
			74	Spiro[2.4]hepta-4,6-diene(Homofulvene)	16, 62, 63
			75	(Bicyclo[2.2.0]hexa-2,5-diene) Norbornadiene	26, 28, 45, 59, 64
	8	10	**76**	1,1′-Dimethylbicyclopropyl-2,2′-diene	65
			77	Spiro[3,4]octa-5,7-diene	63, 66
			78	2,3-Dimethylidenebicyclo[2.1.1]hexane	67, 68
			79	Bicyclo[4.2.0]octa-2,4-diene	69, 70
			80	Bicyclo[4.1.1]octa-2,4-diene	68, 71
			81	Bicyclo[2.2.2]octadiene	16, 45, 56
			82	5-Methylidenebicyclo[2.2.1]hept-2-ene	48
			83	Spiro[2.5]octa-4,6-diene	72
	9	12	**84**	Spiro[4.4]nona-1,3-diene	63, 66
			85	5-Vinylbicyclo[2.2.1]hept-2-ene	73
			86	5-Ethylidenebicyclo[2.2.1]hept-2-ene	73
			87	2,3-Dimethylidenebicyclo[2.2.1]heptane	48
			88	5-Methylidenebicyclo[2.2.2]oct-2-ene	48
			89	*exo*-Bicyclo[4.3.0]nona-3,7-diene	74
			90	*endo*-Bicyclo[4.3.0]nona-3,7-diene	74
			91	Bicyclo[3.2.2]nona-2,6-diene	75
			92	Bicyclo[3.2.2]nona-6,8-diene	75
			93	Bicyclo[4.2.1]nona-2,4-diene	76

TABLE 1. (*continued*)

C_nH_m				Name	References
r	*n*	*m*	No.		
Dienes: $d = 2$					
	10	14	**94**	7-Isopropylidenebicyclo[2.2.1]hept-2-ene	77
			95	2,3-Dimethylbicyclo[2.2.2]octa-2,5-diene	78
			96	2,3-Dimethylidenebicyclo[2.2.2]octane	48
			97	Bicyclo[6.2.0]deca-2,6-diene	51
	11	16	**98**	6,7-Dimethylbicyclo[3.2.2]nona-6,8-diene	78
	12	18	**99**	Hexamethyl-Dewar benzene	58, 79
			100	1,5-Dimethyl-3,7-dimethylidene-bicyclo[3.3.0]octane	80
			101	1,4,5,6-Tetramethyl-2,3-dimethylidene-bicyclo[2.1.1]hexane	67
3	8	8	**102**	*exo*-Tricyclo[4.2.0.0^{2,5}]octa-3,7-diene	81, 82
			103	*endo*-Tricyclo[4.2.0.0^{2,5}]octa-3,7-diene	81, 82
			104	Tricyclo[5.1.0.0^{4,8}]octa-2,5-diene (Semibullvalene)	83
			105	Tricyclo[3.3.0.0^{2,6}]octa-3,7-diene	81
			106	3,4-Dimethylidenetricyclo[3.1.0.0^{2,6}]hexane	67, 68
			107	Tricyclo[4.1.1.0^{7,8}]octa-2,4-diene	58
	9	10	**108**	Nortriquinacene	84
			109	7-Cyclopropylidenenorbornadiene	85
			110	7,8-Methanobicyclo[2.2.2]octa-2,5-diene	86
			111	*exo*-Tricyclo[4.2.1.0^{2,5}]nona-3,7-diene	82
			112	*endo*-Tricyclo[4.2.1.0^{2,5}]nona-3,7-diene	82, 87
			113	Tricyclo[5.1.0.1^{4,8}]nona-2,5-diene	83
	10	12	**114**	Dispiro[2.2.2.2]deca-4,9-diene	54, 88
			115	Dispiro[2.0.2.4]deca-7,9-diene	72
			116	*endo*-Dicyclopentadiene	89, 90
			117	Dihydrobullvalene	91
			118	Tricyclo[5.3.0.0^{2,8}]deca-3,5-diene	92
			119	Twistadiene	93
			120	Dimethylidene-bisnortwistane	93
			121	*syn*-Tricyclo[4.2.1.1^{2,5}]deca-3,7-diene	94
	11	14	**122**	Dispiro[2.0.2.5]undeca-1,5-diene	65
			123	8-Isopropylidenetricyclo[3.2.1.0^{2,4}]octene	77
			124	5,9-Dimethylidene-nortwistane	93
	12	16	**125**	1,5-Dimethyl-3,7-dimethylidene-tricyclo[3.3.0.0^{2,8}]octane	80
			126	1,2,5,6-Tetramethyl-3,4-dimethylidene-tricyclo[3.1.0.0^{2,6}]hexane	67
			127	[4.4.2]Propella-3,11-diene	81, 95
			128	2,5-Dimethylidene[4.2.2]propellane	96
			129	Tricyclo[4.2.2.2^{2,5}]dodeca-1,5-diene	96
			130	Tricyclo[5.5.0.0^{2,8}]dodeca-3,5-diene	92
	13	18	**131**	2,8-Dimethylidene[3.3.3]propellane	97
	14	20	**132**	[4.4.4]propella-2,4-diene	98
	16	24	**133**	3,4,5,6,7,8,12,15-octahydro[2.2]para-cyclophane	99
4	10	10	**134**	Hypostrophene	100, 101

(*continued overleaf*)

TABLE 1. (*continued*)

C_nH_m				Name	References
r	*n*	*m*	No.		
Dienes: $d = 2$					
4	12	14	**135**	Tetracyclo[6.4.0.0^{4,12}. 0^{5,9}]dodeca-2,6-diene	102
			136	4′,5′,6′,7′-Tetrahydrospiro[cyclopropane-1,2′-[4,7]-methano-2*H*-indene]	103
			137	*exo,exo*-1,4,4*a*,5,8,8*a*-Hexahydro-1,4:5,8-dimethanonaphthalene	104
			138	*exo,endo*-1,4,4*a*,5,8,8*a*-Hexahydro-1,4:5,8-dimethanonaphthalene	105
			139	*endo,endo*-1,4,4*a*,5,8,8*a*-Hexahydro-1,4:5,8-dimethanonaphthalene	105
			140	2,5-Ethano[4.2.2]propella-7,9-diene	56
			141	2,5-Etheno[4.2.2]propell-3-ene	56
			142	*syn*-Sesquinorbornadiene	106
			143	*anti*-Sesquinorbornadiene	106
			144	1,5-Dimethyl-3,7-dimethylene-tetracyclo[3.3.0.0^{2,8}.0^{4,6}]octane	80
	14	18	**145**	4′,5′,6′,7′-Tetrahydrospiro[cyclopentane-1,2′-[4,7]-methano-2*H*-indene]	103
5	12	12	**146**	Pentacyclo-[6.4.0.0^{2,5}.0^{3,10}.0^{4,9}]dodeca-6,11-diene	107
	13	14	**147**	[2.2.1]Triblattadiene	108
			148	4,7-Dimethylidene-pentacyclo[6.3.0.0^{2,6}0^{3,10}.0^{5,9}] undecane	108
	16	20	**149**	*endo,endo*-Pentacyclo[10.2.1.1^{5,8}.0^{2,4}.0^{4,9}]hexadeca-6,13-diene	109
6	17	20	**150**	*exo,exo*-1,4,4*a*,5,8,8*a*,9,9*a*,10,10*a*-Decahydro-1,4:5,8:9,10-trimethanoanthracene	109
			151	*endo,endo*-1,4,4*a*,5,8,8*a*,9,9*a*,10,10*a*-Decahydro-1,4:5,8:9,10-trimethanoanthracene	109
7	20	24	**152**	7,12-Dimethylidenehepta-cyclo[6.6.0.0^{2,6}.0^{3,13}.0^{4,11}.0^{5,9}.0^{10,14}]tetradecane	110
			153	Heptacyclo-[10.8.0.0^{2,6}.0^{2,11}.0^{6,17}.0^{7,11}.0^{7,16}]icosa-1(12), 16-diene	111
8	15	12	**154**	Bis(7-quadricyclylidene)methane	112
	22	26	**155**	*endo,endo*-1,4,4*a*,5,5*a*,6,6*a*,7,10,10*a*,11,11*a*,12,12*a*-Tetradecahydro-1,4:5, 12:6, 11:7, 10-tetramethylnonaphthacene	109
9	20	20	**156**	Bissecododecahedradiene	113
10	27	32	**157**	*endo,endo*-1,4,4a,5,5a,6,6a,7,7a,8,11,11a,12,12a,13,13a,14,14a-octadecahydro-1,4:5,14:6, 13:7, 12:8, 11-pentamethano-pentacene	109

TABLE 1. (*continued*)

C_nH_m				Name	References
r	*n*	*m*	No.		
Trienes: $d = 3$					
0	4	4	**158**	Butatriene	16 He(ll), 114, 115
			159	Tetradeuteriobutatriene	114, 115
	5	6	**160**	Penta-1,2,4-triene (Vinylallene)	116
	6	8	**161**	(3*E*)-Hexa-1,3,5-triene	20, 23, 117–119
			162	(3*Z*)-Hexa-1,3,5-triene	20, 23, 117–119
	7	10	**163**	(3*E*, 5*E*)-Hepta-1,3,5-triene	118
			164	(3*E*, 5*Z*)-Hepta-1,3,5-triene	118
			165	(3*E*)-2-Methylhexa-1,3,5-triene	118
			166	(3*E*)-3-Methylhexa-1,3,5-triene	118
			167	Trivinylmethane	120
	8	12	**168**	Tetramethylbutatriene	114, 115
			169	(3*E*)-6-Methylhepta-1,3,5-triene	118
			170	(3*E*,5*E*)-5-Methylhepta-1,3,5-triene	118
			171	(2*E*, 4*E*, 6*E*)-Octa-2,4,6-triene	118
	20	36	**172**	Tetra-*t*-butylbutatriene	114, 115
1	6	6	**173**	[3]Radialene	121–123
			174	3,4-Dimethylidenecyclobutene	124
			175	Fulvene	62, 124–126
	7	8	**176**	1-Methyl-3,4-dimethylidenecyclobutene	127
			177	6-Methylfulvene	125
			178	5-Methylidenecyclohexa-1,3-diene	61
			179	Cyclohepta-1,3,5-triene	50
	8	10	**180**	1,2-Dimethyl-3,4-dimethylidenecyclobutene	127
			181	6-Ethylfulvene	125
			182	6,6-Dimethylfulvene	125
			183	4,5-Dimethylenecyclohexene	48
			184	Cycloocta-1,3,5-triene	50, 70
			185	Cycloocta-1,3,6-triene	50, 70
	9	12	**186**	6-Propylfulvene	125
			187	6-Isopropylfulvene	125
			188	1,6-Dimethylcyclohepta-1,3,5-triene	128
			189	Cyclonona-1,4,7-triene	26, 49
	10	14	**190**	6-Isobutylfulvene	125
			191	6-*t*-Butylfulvene	125
			192	6,6-Diethylfulvene	125
	12	18	**193**	6,6-Dipropylfulvene	125
			194	Hexamethyl-[3]-radialene	129
2	7	6	**195**	Bicyclo[3.2.0]hepta-1,4,6-triene	130
	8	8	**196**	7-Methylidenenorbornadiene	131
			197	Barrelene	26, 86, 122, 132
			198	1,2-Dihydropentalene	133
			199	1,4-Dihydropentalene	133
			200	1,5-Dihydropentalene	133
	9	10	**201**	5,6-Dimethylidenenorborn-2-ene	48
			202	Spiro[4.4]nona-1,3,5-triene	63
			203	Spiro[4.4]nona-1,3,6-triene	63
			204	Bicyclo[3.2.2]nona-2,6,8-triene	75
			205	Bicyclo[4.2.1]nona-2,4,6-triene	49, 76
	10	12	**206**	7-Isopropylidenenorbornadiene	26, 77
			207	4,5-Dimethylidenebicyclo[2.2.2]octene	48
			208	Bicyclo[4.2.2]deca-3,7,10-triene	134
			209	1,4,5,8-Tetrahydronaphthalene	26, 47, 135
			210	6,6-Tetramethylenefulvene	125

(*continued overleaf*)

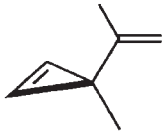
TABLE 1. (*continued*)

C_nH_m				Name	References
r	*n*	*m*	No.		
Trienes: $d = 3$					
	11	14	**211**	Bicyclo[4.4.1]undeca-1,3,5-triene	128
	14	20	**212**	11,12-Dimethylbicyclo[5.3.2]dodeca-1,6,11-triene	117
3	10	10	**213**	Triquinacene	136
			214	Bullvalene	91
			215	7-Cyclopropylidenenorbornadiene	137
			216	Tricyclo[5.3.0.$0^{2,8}$]deca-3,5,9-triene	92
	11	12	**217**	Tricyclo[5.3.1.$0^{1,7}$]undeca-2,4,9-triene	138
			218	Tricyclo[6.2.1.$0^{2,6}$]undeca-2,5,9-triene	139
			219	Tricyclo[6.2.1.$0^{2,6}$]undeca-2,6,9-triene	139
	12	14	**220**	Tricyclo[4.4.1.$1^{2,5}$]dodeca-3,7,9-triene	89
			221	9-Isopropylidene-*endo*-tricyclo[4.2.1.$0^{2,5}$]nona-3,7-diene	82
			222	[4.4.2]Propella-2,4,11-triene	95
			223	[4.4.2]Propella-3,8,11-triene	95
	14	18	**224**	2,8,9-Trimethylidene[3.3.3]propellane	97, 120
4	12	12	**225**	3,7,9-Trimethylidene-tetracyclo[3.3.1.$0^{2,8}$.$0^{4,6}$]dodecane	140
			226	*syn*-Sesquinorbornatriene	106
			227	*anti*-Sesquinorbornatriene	106
	18	24	**228**	Tetracyclo[8.2.2.$2^{2,5}$.$2^{6,9}$]octadeca-1,5,9-triene	141, 142
5	14	14	**229**	[2.2.2]Blattatriene	108
			230	4,7,11-Trimethylidenepentacyclo[5.3.9.$0^{2,6}$.$0^{3,10}$.$0^{5,9}$]undecane	108
6	18	20	**231**	Distella-2,2′,6,6′-triene	143
Tetraenes: $d = 4$					
0	5	4	**232**	Pentatetraene	144
	6	6	**233**	Hexa-1,2,4,5-tetraene (Bisallenyl)	116
	8	10	**234**	(3*E*, 5*E*)-Octa-1,3,5,7-tetraene	23, 145
	9	12	**235**	Tetravinylmethane	35, 120
1	7	6	**236**	6-Methylidenefulvene	146
	8	8	**237**	[4]Radialene	147
			238	*p*-Quinodimethane	148
			239	Cyclooctatetraene	18, 50, 149
	10	12	**240**	2,3-Dimethyl-*p*-quinodimethane	150
			241	2,5-Dimethyl-*p*-quinodimethane	150
			242	Cyclodeca-1,2,6,7-tetraene	151
	12	16	**243**	*trans, trans, trans*-1,2,3,4-Tetravinylcyclobutane	120, 152
			244	*syn, trans, syn*-1,2,3,4-Tetravinylcyclobutane	152
			245	4,9-Dimethylidenecyclodeca-1,6-diene	153
	16	24	**246**	Octamethyl-[4]radialene	154
2	9	8	**247**	[4.4]Spirononatetraene	63, 155
	10	10	**248**	9-Methylidenebicyclo[4.2.1]deca-2,4,7-triene	156
			249	Bicyclo[4.2.2]deca-2,4,7,9-tetraene	157
	11	12	**250**	2,2-Dimethyl(2*H*)indene	26, 121
			251	2,3,5,6-Tetramethylidenenorbornane	158
	12	14	**252**	2,3,5,6-Teramethylidenebicyclo[2.2.2]octane	158
	13	16	**253**	Bicyclo[5.4.2]trideca-7,9,11,12-tetraene	50

TABLE 1. (*continued*)

C_nH_m				Name	References
r	*n*	*m*	No.		
Tetraenes: $d = 4$					
3	10	8	**254**	[4.2.2]Propellatetraene	56
	12	12	**255**	[4.4.2]Propella-3,7,9,11-tetraene	69
			256	Tricyclo[[6.4.0.0^{1,7}]dodeca-3,5,9,11-tetraene	95
			257	9,19-Dimethylidene-tricyclo[5.3.0.0^{2,8}]deca-3,5-diene	92
			258	Tricyclo[5.5.0.0^{2,8}]dodeca-3,5,9,11-tetraene	92
	14	16	**259**	1,4,5,6,9,11-Hexahydroanthracene	47
			260	[4.4.4]Propella-2,4,7,9-tetraene	98
	16	20	**261**	*anti*-1,2,5,6-Tetramethyl-3,4,7,8-tetramethylidenetricyclo[4.2.0.0^{2,5}]octane	159
			262	1,2,5,6-Tetramethyl-3,4,7,8-tetra-methylidenetricyclo[3.3.0.0^{2,6}]octane	159
			263	2,3′,5,6′-Tetrahydro[2.2]paracyclophane	99
4	12	10	**264**	2,5-Etheno-[4.2.2]propella-3,7,9-triene	56
5	15	14	**265**	Dispiro-(bicyclo[2.2.1]hepta-2,5-diene-7,1′-cyclopropane-2′,7″-bicyclo[2.2.1]hepta-2″,5″-diene	112
	20	24	**266**	2,2′,5,5′-Tetrahydro[2.2.2.2](1,3,4,6)(1′,3′,4′,6′)cyclophane	99
8	29	18	**267**	Octacyclo-[12.5.1.0^{2,7}.0^{2,13}.0^{7,18}.0^{8,13}.0^{8,16}.0^{17,20}]ei-cosa-3,5,9,11-tetraene	160
Polyenes: $d \geqslant 5$					
				$d = 5$	
2	10	8	**268**	2-Methylidene-(2H)indene	161
	12	12	**269**	5,6,7,8-Tetramethylidenebicyclo[2.2.2]oct-7-ene	158
3	12	10	**270**	2a,8b-Dihydrocyclopenta[*c*,*d*]azulene	128
			271	[4.4.2]Propellapentaene	95
4	18	20	**272**	1,4,5,6,7,10,12-Octahydronaphthacene	47
				$d = 6$	
2	12	10	**273**	2,6-Azulylene	162
	14	14	**274**	2,3,5,6,7,8-Hexamethylidene-bicyclo[2.2.2]octane	163
3	14	12	**275**	[4.4.4]Propellahexaene	98
4	15	12	**276**	Bis(7-norbornadienylidene)methane	112
				$d = 7$	
4	20	20	**277**	2,7-Dihydro-2,2,7,7-tetramethylpyrene	164
				$d = 8$	
3	22	24	**278**	7,14-Diisopropylidene-7,14-dihydro-*syn*-1,6:8,13-bismethano[14]annulene	165
				$d = 11$	
2	40	56	**279**	β-Carotene	166, 167
			280	(15*Z*)-β-Carotene	168

[a]IUPAC name is given first, followed by trivial name in parentheses.



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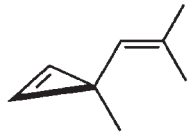

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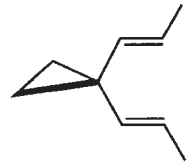

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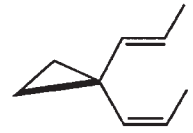

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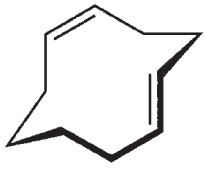

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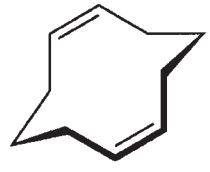

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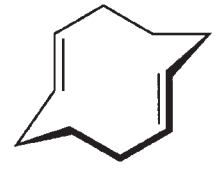

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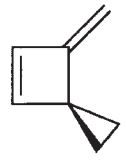

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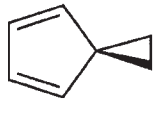

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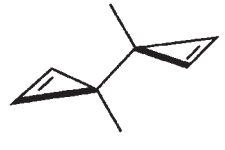

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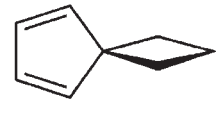

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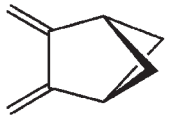

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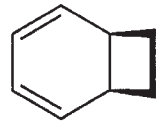

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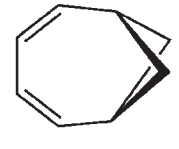

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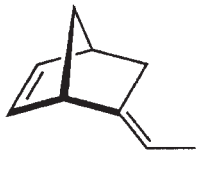

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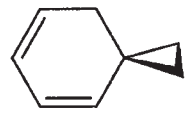

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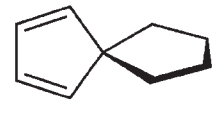

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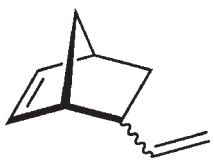

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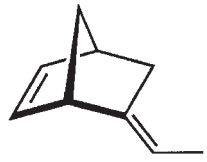

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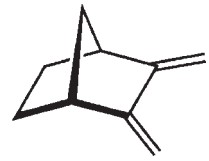

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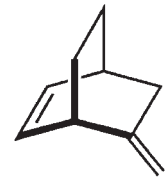

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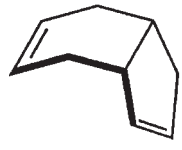

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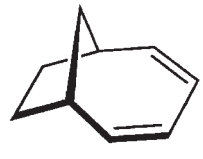

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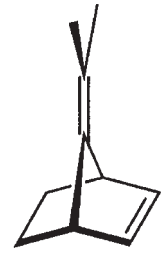

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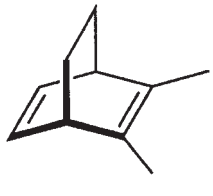

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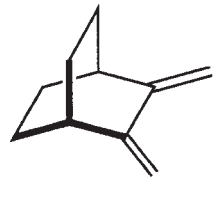

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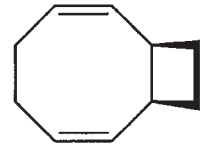

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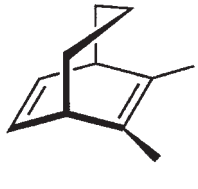

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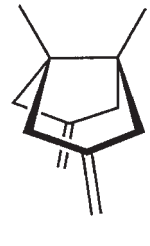

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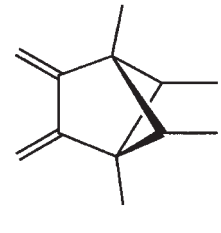

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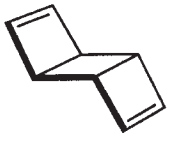

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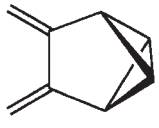

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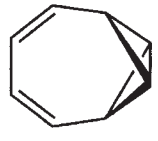

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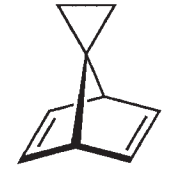

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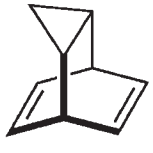

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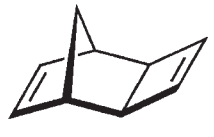

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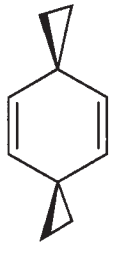

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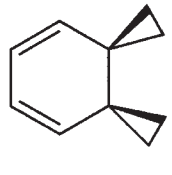

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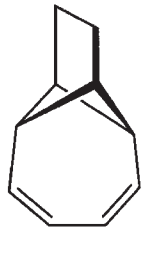

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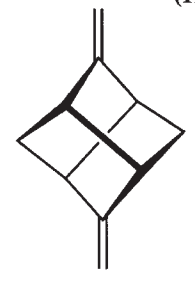

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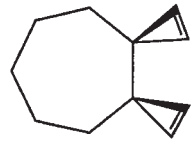

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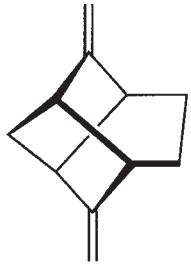

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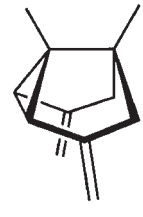

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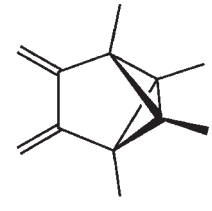

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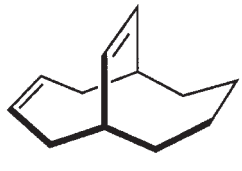

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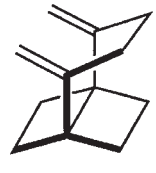

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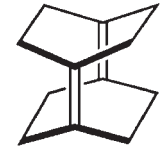

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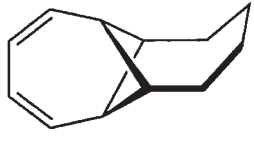

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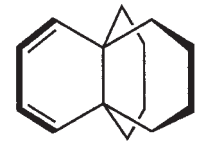

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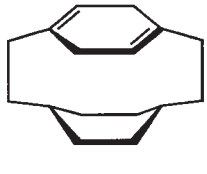

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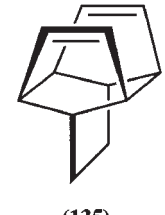

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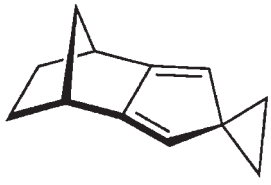

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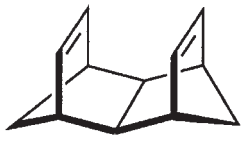

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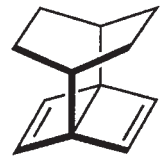

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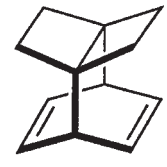

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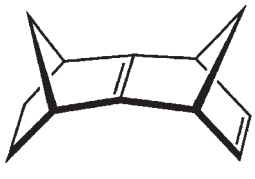

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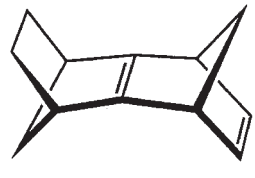

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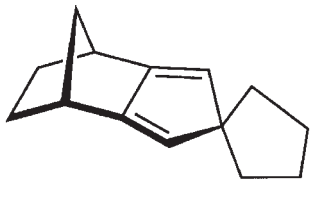

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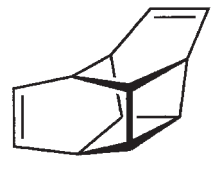

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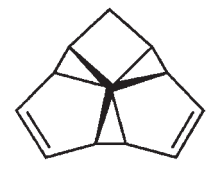

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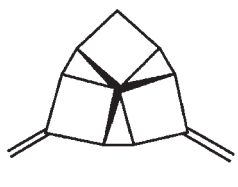

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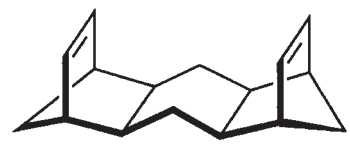

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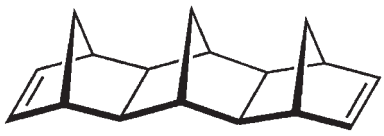

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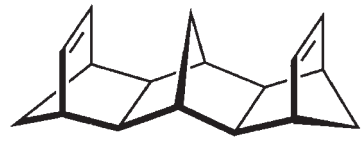

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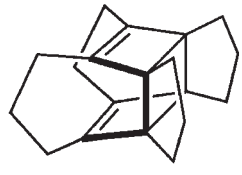

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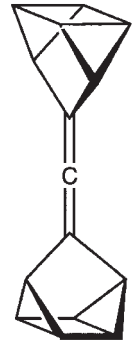

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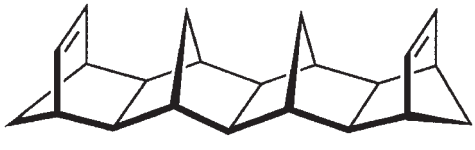

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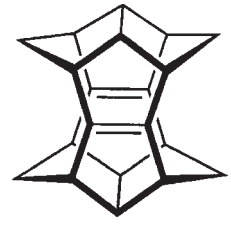

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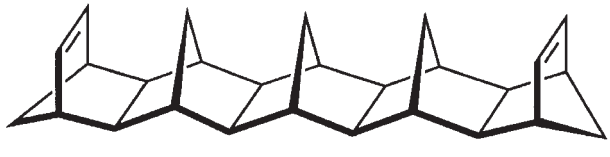

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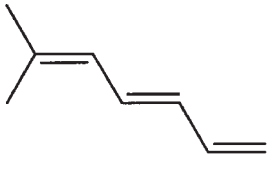

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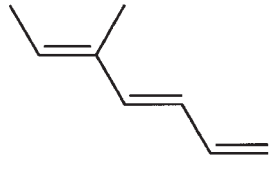

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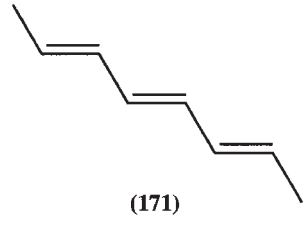

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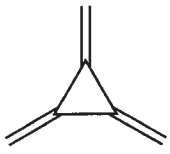

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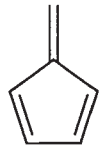

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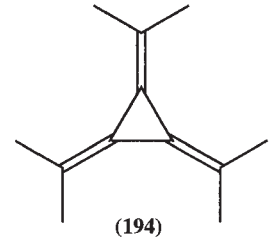

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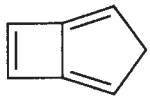

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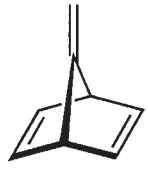

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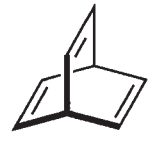

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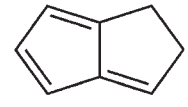

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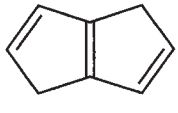

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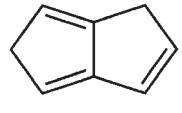

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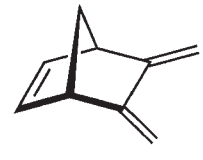

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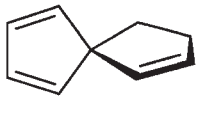

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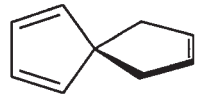

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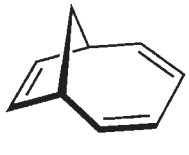

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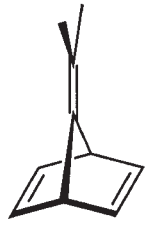

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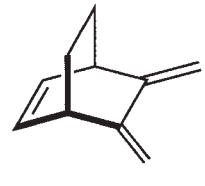

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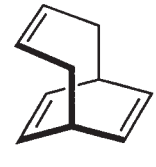

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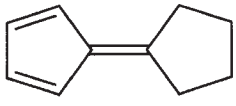

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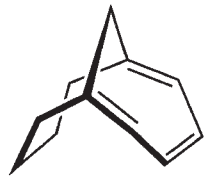

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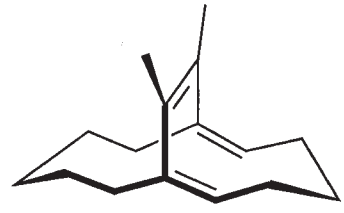

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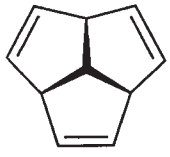

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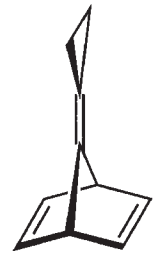

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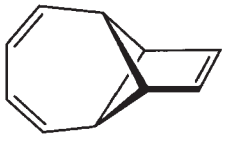

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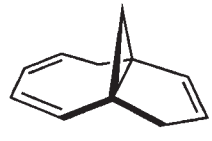

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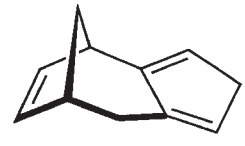

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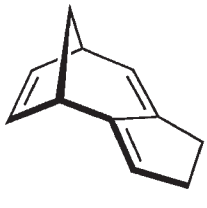

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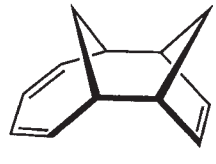

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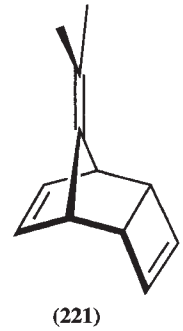

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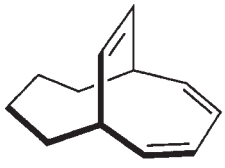

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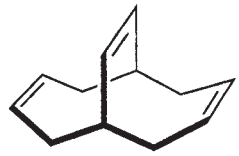

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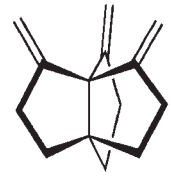

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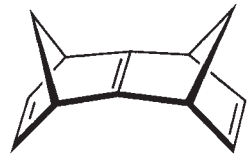

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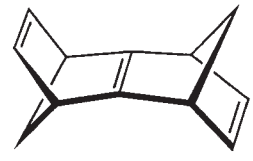

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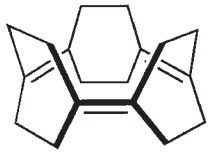

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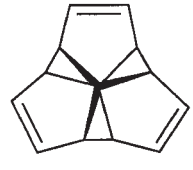

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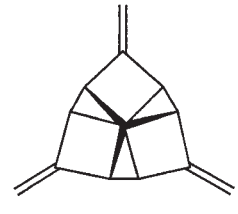

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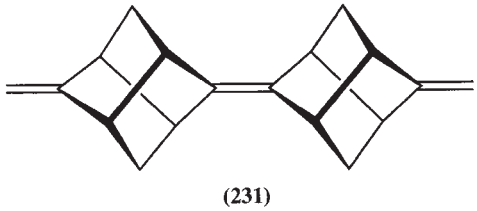

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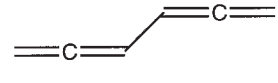

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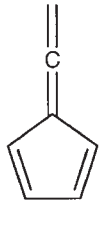

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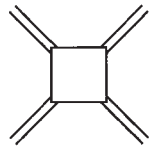

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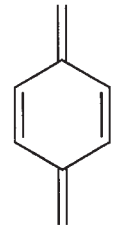

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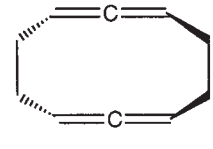

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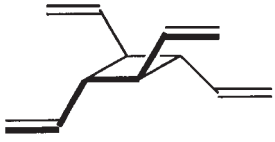

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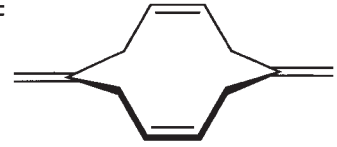

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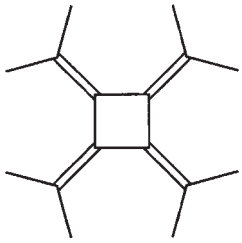

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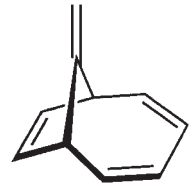

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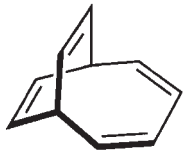

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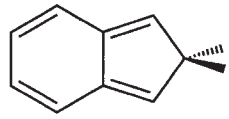

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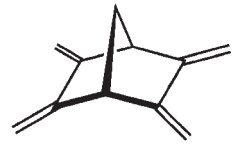

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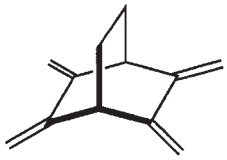

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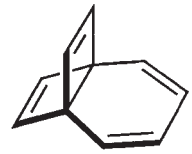

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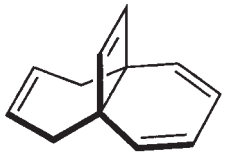

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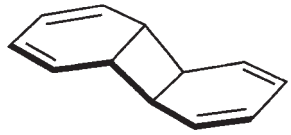

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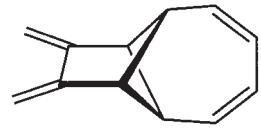

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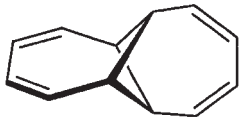

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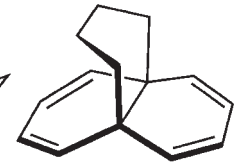

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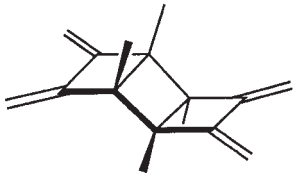

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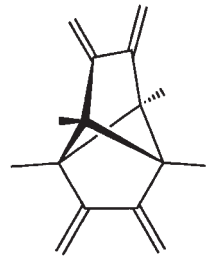

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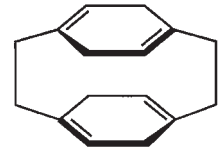

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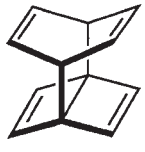

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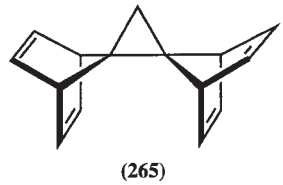

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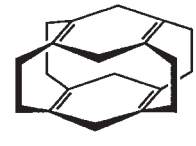

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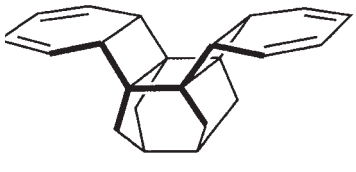

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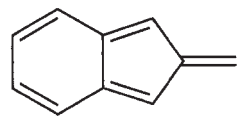

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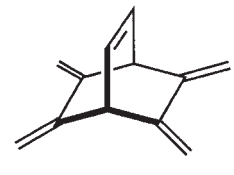

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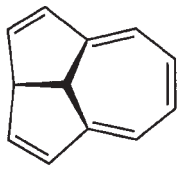

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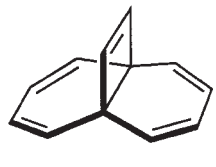

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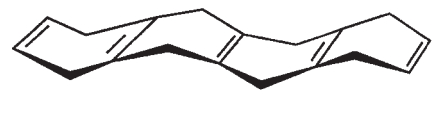

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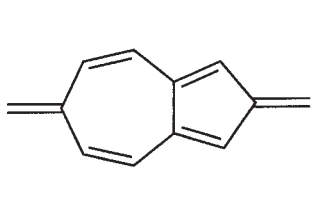

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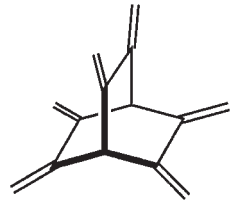

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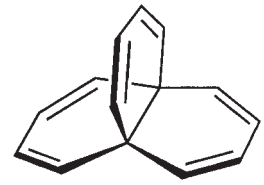

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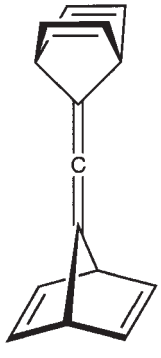

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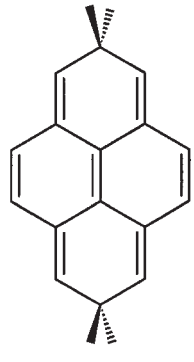

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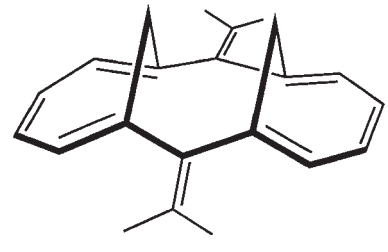

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C. Interpretation of PE Spectra

In principle, refined and relatively reliable quantum-theoretical methods are available for the calculation of the energy change associated with the process of equation 2. They take into account the changes in geometry, in electron distribution and in electron correlation which accompany the transition $M(^1\Psi_0) \rightarrow M^{+\bullet}(^2\tilde{\Psi}_j)$, and also vibronic interactions between the radical cation states. Such sophisticated treatments yield not only reliable predictions for the different ionization energies I_j^a, I_j^v or I_j^m, but also rather precise Franck–Condon envelopes for the individual bands in the PE spectrum. However, the computational expenditure of these methods still limits their application to smaller molecules. We shall mention them later in connection with examples where such treatments are required.

For most practical purposes — and certainly for the discussions in this chapter — much simpler models are entirely adequate for a qualitative or semiquantitative rationalization of the features of PE spectra of dienes and polyenes. Before using such models, we first situate them within the genealogy of quantum-mechanical treatments.

A convenient starting point is an *ab initio*[169] or semiempirical[170] SCF calculation yielding the singlet ground configuration $^1\Phi_0$ for a closed-shell molecule M with $2n$ electrons, which is assumed to be a sufficiently good approximation for the ground-state $^1\Psi_0$ of M. This configuration $^1\Phi_0$ is written as a Slater determinant in terms of the n doubly occupied canonical molecular orbitals (CMO) φ_k (equation 7). By convention φ_k

represents a CMO occupied by an electron with spin α, and $\bar{\varphi}_k$ with spin β:

$$^1\Phi_0 = \left\|\varphi_1\bar{\varphi}_1\varphi_2\bar{\varphi}_2\cdots\varphi_j\bar{\varphi}_j\cdots\varphi_n\bar{\varphi}_n\right\| \tag{7}$$

The next approximation is to assume that exactly the same CMOs φ_k can be used for writing the electronic doublet configurations $^2\tilde{\Phi}_j$ of the radical cation M^+, by simply removing one of the two electrons occupying the CMO φ_j in the closed-shell molecule M. This yields

$$2\tilde{\Phi}_j = \begin{cases} \left\|\varphi_1\bar{\varphi}_1\varphi_2\bar{\varphi}_2\cdots\varphi_j\cdots\varphi_n\bar{\varphi}_n\right\| \\ \left\|\varphi_1\bar{\varphi}_1\varphi_2\bar{\varphi}_2\cdots\bar{\varphi}_j\cdots\varphi_n\bar{\varphi}_n\right\| \end{cases} \tag{8}$$

In agreement with the convention for the states $^2\tilde{\Psi}_j$ of radical cations, their configurations $^2\tilde{\Phi}_j$ are again characterized by a 'tilde'. The top line of equation 8 corresponds to the component of $^2\tilde{\Phi}_j$ with spin $S_z = \hbar/2$, and the bottom one to $S_z = -\hbar/2$. Figure 3 shows on the left the energy-level diagram of the lowest three states $^2\tilde{\Psi}_j$ of a radical cation $M^{+\bullet}$ relative to the level of the electronic ground-state $^1\Psi_0$ of the neutral parent molecule M, and on the right side the symbolic representations of the corresponding configurations (equations 7 and 8), i.e. of $^1\Phi_0$ and $^2\tilde{\Phi}_j$.

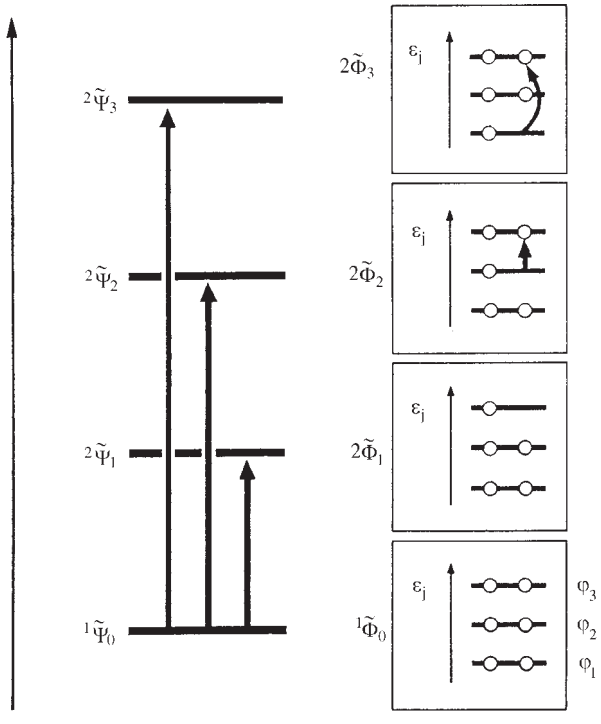


FIGURE 3. Graphical representation of the electron configuration $^1\Phi_0$ of a closed-shell molecule M and of the configurations $^2\tilde{\Phi}_j$ of its radical cation $M^{+\bullet}$ as approximations to the states $^1\Psi_0$ and $^2\tilde{\Psi}_j$ ($j = 1, 2, 3$). The arrows in the representations of $^2\tilde{\Phi}_2$ and $^2\tilde{\Phi}_3$ indicate that these configurations correspond to electronic excitations of M^+, relative to its ground-state configuration $^2\tilde{\Phi}_1$

The approximation underlying the expression in equation 8 and Figure 3, i.e. using frozen CMOs φ_j, not only implies that M and $M^{+\bullet}$ have the same geometry, but also that we disregard electron rearrangement, i.e. changes in the CMOs φ_k when an electron is removed from φ_j, and changes in electron correlation. Notwithstanding these restrictions, the energy change $E(^2\tilde{\Phi}_j) - E(^1\Phi_0)$ is then a useful approximation for the vertical ionization energy I_j^v:

$$E(^2\tilde{\Phi}_j) - E(^1\Phi_0) = I_j^v \tag{9}$$

It has been shown by Koopmans[171] that under the above simplifications (same rigid geometry of M and $M^{+\bullet}$, frozen CMOs φ_k) the energy difference $E(^2\tilde{\Phi}_j) - E(^1\Phi_0)$ is equal, up to sign, to the orbital energy $\mathcal{E}_j$ of the CMO φ_j of the neutral molecule M from which the electron has been ejected:

$$E(^2\tilde{\Phi}_j) - E(^1\Phi_0) = -\mathcal{E}_j \tag{10}$$

The resulting relationship

$$I_j^v = -\mathcal{E}_j \tag{11}$$

known as the Koopmans theorem[171], is the basis of almost all qualitative and many semiquantitative discussions of PE spectra.

Under the above assumption that removal of an electron from a CMO φ_j of M will leave the geometry of the system unchanged, both the closed-shell molecule M and the radical cation $M^{+\bullet}$ belong to the same symmetry group $\mathcal{G}$. Because the closed-shell ground configuration $^1\Phi_0$ is totally symmetric, the radical cation configurations $^2\tilde{\Phi}_j$ must necessarily belong to the same irreducible representation of the group $\mathcal{G}$ as the vacated CMO φ_j. It follows that a discussion of ionization energies based on the Koopmans theorem can be carried out, without loss of generality, on the level of the CMOs φ_k. All that is needed in this approximation are the orbital energies $\mathcal{E}_j$ of the CMOs φ_j of M, their nodal properties, the irreducible representations of $\mathcal{G}$ to which they belong and — in some cases — additional characteristic values that can be derived from the set of the occupied CMOs φ_j, such as bond orders (bond populations) or charge distributions.

All this suggests a further simplification, which has proved to be eminently successful in many cases. It is known that independent electron treatments, such as the Hückel (HMO) treatment[2] or the extended Hückel treatment (EHT)[172], which do not take the electron–electron interaction explicitly into account, yield — by and large — orbitals φ_j which are close approximations to those derived from sophisticated SCF calculations. In particular, the HMO and ETH molecular orbitals reflect faithfully the symmetry and nodal properties of their counterparts obtained from SCF treatments.

In the following we shall discuss the different models in context with their application to particular problems arising in the discussion of diene and polyene PE spectra.

D. Planar Conjugated Polyenes

1. Introductory remarks

This section concerns unsubstituted planar polyenes C_nH_m, n even and $m = n+2(1-r)$, r being the number of rings, i.e. π-systems with all atoms, C and H, in a common plane. Low man on the totem pole of quantum-chemical models adequate for such polyenes (and, of course, for aromatic π-systems) is the Hückel (HMO) treatment[2] which assumes strict orthogonality between the molecular σ- and π-orbitals. Under the assumption of this so-called 'σ/π-separation' the π-orbitals can be dealt with independently of the σ manifold

by forming linear combinations of appropriate basis orbitals η_μ which are antisymmetric with respect to reflection through the molecular plane:

$$\varphi = \sum_\mu \eta_\mu c_\mu \tag{12}$$

With respect to an otherwise unspecified operator $\mathbf{H}$ one defines the energy a_μ of a basis function η_μ and the interaction term $b_{\mu\nu}$ between two basis functions η_μ and η_ν as

$$a_\mu = \langle \eta_\mu \, | \mathbf{H} | \, \eta_\mu \rangle \tag{13}$$

and

$$b_{\mu\nu} = \langle \eta_\mu \, | \mathbf{H} | \, \eta_\nu \rangle. \tag{14}$$

To obtain the π-orbitals φ_j of the polyene model system and their orbital energies $\mathcal{E}_j$ one first diagonalizes the $N \times N$ matrix defined by equation 15, N being the number of basis functions η_μ:

$$\mathbb{H} = \begin{pmatrix} a_1 & b_{12} & b_{13} & \cdots & b_{1N} \\ b_{21} & a_2 & b_{23} & \cdots & b_{2N} \\ b_{31} & b_{32} & a_3 & \cdots & b_{3N} \\ \vdots & \vdots & \vdots & \vdots & \vdots \\ b_{N1} & b_{N2} & b_{N3} & \cdots & a_N \end{pmatrix} \tag{15}$$

This yields the N orbital energies (eigenvalues)

$$\mathcal{E}_j = \mathcal{E}_j(\cdots a_\mu \cdots b_{\mu\nu} \cdots) \tag{16}$$

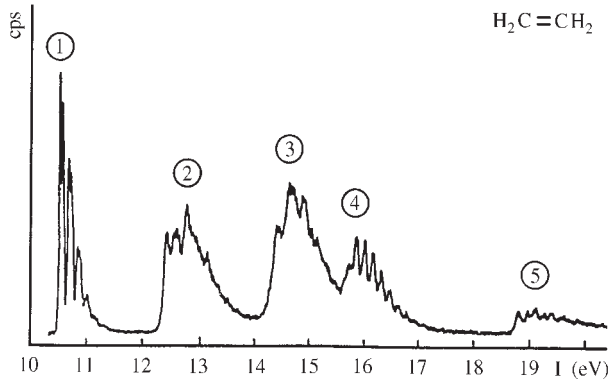
and the corresponding N eigenvectors $\mathbb{C}_j = (c_{\mu j})^{\mathrm{T}}$, the components $c_{\mu j}$ of which define the molecular orbitals

$$\varphi_j = \sum_\mu \eta_\mu c_{\mu j} \tag{17}$$

The orbital energies $\mathcal{E}_j$ so obtained depend, as shown in equation 16, on the parameters a_μ and $b_{\mu\nu}$, which are thus available for calibration by comparison with experimental data, i.e. by matching the $\mathcal{E}_j$ to observed band positions I_j^{m} for a series of polyenes. To this end we postulate that $I_j^{\mathrm{v}} = -\mathcal{E}_j$. Although this looks suspiciously like the Koopmans theorem (equation 11) it should be realized that $I_j^{\mathrm{v}} = -\mathcal{E}_j$ is now simply the consequence of assuming independent electrons. Whereas $\mathcal{E}_j$ in equation 11 contains the explicit interactions of an electron in φ_j with all the other $2n$ - 1 electrons of the molecule M, this is no longer the case if $\mathcal{E}_j$ is calculated by an independent electron procedure. (Notwithstanding this important difference, it has become customary to refer to $I_j^{\mathrm{v}} = -\mathcal{E}_j$ as the Koopmans theorem even if it is applied to an independent electron model.) Once the parameters a_μ and $b_{\mu\nu}$ have been calibrated using a limited set of polyenes, it is found that they allow the computation of reasonably reliable predictions of ionization energies for other polyenes.

2. Linear combination of two-centre π-orbitals

The simplest model of this kind — and admittedly a rather naive one — is to choose two-centre π-orbitals π_μ as basis functions. The prototype for the π_μ is the π-orbital of ethene. Because ejection of an electron from this orbital yields the low-energy band, at $I_1^{\mathrm{v}} = 10.5$ eV, in the ethene PE spectrum shown in Figure 4, $A = -I_1^{\mathrm{v}} = -10.5$ eV is



Band	State	I_v^m (eV)
①	$\tilde{X}$	10.51 (π-band)
②	$\tilde{A}$	12.85
③	$\tilde{B}$	14.66 (σ-bands)
④	$\tilde{C}$	15.87
⑤	$\tilde{D}$	19.1

FIGURE 4. Photoelectron spectrum of ethene:

a first, rough estimate of the basis energy of the two-centre π-orbitals π_μ. We introduce the following simplifications:

(1) The basis energies (equation 13) are assumed to be the same for all basis functions π_μ, i.e. $a_\mu = A$:

$$\langle \pi_\mu \,|\mathbf{H}|\, \pi_\mu \rangle = A \text{ for all } \mu \tag{18}$$

(2) The cross terms (equation 14) differ from zero only if π_μ and π_ν are conjugated, in which case they are assigned the same value B:

$$\begin{aligned} \langle \pi_\mu \,|\mathbf{H}|\, \pi_\nu \rangle &= B \quad \text{if } \mu, \nu \text{ conjugated} \\ &= 0 \quad \text{otherwise} \end{aligned} \tag{19}$$

Under these conditions the π-system of a given polyene with N double bonds can be characterized by a graph $\mathcal{G}$ in which each of the N basis π-orbitals π_μ is represented by a node and each cross term B by an edge, as shown in Figure 5. Such a graph translates into an adjacency matrix $\mathbb{A} = (A_{\mu\nu})$ with $A_{\mu\nu} = 1$ if μ and ν are connected by an edge, and zero otherwise. (Do not confuse A with $A_{\mu\nu}$!) To give an example, the adjacency matrix $\mathbb{A}$ of (3*E*)-hexa-1,3,5-triene **161** (cf Figure 5) is

$$\begin{pmatrix} 0 & 1 & 0 \\ 1 & 0 & 1 \\ 0 & 1 & 0 \end{pmatrix} \tag{20}$$

Diagonalization of $\mathbb{A}$ yields the eigenvalues X_j and the corresponding eigenvectors $\mathbb{C}_j = (C_{\mu j})$. From these one obtains the N orbital energies

$$\mathcal{E}_j = A + X_j B \tag{21}$$

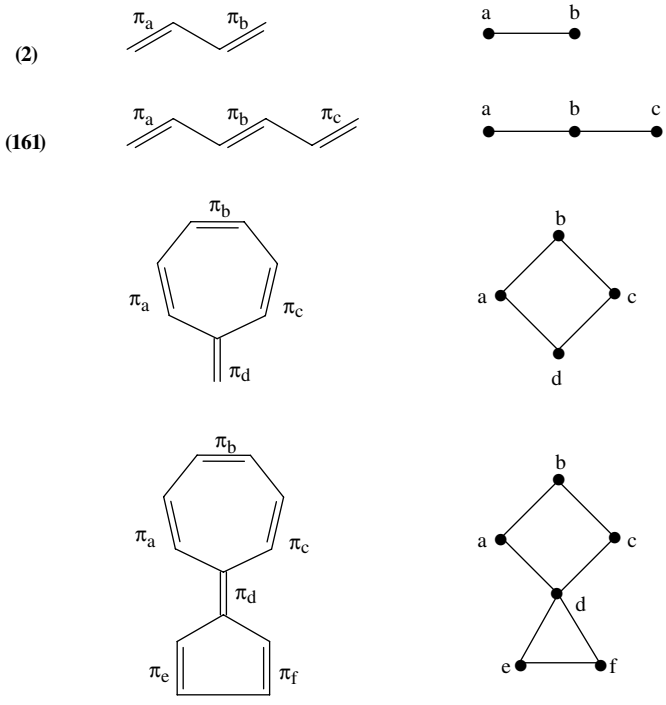


FIGURE 5. Representative graphs $\mathcal{G}$ for an independent electron model based on linear combinations of two-centre π-orbitals π_μ. Examples: 1,3-butadiene **2**, (3*E*)-hexa-1,3,5-triene **161**, heptafulvene and sesquifulvalene

and the N molecular orbitals

$$\varphi_j = \sum_\mu \pi_\mu C_{\mu j} \tag{22}$$

Thus the diagonalization of the matrix 20 yields $X_1 = -\sqrt{2}$, $X_2 = 0$, $X_3 = \sqrt{2}$ and, according to equation 21, $\mathcal{E}_1 = A - \sqrt{2}B$, $\mathcal{E}_2 = A$ and $\mathcal{E}_3 = A + \sqrt{2}B$. Using the Koopmans theorem (equation 11) the π-bands in the PE spectrum of (3*E*)-hexa-1,3,5-triene **161** are therefore expected at positions $I_1^{\mathrm{v}} = -A + \sqrt{2}B$, $I_2^{\mathrm{v}} = -A$ and $I_3^{\mathrm{v}} = -A - \sqrt{2}B$. If this procedure is applied to a series of planar π-systems, e.g. ethene, 1,3-butadiene **2**, (3*E*)-hexa-1,3,5-triene **161**, fulvene **175** and other unsubstituted polyenes, and if the computed ionization energies $I_{j,\mathrm{calc}}^{\mathrm{v}} = -\mathcal{E}_j$ are compared to the corresponding experimental values I_j^{v} or I_j^{m} by means of linear regression techniques, one obtains roughly $A \approx -10.2$ eV and $B \approx -1.2$ eV. Using these values for e.g. (3*E*,5*E*)-octa-1,3,5,7-tetraene **234**, one finds, according to the above procedure, $I_{1,\mathrm{calc}}^{\mathrm{v}} = 8.3$ eV, $I_{2,\mathrm{calc}}^{\mathrm{v}} = 9.5$ eV, $I_{3,\mathrm{calc}}^{\mathrm{v}} = 10.9$ eV and $I_{4,\mathrm{calc}}^{\mathrm{v}} = 12.1$ eV, which compare favourably with the experimental findings for **234** shown in Figure 6 and in Table 2.

The limitations of this naive approach are immediately obvious, if one considers that the molecules [3]radialene **173**, 3,4-dimethylidenecyclobutene **174** and fulvene **175** give rise to the same graph $\mathcal{G}$ (see display 23) and thus to identical predictions for their three π ionization energies. Using the above parameters one finds $I_{1,\mathrm{calc}}^{\mathrm{v}} = I_{2,\mathrm{calc}}^{\mathrm{v}} = 9.0$ eV,

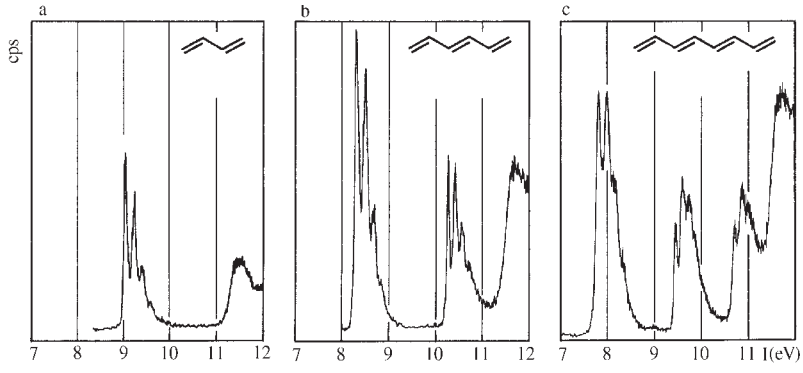
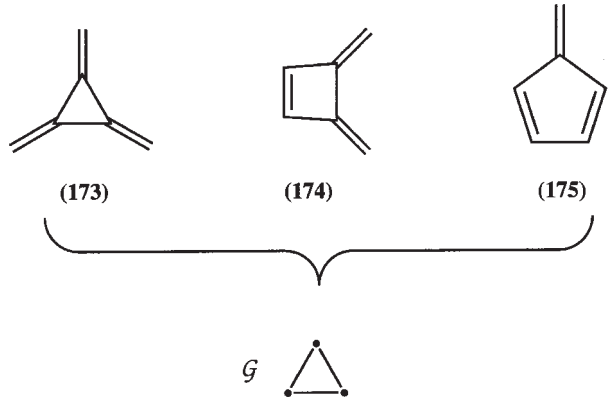


FIGURE 6. Photoelectron spectra of (a) 1,3-butadiene **2**, (b) (*E*)-hexa-1,3,5-triene **161** and (c) (3*E*, 5*E*)-octa-1,3,5,7-tetraene **234**

and $I^{v}_{3,\mathrm{calc}} = 12.6$ eV, the first two values being degenerate because of the D_{3h} symmetry of the graph $\mathcal{G}$. Whereas this result is compatible with the experimental results for **173** of the same symmetry as $\mathcal{G}$ (see Table 2), it is at odds with those for **174** and **175**, which lack the symmetry of $\mathcal{G}$.



(23)

This shortcoming could be avoided and the treatment improved by assigning different basis energies A_{exo} and A_{endo} to exocyclic and endocyclic basis orbitals π_μ and by adjusting the cross terms, but this is not really worthwhile. (For a more detailed discussion of the model see elsewhere[173].)

3. The standard Hückel treatment

In the familiar standard Hückel treatment[2,174] of planar π-systems, the basis functions are atomic orbitals (AO) $2p_{z,\mu} \equiv \phi_\mu$, z being the coordinate perpendicular to the molecular plane. In analogy to the previous model, the basis energies of the atomic orbitals ϕ_μ and the cross terms between neighbouring pairs of AOs, ϕ_μ and ϕ_ν, are defined by

$$\langle \phi_\mu \,|\mathbf{H}|\, \phi_\mu \rangle = \alpha \text{ for all } \mu \tag{24}$$

and

$$\langle \phi_\mu \, |\mathbf{H}| \, \phi_\nu \rangle = \beta \text{ if } \mu, \nu \text{ conjugated} \qquad (25)$$
$$= 0 \text{ otherwise}$$

Under these conditions a π-system extending over N carbon centres is represented by a graph $\mathcal{G}$[175] in which the nodes correspond to the basis orbitals ϕ_μ and the edges to those cross terms (equation 25) which are equal to β. Diagonalization of the corresponding adjacency matrix $\mathbb{A}$ — sometimes called the Hückel matrix — yields N eigenvalues x_j and the corresponding eigenvectors $\mathbb{C}_j = (c_{\mu j})$. These quantities define the orbital energies $\mathcal{E}_j$ and the Hückel molecular orbitals φ_j (HMO) according to

$$\mathcal{E}_j = \alpha + x_j \beta \qquad (26)$$

and

$$\varphi_j = \sum_\mu \phi_\mu c_{\mu j} \qquad (27)$$

To demonstrate the quality of this simple approach we show in Figures 6 and 7 the PE spectra of 1,3-butadiene **2**, (3*E*)-hexa-1,3,5-triene **161**, (3*E*, 5*E*)-octa-1,3,5,7-tetraene **234**, [3]radialene **173**, 3,4-dimethylidenecyclobutene **174** and fulvene **175**. The observed positions I_j^{m} of the π-bands are collected in the third column of Table 2, and the eigenvalues x_j obtained from standard HMO models in the fourth. A least-squares calculation yields the linear regression

$$I_j^{\mathrm{m}} \text{ (eV)} = 7.15 + 2.60\, x_j \qquad (28)$$

shown in Figure 8. As can be seen, the agreement is rather satisfactory in view of the simplicity of the treatment. The values $I_{j,\mathrm{calc}}^{\mathrm{v}}$ calculated according to equation 23 are listed in the last column of Table 2. Using the Koopmans theorem (equation 11) in conjunction with equations 26 and 28, the following calibration of the basic parameters is obtained:

$$\alpha = -7.15 \text{ eV}, \quad \beta = -2.60 \text{ eV} \qquad (29)$$

4. Alkyl-substituted planar dienes and polyenes

Restricting ourselves, as before, to molecules C_nH_m we shall discuss only the consequences due to the replacement of hydrogen atoms by alkyl groups R. The influence of the substituents R on the orbital energies $\mathcal{E}_j$ of the π-orbital φ_j of the parent molecule — and thus, according to the Koopmans theorem, on the ionization energy $I_{j,\mathrm{calc}}^{\mathrm{v}}$ — is assigned, within an HMO treatment, to two causes:(a) to an inductive effect and (b) to hyperconjugation.

(a) *Inductive effect*. If a hydrogen atom in position ρ of a planar π-system is replaced by an alkyl group R_ρ, the inductive effect of R_ρ is assumed to change the basis energy of the atomic orbital ϕ_ρ from α to

$$\alpha_\rho(R_\rho) = \alpha + \delta\alpha_\rho(R_\rho) \qquad (30)$$

The perturbation $\delta\alpha_\rho(R_\rho)$ is positive for all alkyl groups, increasing with increasing size of the group R_ρ. The change $\delta\mathcal{E}_{j,\mathrm{ind}} = \mathcal{E}'_j - \mathcal{E}_j$ of the orbital energy $\mathcal{E}_j$ due to the inductive influence of alkyl substituents R_ρ in positions ρ of the parent molecule can be

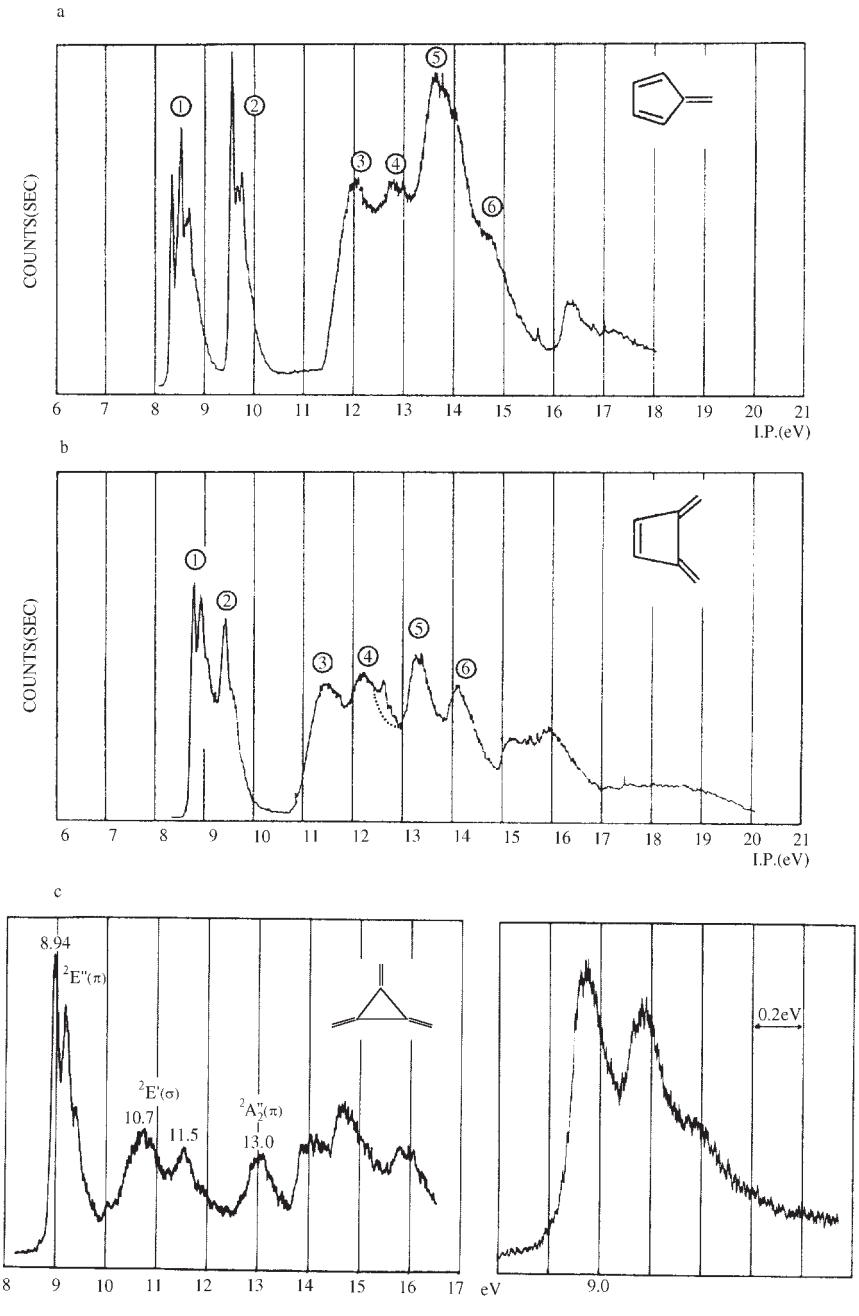


FIGURE 7. Photoelectron spectra of (a) fulvene **175**, (b) dimethylidenecyclobutene **174** and (c) [3]radialene **173**

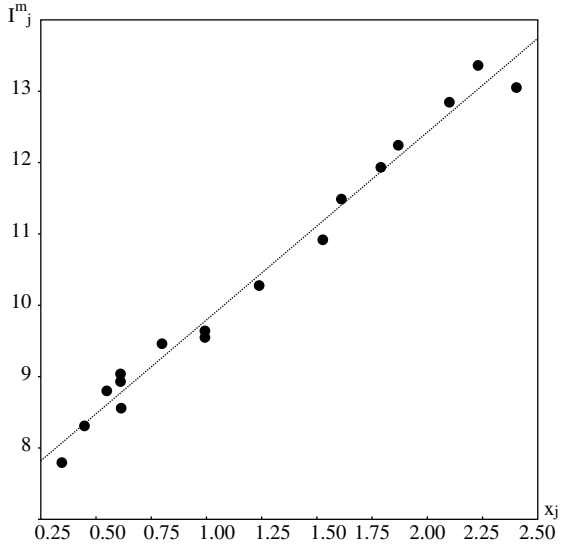


FIGURE 8. Regression of observed vertical ionization energies I_j^m on the corresponding HMO x_j values for the set of planar polyenes listed in Table 2

TABLE 2. Observed band positions I_j^m and calculated HMO ionization energies $I_{j,calc}^v$ for some polyenes

	Polyene	I_j^m(eV)	x_j	$I_{j,calc}^v$ (eV)
2	Butadiene	9.03	0.618	8.73
		11.46	1.618	11.33
161	(3*E*)-Hexa-1,3,5-triene	8.29	0.445	8.28
		10.26	1.247	10.37
		11.90	1.802	11.81
234	(3*E*, 5*E*)-Octa-1,3,5,7-tetraene	7.79	0.347	8.03
		9.61	1.000	9.37
		10.89	1.532	11.11
		12.20	1.879	12.01
173	[3]Radialene	8.94	0.618	8.94
		13.00	2.414	13.40
174	3,4-Dimethylidenecyclobutene	8.80	0.555	8.57
		9.44	0.802	9.44
		13.30	2.247	13.30
175	Fulvene	8.55	0.618	8.73
		9.54	1.000	9.72
		12.80	2.115	12.62

estimated by a first-order perturbation calculation according to

$$\delta\mathcal{E}_{j,\mathrm{ind}} = \sum_{\rho} \delta\alpha_{\rho}(R_{\rho}) c_{\rho j}^2 \tag{31}$$

where the summation carries only over the substituted positions ρ. According to the Koopmans theorem (equation 11) the corresponding change $\delta I_{j,\mathrm{ind}}^v$ of the ionization energy

$I^{v}_{j,\mathrm{calc}}$ is then given by

$$\delta I^{v}_{j,\mathrm{ind}} = -\delta\mathcal{E}_{j,\mathrm{ind}} = -\sum_{\rho} \delta\alpha_{\rho}(\mathrm{R}_{\rho}) c^{2}_{\rho j} \tag{32}$$

Note that the shift $\delta I^{v}_{j,\mathrm{ind}}$ is always negative, meaning that the inductive influence of alkyl substituents leads to a reduction of the ionization energies $\mathrm{I}^{v}_{j,\mathrm{calc}}$ relative to the values calculated for the parent molecule.

If one assumes that the substituents R exert only an inductive effect, a crude calibration of $\delta\alpha_{\rho}(\mathrm{R}_{\rho})$ is obtained from π-ionization energy shifts δI^{v}_{1} observed for alkyl-substituted ethenes[176], as shown in Figure 9. It is seen that the size of $\left|\delta I^{v}_{1}\right|$ increases with increasing number of C-atoms of the alkyl group. Because both atomic orbital coefficients of the ethene π-orbital $\pi = (\phi_1 + \phi_2)/\sqrt{2}$ are equal to $1/\sqrt{2}$, one obtains from equation 32 the following (upper) estimates for $\delta\alpha_{\rho}(\mathrm{R}_{\rho})$: $\delta\alpha(\mathrm{Me}) = 1.6$ eV; $\delta\alpha(\mathrm{Et}) = 1.8$ eV; $\delta\alpha(i\text{-Pr}) = 2.0$ eV; $\delta\alpha(t\text{-Bu}) = 2.2$ eV. [Note that these $\delta\alpha(\mathrm{R}_{\rho})$ values correlate linearly with the differences $\Delta\sigma^{*}(\mathrm{R}) = \sigma^{*}(\mathrm{R}) - \sigma^{*}(\mathrm{H})$ of Taft's inductive parameters $\sigma^{*}(\mathrm{R})$[177]: $\Delta\sigma^{*}(\mathrm{Me}) = 0.49$, $\Delta\sigma^{*}(\mathrm{Et}) = 0.59$, $\Delta\sigma^{*}(i\text{-Pr}) = 0.68$, $\Delta\sigma^{*}(t\text{-Bu}) = 0.79$.]. Such a parametrization has to be taken with a grain of salt, as it implies that alkyl groups exert only an inductive effect. In addition, it refers only to single substitution at a double bond. If a double bond is multiply substituted, the observed shift δI^{v}_{1} is smaller than the sum of the individual $\delta I^{v}_{j,\mathrm{ind}}$ values calculated according to equation 32 for each of the substituting alkyl groups.

(b) *Hyperconjugation*. Hyperconjugation between a π-orbital φ_j and a pseudo π-orbital ϕ_{R} of a substituting alkyl group R can be taken care of by a model first proposed by Mulliken[178]. To this end one assigns a basis energy α_{R} to ϕ_{R} and a cross term

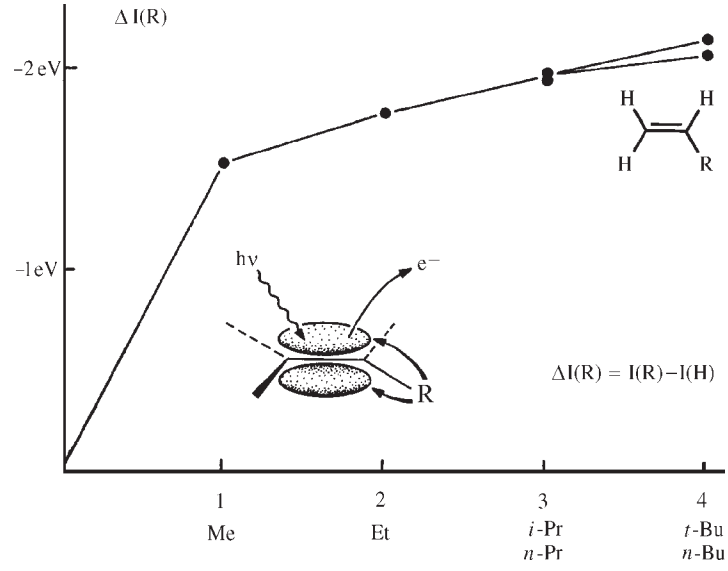


FIGURE 9. Shifts $\Delta I(\mathrm{R})$ of the π-ionization energy of ethene induced by a single alkyl group R = Me, Et, *n*-Pr, *i*-Pr, *n*-Bu and *t*-Bu

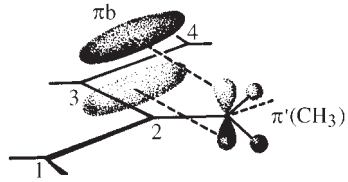
$\beta_{\rho R} = \langle \phi_\rho | \mathbf{H} | \phi_R \rangle$ to the interaction of ϕ_R with the atomic orbital ϕ_ρ at the point of substitution. The shift $\delta\mathcal{E}_{j,\text{hyp}}$ caused by a single substitution can be estimated by second-order perturbation theory according to

$$\delta\mathcal{E}_{j,\text{hyp}} = (c_{\rho j}\beta_{\rho R})^2/(\mathcal{E}_j - \alpha_R) \tag{33}$$

If this is rewritten in the form $\delta\mathcal{E}_{j,\text{hyp}} = [\beta_{\rho R}^2/(\mathcal{E}_j - \alpha_R)]c_{\rho j}^2$, one sees that for a given alkyl group R this hyperconjugative shift is again proportional to $c_{\rho j}^2$ in analogy to the inductive shift (equation 32). The expression in square brackets increases with decreasing difference $\mathcal{E}_j - \alpha_R$, which is in general positive for the top π-orbitals. This means that π-orbitals φ_j lying closer in energy to the pseudo π-orbital ϕ_R are more strongly affected by hyperconjugation than the upper ones. As long as the π-orbital φ_j lies above ϕ_R, the hyperconjugative shift $\delta I_{j,\text{hyp}}^v = -\delta\mathcal{E}_{j,\text{hyp}}$ calculated according to equation 33 is again towards lower ionization energies, adding to the one due to the inductive effect (see equation 32), with the result that the total shift $\delta I_{j,\text{calc}}^v = \delta I_{j,\text{ind}}^v + \delta I_{j,\text{hyp}}^v$ is given — within our simple model — for a multiply substituted π-system by

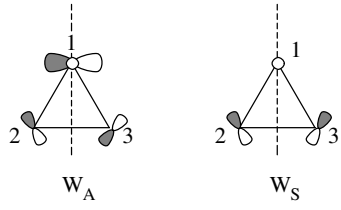
$$\delta I_{j,\text{calc}}^v = -\sum_\rho \left(\delta\alpha_\rho(R_\rho) + \beta_{\rho R}^2/(\mathcal{E}_j - \alpha_R)\right) c_{\rho j}^2 \tag{34}$$

Hoffmann has pointed out[179] that one should also expect significant through-space interaction (i.e. hyperconjugation) between alkyl groups R and two-centre π-orbitals which are not directly bonded, as shown schematically in diagram 35 for R = Me. (In this example we have used the model described in Section II.D.2, i.e. using as basis a two-centre orbital π and a pseudo π-orbital $\pi'(CH_3)$ for the methyl group.) The effect of this type of interaction can be shown by comparison of the two π-ionization energies I_1^v and I_2^v of (2*E*,4*E*)-hexa-2,4-diene **10** and of 2,3-dimethylbuta-1,3-diene **11**[20]. Whereas the mean π-ionization energy $(I_1^v + I_2^v)/2$ is the same for both molecules, i.e. 11.33 eV and 11.31 eV respectively, the split $I_2^v - I_1^v$ is quite different, namely 3.07 eV and 2.28 eV. These observations are nicely explained by Hoffmann's theory, as shown in Figure 10 which is self-explanatory.



(35)

A special case is met when the substituent is the cyclopropyl group, because of the presence of high-lying almost π-type σ-orbitals. These orbitals, W_A and W_S, shown schematically in diagram 36, have been introduced by Walsh[180] to explain the properties of molecules containing the cyclopropane moiety.



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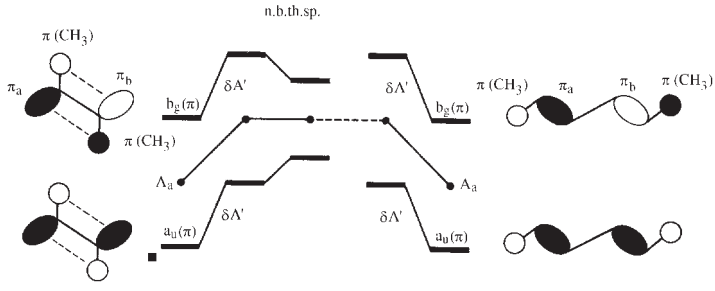
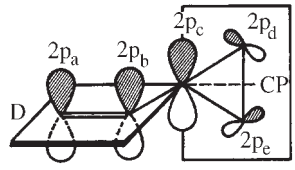


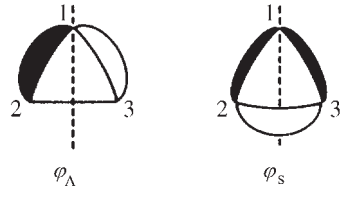
FIGURE 10. Correlation diagram showing the influence of non-bonded through-space (n.bd.th.sp) interaction between the pseudo π-orbitals $\pi(CH_3)$ (circles) and the double-bond π-orbitals π_a and π_b (ovals) on the π-orbital energies of the butadiene π-system. A_a is the basis energy of π_a and π_b and δA the inductive and hyperconjugative destabilization (see equation 34)

Because these orbitals — which are degenerate in cyclopropane because of its D_{3h} symmetry — are close in energy to two-centre π-orbitals, and because the antisymmetric Walsh orbital W_A consists essentially of a 2p-orbital in position 1, a cyclopropyl substituent acts almost as another two-centre π-orbital in direct conjugation with that of the substituted double bond, as sketched in diagram 37. It follows that the PE spectra of molecules in which the cyclopropyl group is ideally aligned for optimal conjugation with a planar π-system, will be very similar to that of the corresponding polyene. For example, the PE spectrum of spiro[2.4]hepta-4,6-diene (homofulvene) **74** resembles that of fulvene **175**, as shown in Figure 11.



(37)

However, for a more detailed and reliable rationalization of the PE spectroscopic consequences due to conjugation with a cyclopropyl moiety, it is of advantage to use a model originally proposed by Förster[181] and later by Coulson and Moffitt[182]. The advantages of this model, where the high-lying cyclopropane orbitals are written in terms of localized CC σ-orbitals (diagram 38), have been discussed elsewhere[183].



(38)

5. Special cases

a. Deviations from planarity. The moderate bending and twisting of a single double bond has only a very small effect on its π-ionization energy because of an internal

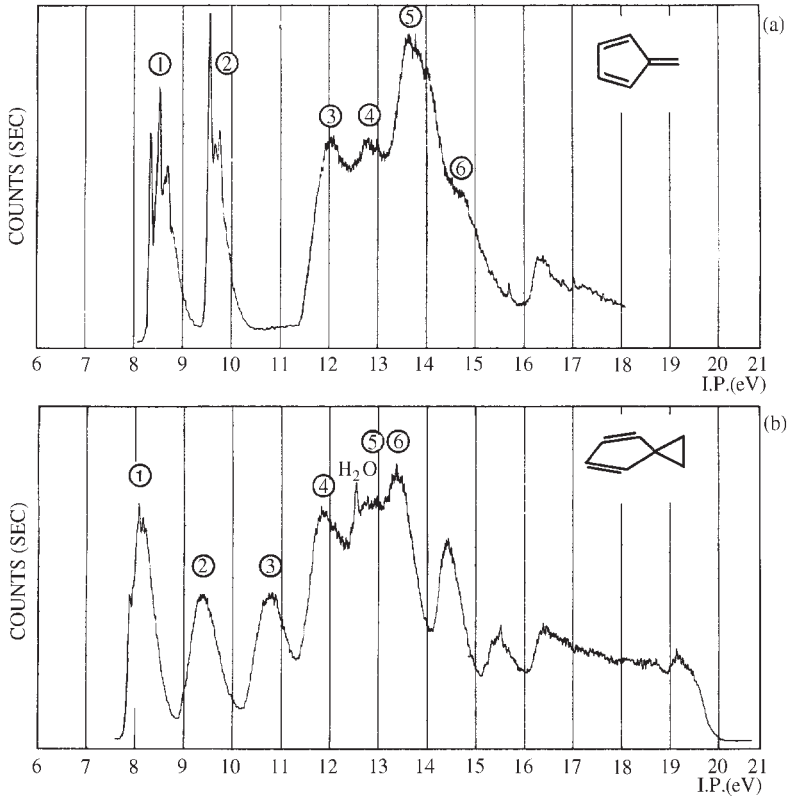


FIGURE 11. Comparison of the PE spectra of (a) fulvene **175** and (b) homofulvene (spiro[2.4]hepta-4,6-diene) **74**

compensation of different electronic effects[184]. (An example is provided by the analysis of the PE spectrum of tricyclo[4.2.2.2^{2,5}]dodeca-1,5-diene **129**[96].) In contrast, the twisting about the single bond connecting two conjugated double bonds, e.g. in butadiene **2**, has a large effect on both π-ionization energies I_1^v and I_2^v leading in particular to a significant reduction of the gap $\Delta I = I_2^v - I_1^v$. As shown by Maier and Turner[185] this effect can be accounted for within an independent electron model by assuming that the cross term between the two conjugated π-orbitals π_1 and π_2 or between their linked atomic orbitals ϕ_2 and ϕ_3 depends on the twisting angle τ according to the equations

$$\langle \pi_1 | \mathbf{H} | \pi_2 \rangle = B_{1,2} = B \cos \tau \tag{39}$$

or

$$\langle \phi_2 | \mathbf{H} | \phi_3 \rangle = \beta_{2,3} = \beta \cos \tau \tag{40}$$

where $\tau = 0^\circ$ for the s-*trans* conformation. As a result the observed ionization energy gap depends on τ

$$\Delta I_\tau = I_2^v - I_1^v = \Delta I_{\tau=0} \cos \tau \tag{41}$$

This relationship has been used with success to derive the twisting angles τ between two conjugated double bonds[185], and a particularly nice example is provided by the PE spectroscopic determination of the dihedral angle $\tau = 58°$ which perfluorobutadiene assumes in the gas phase[19,186]. Figure 12 presents the PE spectra of the three isomers (2*Z*,4*Z*)-, (2*Z*,4*E*)- and (2*E*,4*E*)-3,4-dimethylhexa-2,4-diene (**26, 27** and **28**)[37], from which it is seen that the gap ΔI_τ decreases with increasing steric interference between the two methyl groups, whereas the mean π-ionization energy $\overline{I^v} = (I_1^v + I_2^v)/2$ remains constant.

Molecule	**26** (2*Z*,4*Z*)	**27** (2*Z*,4*E*)	**28** (2*E*,4*E*)
ΔI_τ (eV)	1.65	0.60	0.30
$\overline{I^v}$ (eV)	8.93	8.90	8.90
τ	0°	69°	80°

(42)

Assuming that the π-system of the (2*Z*,4*Z*) isomer **26** is flat, $\tau = 0°$, equation 41 yields the twist angles τ indicated in the last line of display 42 for the other two isomers. A further example of strong steric prohibition of coplanarity is provided by 2,3-di-*t*-butylbuta-1,3-diene **35**[37], whose PE spectrum yields a gap $\Delta I_\tau = 0.3$ eV, corresponding to a twist angle $\tau = 80°$.

Application of an extension of the above treatment to cyclooctatetraene **239** and other cyclic polyenes[50] yields a satisfactory determination of the twist angles τ between conjugated pairs of their double bonds, in excellent agreement with those derived by other methods.

b. Cumulenes. Although the formulae of the cumulenes allene **1**, butatriene **158** and pentatetraene **232** look deceptively simple, their PE spectra are among the most difficult to interpret. Allene, first investigated by Baker and Turner[187], and pentatetraene exhibit D_{2d} symmetry, with the result that their highest occupied molecular orbitals are degenerate. Removing an electron from this orbital pair leads to a degenerate doublet state of the corresponding radical cation, which therefore undergoes a Jahn–Teller distortion. This distortion can lead to a radical cation of C_{2v} or D_2 symmetry, depending on whether the distortion proceeds along the stretching B_2 or the twisting B_1 mode of vibration of the parent hydrocarbon, as has been shown by Haselbach[188]. The resultant Franck–Condon envelopes are thus rather complicated and difficult to analyse. This complication can be partially avoided by breaking the D_{2d} symmetry, i.e. by correlating the π-band positions in the PE spectrum of allene with those in the spectra of methyl-substituted allenes **3**, **6**, **7**, **15** and **18**[17], or of tetrafluoroallene[115].

Butatriene **158**, belonging to the symmetry group D_{2h}, is planar, and therefore lacks degenerate orbitals. Notwithstanding this simplification its PE spectrum is far from simple. In particular, the first π-band at 9.15 eV is accompanied at higher energy by a second 'mystery band' at 9.63 eV, as shown in Figure 13[114]. This feature cannot be accounted for by an independent electron model, and not even by SCF models. It has been shown by von Niessen, Cederbaum and their coworkers[189] that it arises as a consequence of vibronic mixing of the $^2B_{2g}$ and $^2B_{3u}$ states of the butatriene radical cation. Supporting evidence for this interpretation is provided by an analysis of the PE spectra of terafluorobutatriene, tetramethylbutatriene **168** and tetra-*t*-butylbutatriene **172**[115]. It follows that the PE spectra of molecules containing cumulated double bonds cannot be interpreted with reference to the usual, naive, independent electron-orbital picture.

c. π-Systems exhibiting second-order bond fixation. A special case is given by cyclic π-systems for which two or more Kekulé structures can be written, but which tend to

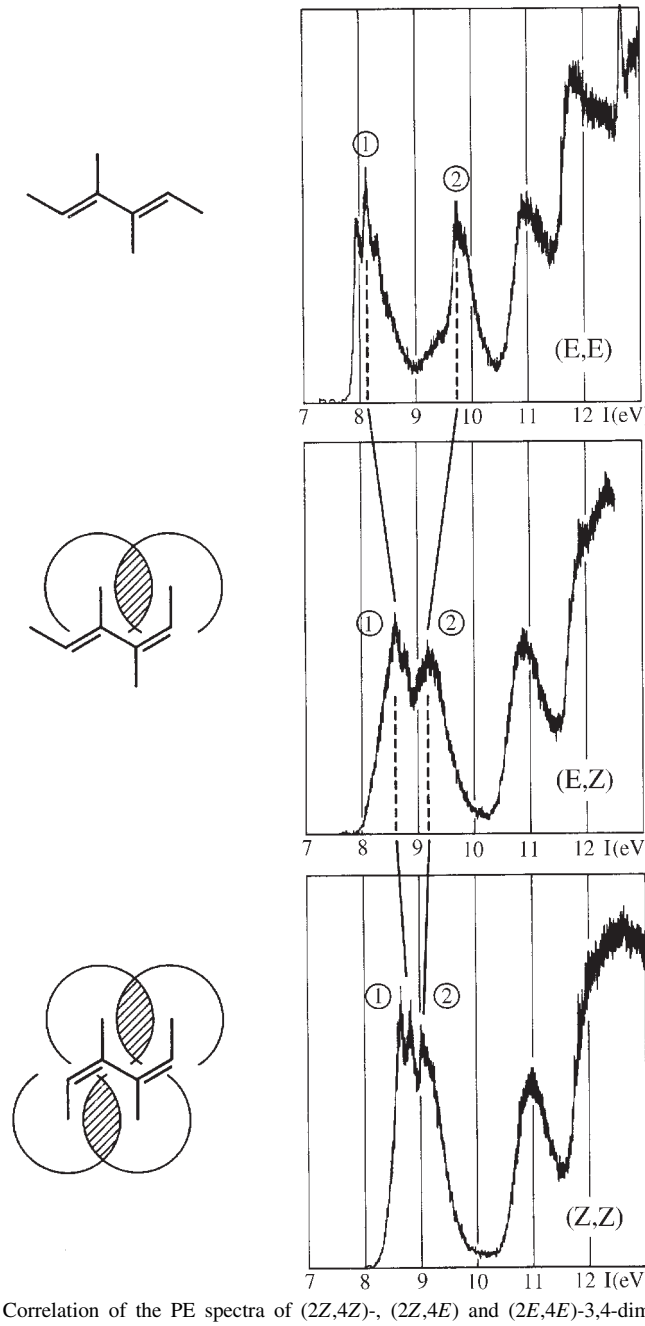


FIGURE 12. Correlation of the PE spectra of (2*Z*,4*Z*)-, (2*Z*,4*E*) and (2*E*,4*E*)-3,4-dimethylhexa-2,4-diene (**26**, **27** and **28**, respectively

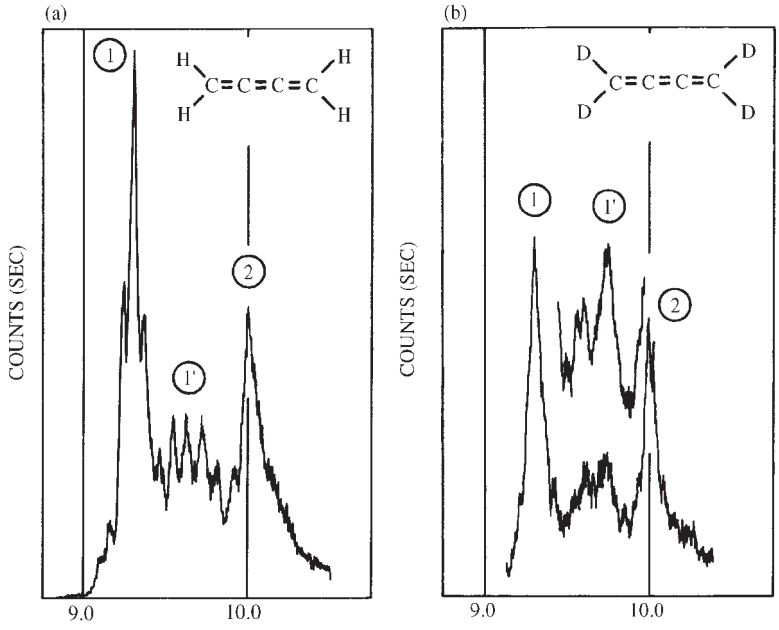


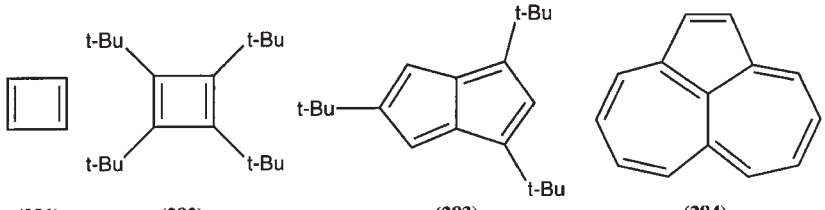
FIGURE 13. Franck–Condon envelopes of the low-energy part of the PE spectra of (a) butatriene **158** and (b) tetradeuteriobutatriene **159**. The central feature labeled 1′ is the 'mystery band' mentioned in the text

localize their double bonds to assume a structure corresponding to only one or other of these Kekulé structures. It has been shown by Longuet-Higgins and Salem[14] that this is a second-order effect which occurs in annulenes above a critical size. The tendency of a molecule towards second-order bond localization can be linked to the bond–bond polarizabilities $\pi_{\mu\nu,\rho\sigma}$ of its π-system[190,191]. Typical examples are hydrocarbons containing cyclobutadiene, pentalene or heptalene moieties. Because bond–bond polarizabilities $\pi_{\mu\nu,\rho\sigma}$ of the neutral ground-state molecule M change when an electron is removed from an orbital φ_j, the tendency of the radical cation $M^{+\bullet}$ to localize its double bonds varies, depending on the electronic state $^2\tilde{\Psi}_j$ of $M^{+\bullet}$[190]. This effect complicates the analysis of the PE spectra of such molecules.

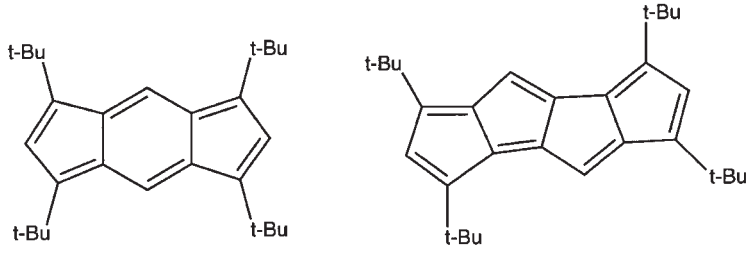
The PE spectra of cyclobutadiene **281**[192], tetra-*t*-butylcyclobutadiene **282**[193], 1,3,5-tri-*t*-butylpentalene **283**[194] and aceheptylene **284**[195], all of which are subject to second-order bond localization, have been described in the literature. Further examples are 1,3,5,7-tetra-*t*-butyl-*s*-indacene **285** (which exhibits a first double band 1,2 at $I^v_{1,2} = 6.75$ eV, followed by two bands at $I^v_3 = 8.50$ eV and $I^v_4 = 9.30$ eV) and the tetracyclic hydrocarbon 1,3,6,8-tetra-*t*-butylpentaleno[2,1-*a*]pentalene **286** (the first two bands of which are observed at 6.40 eV and 7.65 eV)[196].

6. Some cautionary remarks

The simple HMO model[2] has proved useful in many cases — and is in fact still used — for a first rationalization of the PE spectra of planar — almost planar — polyenes.



(281) (282) (283) (284)



(285) (286)

Notwithstanding its advantages, its limitations must be taken into account, even if it is applied only qualitatively and certainly if a semiquantitative discussion is intended. In this connection the following points are worth mentioning.

(1) The Hückel treatment and its simpler version presented in Section II.D.2 make the implicit assumption that the manifold of π-orbitals lies above and is well separated from the σ-orbital manifold. Whereas the first bands in the PE spectrum of a planar polyene with N conjugated double bonds are indeed due to ejection of an electron from π-orbitals, this is not necessarily true for all of its first N bands. The reason is that σ-orbitals are delocalized over the whole of the σ-frame of the molecule M — sometimes even more so than the π-orbitals — with the result that the top σ-orbitals move to higher energies with increasing size of the molecule. To give an example: the first band in the PE spectrum of ethane is found at $I_1^m = 11.5$ eV but that of the saturated tetracyclic hydrocarbon perhydropyrene is at $I_1^m = 9.0$ eV[197]. This shift towards lower ionization energies occurs also if the σ-frame consists of sp^2–sp^2 single bonds[197]. As a consequence, the third band observed in the PE spectrum of (3*E*)-hexa -1,3,5-triene **161** at 11.9 eV (Figure 6 and Table 2) is due to the superposition of the third π-band and of the first σ-band, and the fourth band at 11.7 eV in the PE spectrum of (3*E*, 5*E*)-octa -1,3,5,7-tetraene **234** (Figure 6 and Table 2) is a σ-band preceding the fourth π-band at 12.2 eV. The implications will be discussed in a later section.

(2) Because independent electron treatments do not take electron–electron interactions into account explicitly, the ground configuration $^1\Phi_0$ or the configurations $^2\tilde{\Phi}_j$ obtained by removing a single electron from one of the orbitals φ_j will not mix with excited configurations. This excludes configuration interaction known to be an important factor. For instance, some of the standard Hückel molecular orbitals φ_j derived for molecules such as heptafulvene **287** or sesquifulvalene **288** are completely localized on only part of the molecule, e.g. on either the five- or the seven-membered ring of **288**. Removing an electron from such an orbital leads to a radical cation in which the positive charge is concentrated on one of the rings only. Obviously, the radical cation will avoid this unfavourable distribution by spreading the charge over the remainder of the system, thereby lowering its energy. It follows that the observed π-band positions in the PE spectra of **287** and

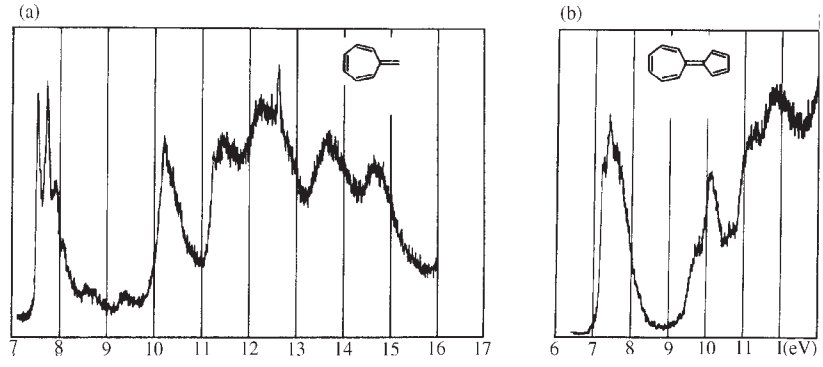
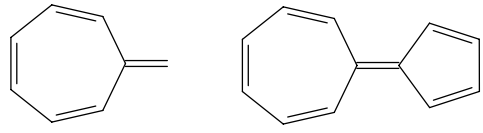


FIGURE 14. Photoelectron spectra of (a) heptafulvene **287** and (b) sesquifulvalene **288**

288 shown in Figure 14 173 — and of similar molecules — will not fit the results of independent electron-model calculations. Spanguet-Larsen has shown[198] that the reasons for this failure are in fact more complicated than stated above.



(287) **(288)**

(3) The assumption of constant interaction terms B between conjugated π_μ basis orbitals or of β between bonded $2p_z(\phi_\mu)$ orbitals assumes that all bonds in the polyene, both double and single, have the same length R_0 both in the neutral molecule M and in the radical cation $M^{+\bullet}$, independent of its different configurations $^2\tilde{\Phi}_j$. However, this is not the case. In a first, crude approximation the interatomic distances $R_{\mu\nu}$ of the neutral molecule are linear functions of the bond orders $p_{\mu\nu}$ and those of the radical cation, $R^+_{\mu\nu,j}$, of the bond orders $p^+_{\mu\nu,j} = p_{\mu\nu} - c_{\mu j}c_{\nu j}$, j being the quantum number of the vacated orbital φ_j. It has been shown[199] that this effect can be taken care of by a perturbation treatment (thereby improving the agreement) of the computed $I^{\mathrm{v}}_{j,\mathrm{calc}}$ values with the observed I^{m}_j ionization energies.

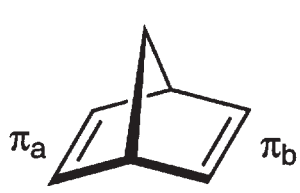
The take-home lesson is that independent electron treatments, e.g. the HMO model, should be used with caution, especially if semiquantitative predictions are intended. *Warning*: Concerning limitations and possible side-effects consult your PE spectroscopist or your neighbour theoretician.

E. Interaction Between Non-conjugated π-Orbitals

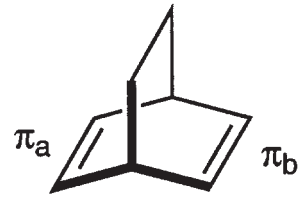
1. A naive, independent electron model

The disproof of the naive expectation that the PE spectrum of a (non-planar) hydrocarbon containing z non-conjugated double bonds would show z π-bands, where each one corresponds to the removal of an electron from only one of the z localized two-centre π-orbitals, was one of the earliest successes of PE spectroscopy. In particular, if in a

diene M the two double bonds, and thus the two π-orbitals π_a and π_b, are symmetry equivalent, one does not observe a single peak due to the superposition of two bands of the same ionization energy $I_a^v = I_b^v$ but two well-separated bands, as shown for example in the PE spectra of 1,1-divinylcyclopropane **46** (Figure 2), or norbornadiene **75** or of bicyclo[2.2.2]octadiene **81** (Figure 15). This means that there exists a large interaction between π_a and π_b.

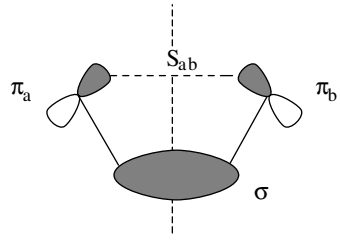


(75)



(81)

Although *ab initio* or semiempirical SCF calculations account rather well for this observation, it has proved extremely enlightening, especially from a qualitative point of view, to discuss the interactions between non-conjugated π-orbitals in terms of the concepts of 'through-space' and 'through-bond' interactions introduced by Roald Hoffmann[200–203]. With reference to the schematic diagram 43 of a non-planar diene, these interactions are defined as follows:



(43)

(1) '*Through-space interaction*'. Although the two π-orbitals π_a and π_b are not in conjugation, there exists a small but finite cross term B between them which, to a first approximation, will be proportional to their overlap integral $S_{ab} = \langle \pi_a | \pi_b \rangle$.

(2) '*Through-bond interaction*'. Because of the molecule's lack of planarity, each of the two π-orbitals π_a and π_b will interact with those of the σ-frame's σ-orbitals which exhibit the appropriate symmetry behaviour.

To illustrate the principles involved we shall use the independent electron model presented in Section II.D.2. For simplicity, we assume that we are dealing with a diene in which the basis π-orbitals π_a and π_b are symmetry equivalent, as is the case for the dienes **75** and **81**, both of which belong to the point group C_{2v}. (The same assumption underlies the schematic diagram 43). Disregarding the 1s orbitals of the carbon atoms, such a diene C_nH_m has $2(n-1)+m/2$ σ-orbitals. Of these we shall consider only a single one (σ), symmetric with respect to the operations which transform the linear combination $\pi_a + \pi_b$ into itself. (The extension to more σ-orbitals is trivial.) Under these conditions we are dealing with a mini-model — depicted in diagram 43 — that can be represented by a graph $\mathcal{G}$ with only three nodes representing π_a, π_b and σ, and three labelled edges, B representing the 'through-space' and Γ the 'through-bond' cross terms. Note that in

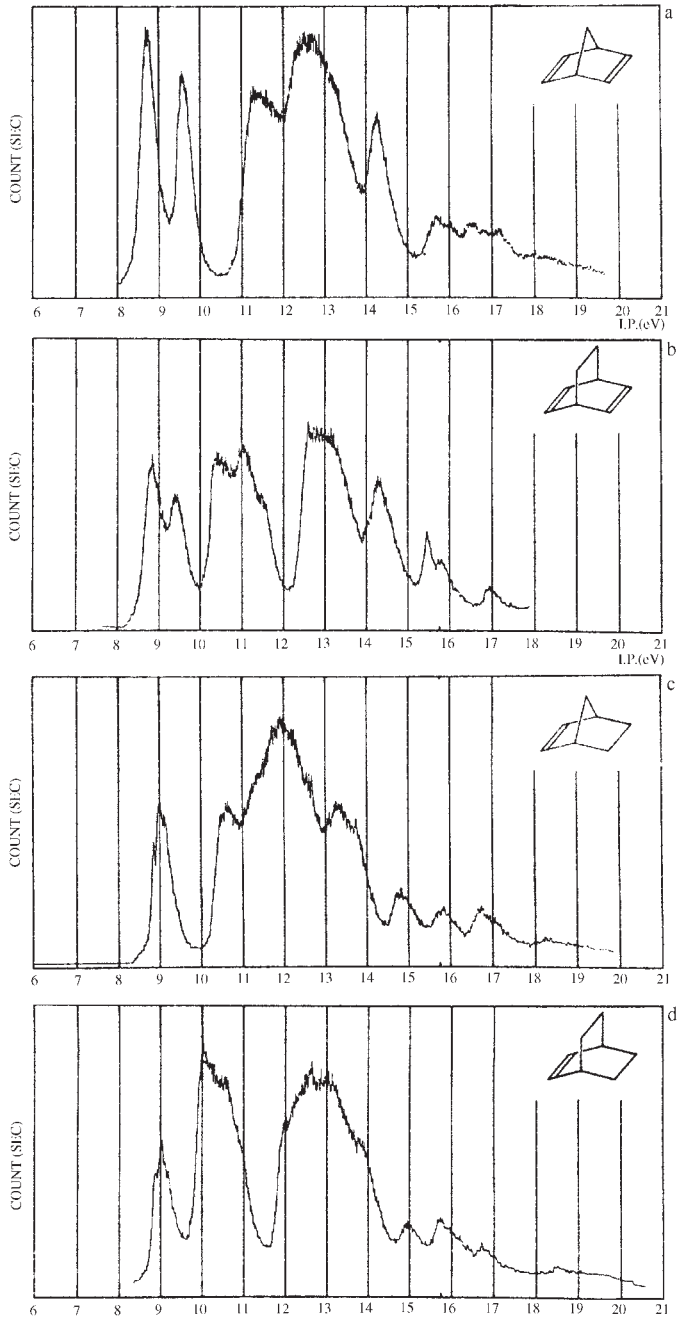
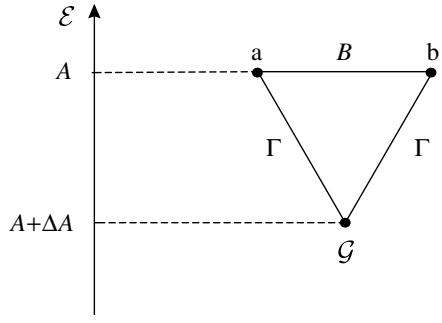


FIGURE 15. Photoelectron spectra of (a) norbornadiene **75** and (b) bicyclo[2.2.2]octadiene **81**, compared to those of (c) norbornene and (d) bicyclo[2.2.2]octene

presentation 44 the graph $\mathcal{G}$ has been drawn in such a way that the projections of the nodes onto an energy ordinate labeled $\mathcal{E}$ corresponds qualitatively to the relative energies of the basis orbitals.



(44)

The parameters are defined in equations 45–48. The parameters A, B and Γ are negative quantities if the orientation of the basis orbitals is defined as shown in diagram 43, and the same is true for ΔA if we assume that the energy of the σ-orbital lies below that of the two π-orbitals as indicated in presentation 44. The orbital energies $\mathcal{E}_j$ are obtained by solving the secular determinant given by equation 49, which yields the solutions given in equations 50.

$$\langle \pi_a | \mathbf{H} | \pi_a \rangle = \langle \pi_b | \mathbf{H} | \pi_b \rangle = A \tag{45}$$

$$\langle \pi_a | \mathbf{H} | \pi_b \rangle = B \tag{46}$$

$$\langle \sigma | \mathbf{H} | \sigma \rangle = A + \Delta A, \text{ with } \Delta A < 0 \tag{47}$$

$$\langle \pi_a | \mathbf{H} | \sigma \rangle = \langle \pi_b | \mathbf{H} | \sigma \rangle = \Gamma \tag{48}$$

$$\begin{Vmatrix} A-\mathcal{E} & B & \Gamma \\ B & A-\mathcal{E} & \Gamma \\ \Gamma & \Gamma & A+\Delta A-\mathcal{E} \end{Vmatrix} = 0 \tag{49}$$

$$\begin{aligned} \mathcal{E}_{1,3} &= A + (\Delta A + B)/2 \pm \sqrt{[(B-\Delta A)/2]^2 + 2\Gamma^2} \\ \mathcal{E}_2 &= A - B \end{aligned} \tag{50}$$

Of the corresponding linear combinations φ_1 and φ_3 are symmetric, and φ_2 antisymmetric, as shown in Figure 16. To give an example, one obtains for the values $\Delta A = -2$ eV and $\Gamma = -1$ eV the dependence of $\mathcal{E}_1$, $\mathcal{E}_2$ and $\mathcal{E}_3$ on the through-space parameter B shown in display 51.

B	$\mathcal{E}_1 - A$ (eV)	$\mathcal{E}_2 - A$ (eV)	$\mathcal{E}_3 - A$ (eV)
0.0	−2.732	0.000	0.732
−0.2	−2.776	0.200	0.576
−0.4	−2.825	0.400	0.425
−0.6	−2.878	0.600	0.278
−0.8	−2.936	0.800	0.136
−1.0	−3.000	1.000	0.000

(51)

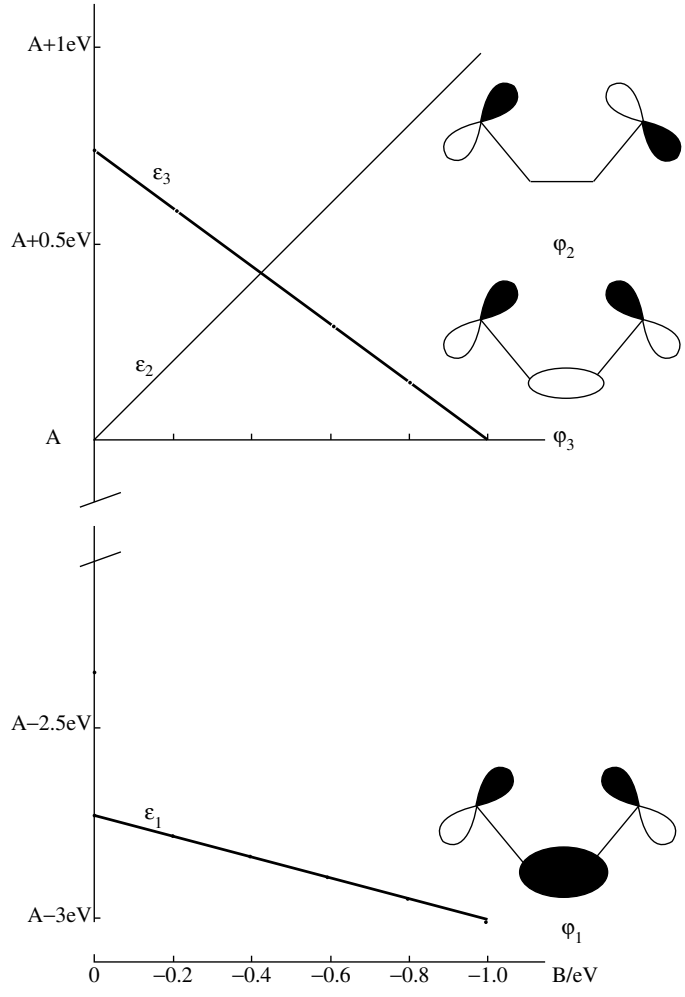


FIGURE 16. Dependence of the eigenvalues $\mathcal{E}_1, \mathcal{E}_2$ and $\mathcal{E}_3$ (see equations 50 and display 51) on the through-space interaction parameter B for fixed $\Gamma = -1$ eV and $\Delta A = -2$ eV. The orbital diagrams are based on the sign convention for the basis orbitals shown in schematic diagram 43

It can be seen from display 51 and Figure 16 that pure through-bond interaction ($B = 0$) places the symmetric orbital φ_3 on top of the antisymmetric orbital φ_2. This is known as the 'reversed' order. With increasing through-space interaction ($|B| > 0$), the energy gap $\mathcal{E}_3 - \mathcal{E}_2$ between φ_3 and φ_2 first decreases, then becomes zero, leading finally to a 'normal' order of φ_3 below φ_2. The cross-over occurs when the parameters obey the condition

$$\Gamma = -\sqrt{B(B + \Delta A)} \tag{52}$$

i.e., for the example given above, if $B = -(\sqrt{2} - 1)$ eV $= 0.41$ eV.

2. A more detailed analysis of through-space and through-bond interactions

The heuristic success of the concepts of through-space and through-bond interactions introduced by Hoffmann[200] made it desirable to link it to many electron procedures, at least on the level of semiempirical or *ab initio* SCF calculations. Such a treatment, which had been proposed some time ago[204], has been reviewed in detail elsewhere[173]. For this reason we shall only sketch the essential steps involved, using norbornadiene **75** as an example.

Step 1. Norbornadiene C_7H_8 of symmetry C_{2v} contains 8 CH single, 8 CC single and 2 π-bonds, occupied by 36 electrons. (We disregard the inner carbon 1s-orbitals). Accordingly, a SCF treatment yields 18 bonding canonical molecular orbitals (CMOs) φ_j ($j = 1, 2, \ldots, 18$) of which 7 belong to the irreducible representation A_1, 2 to A_2, 4 to B_1 and 5 to B_2. We collect these 18 CMOs in a column vector

$$\boldsymbol{\varphi} = (\varphi_1, \varphi_2, \ldots, \varphi_j, \ldots, \varphi_{18})^{\mathrm{T}} \tag{53}$$

Step 2. The set of CMOs φ_j is now transformed into an equivalent set of 18 localized, orthogonal molecular orbitals (LMOs) λ_j using, e.g., Ruedenberg's localization criterion[205]. This is achieved by multiplying $\boldsymbol{\varphi}$ with an appropriate unitary transformation matrix $\mathbb{L}$:

$$\mathbb{L}\boldsymbol{\varphi} = \boldsymbol{\lambda} = (\lambda_1, \lambda_2, \ldots, \lambda_j, \ldots, \lambda_{18})^{\mathrm{T}} \tag{54}$$

This transformation leaves invariant all observable molecular properties of ground-state norbornadiene that can be derived from our SCF model. Note that the two localized orbitals describing a double bond are two 'banana' LMOs $\lambda_{b,up}$ and $\lambda_{b,down}$, as shown on the left of Figure 17, Their normalized, out-of-phase linear combination

$$\pi = (\lambda_{b,up} - \lambda_{b,down})/\sqrt{2} \tag{55}$$

represents the double-bond π-orbital as shown on the right of Figure 17, and their in-phase combination $\sigma = (\lambda_{b,up} + \lambda_{b,down})/\sqrt{2}$ the double-bond σ-orbital.

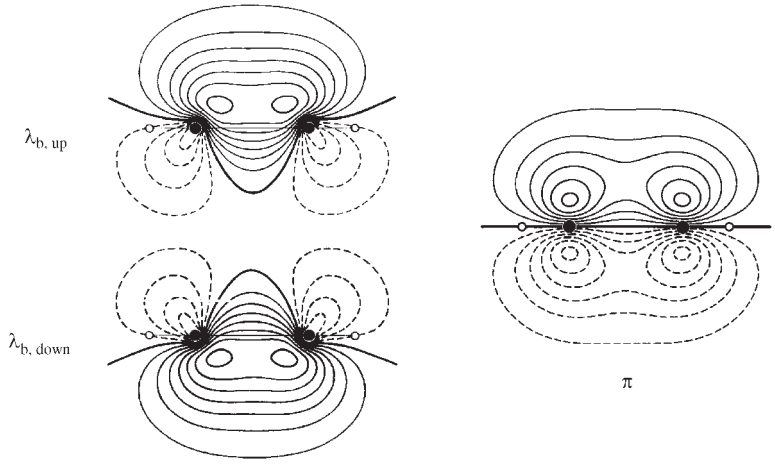


FIGURE 17. On the left is shown the pair of localized banana bond orbitals $\lambda_{b,up}$ and $\lambda_{b,down}$ obtained according to step 2 of Section II.E.2. Their out-of-phase linear combination $\pi = (\lambda_{b,up} - \lambda_{b,down})/\sqrt{2}$ defined in equation 5 yields the π basis orbital shown on the right

Step 3. We first remove the two π-orbitals π_a and π_b (located in positions 2,3 and 5,6 of the norbornadiene skeleton) from the set of LMOs, and form their linear combinations

$$\pi_+ = (\pi_a + \pi_b)/\sqrt{2} \quad \text{and} \quad \pi_- = (\pi_a - \pi_b)/\sqrt{2} \tag{56}$$

The combination π_+ belongs to the irreducible representation A_1 and π_+ to B_2. The remaining 16 σ-orbitals of norbornadiene are now transformed into 16 orthogonal linear combinations of which 6 belong to A_1, 4 to B_2, 2 to A_2 and 4 to B_1. Only the former two sets, belonging to A_1 and B_2, shown qualitatively in Figure 18, can interact with the target π-orbitals π_+ and π_- depicted on the right, thus serving as relay orbitals for through-bond interaction.

Step 4. This last step consists in calculating first the energies $\mathcal{E}(\pi_+)$ and $\mathcal{E}(\pi_-)$ corresponding to the linear combinations in equation 56. The differences relative to the energy $\mathcal{E}(\pi)$ of a single π-orbital defined according to equation 55 are those due to through-space interaction between π_a and π_b. Finally, the cross terms between π_+ and the set of relay orbitals of the same symmetry behaviour A_1 (top row of Figure 18), and of π_- with the B_2 relay orbitals (bottom row of Figure 18), are calculated. In analogy to our naive treatment discussed in Section II.E.1, this yields the energy shifts due to through-bond interaction.

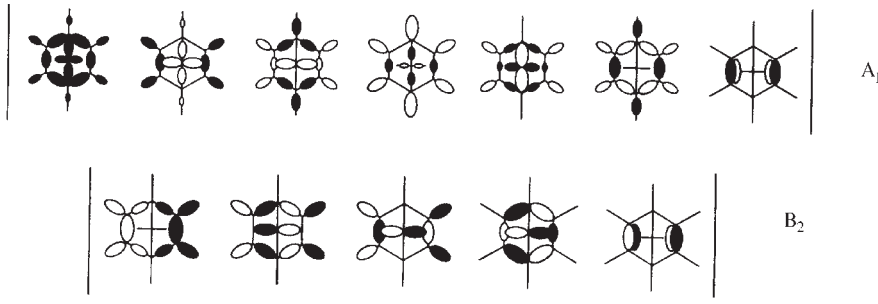
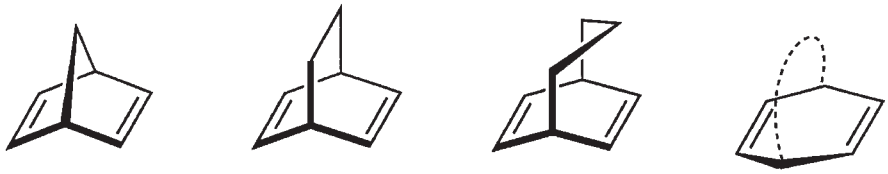


FIGURE 18. The symmetry-adapted, orthogonal linear combinations of the localized σ-orbitals of norbornadiene **75** belonging to the irreducible representations A_1 and B_2 of the point group C_{2v}. The A_1 and B_2 combinations are the relay orbitals for through-bond interaction between π_a and π_b which define, according to equation 56, the orbitals π_+ and π_-

3. Some special cases of interaction between non-conjugated π-orbitals

The consequences of interactions between non-conjugated π-orbitals and their interpretation in terms of through-bond and through-space interactions have been reviewed extensively, by Hoffmann[201], Gleiter[202] and more recently by Gleiter and Schäfer[206]. Although some of the PE spectroscopic consequences of these types of interaction have been summarized before[10,207], the interested reader is referred to the detailed and authoritative review by Mirjana Eckert-Maksic[208] who reports the relevant data and their quantum-chemical interpretation. For this reason we shall only refer briefly to a few typical examples.

a. The interplay of through-bond and through-space interactions in norbornadiene homologues. Bridging the positions 3 and 6 of cyclohexa-1,4-diene **45** by a polymethylene chain, $-(CH_2)_n-$, yields the bicyclic dienes norbornadiene **75** ($n = 1$), bicyclo[2.2.2]octadiene **81**, bicyclo[3.2.2]nona-6,8-diene **92** etc.



(75) **(81)** **(92)**

$n=1$ 2 3 '∞ '

With increasing length n of the polymethylene bridge, the dihedral angle ω between the two C−CH=CH−C moieties increases from $\omega = 110°$ in norbornadiene **75** ($n = 1$), to $\omega = 170°$ to 180° in a hypothetical bicyclo[n.2.2]diene with $n \rightarrow \infty$, i.e. to the ω value observed in cyclohexa-1,4-diene **45**. Figure 19 shows the observed π-ionization energies of the bridged dienes as a function of ω (or of n), which correspond to the ejection of an electron from one or other of the two top orbitals φ_2 or φ_3 which are of the type depicted in Figure 16.

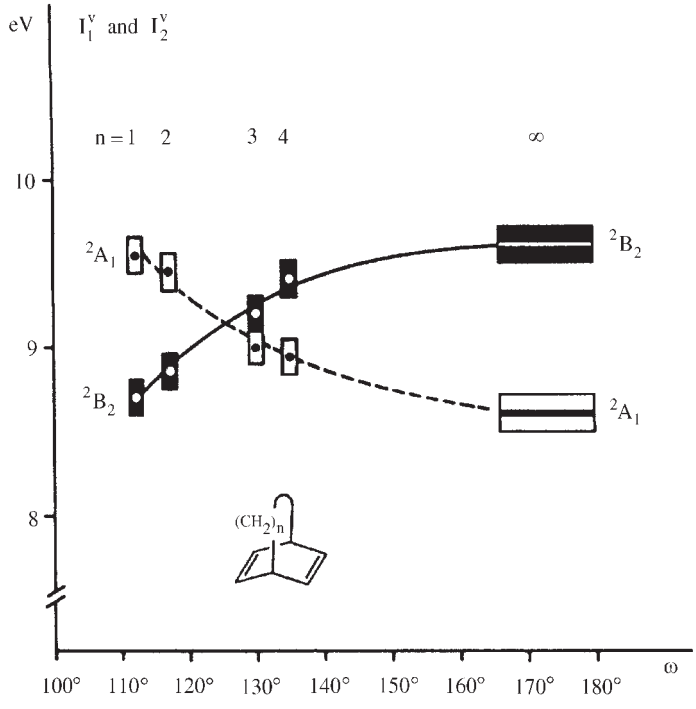


FIGURE 19. Correlation diagram of the π-ionization energies I_1^v and I_2^v of cyclohexa-1,4-diene, bridged in positions 3,6 by a polymethylene chain $-(CH_2)_n-$, as a function of the dihedral angle ω. The radical cation states $^2\tilde{A}_1$ and $^2\tilde{B}_2$ are those obtained by electron ejection from the π-orbitals a_1 and b_2, respectively

With increasing ω the overlap integral $S_{ab} = \langle \pi_a | \pi_b \rangle$ between the two π-orbitals π_a and π_b decreases, and thus their cross term B decreases (see presentation 44 and equation 46). With reference to Figure 16 one sees that for small values of ω, i.e. for large values of B, the through-space interaction dominates, leading to the 'natural' order of the antisymmetric linear combination $\varphi_2(B_2)$ above the symmetric combination $\varphi_3(A_1)$. (The symmetry labels refer to an assumed symmetry C_{2v} of the dienes.) According to the Koopmans theorem (equation 11), this means that I_1^v, corresponding to $^2B_2$ is smaller than I_2^v, corresponding to $^2A_1$, as shown in Figure 19. As ω increases and B decreases, through-bond interaction, characterized by the cross term Γ (see presentation 44 and equation 48), overcompensates the through-space interaction, yielding the 'reversed' order of $\varphi_3(A_1)$ above $\varphi_2(B_2)$. As can be seen from Figure 19, a cross-over occurs for $\omega \approx 125^\circ$, i.e. at a point where B and Γ satisfy the condition given by equation 52. At this point the orbital energies (equation 50) of $\varphi_2(B_2)$ and $\varphi_3(A_1)$ are

$$\mathcal{E}_2 = \mathcal{E}_3 = A + \Delta A/2 + \tfrac{1}{2}\sqrt{(\Delta A^2 + 4\Gamma^2)} \tag{57}$$

These orbital energies are equal to the orbital energy $\mathcal{E}_\pi$ of a single π-orbital, say π_a, interacting with the σ-orbitals of the monoene which corresponds to the diene in question. $\mathcal{E}_\pi$ is the result of solving the 2×2 determinant obtained by striking out the first row and first column of the determinant given by equation 49, i.e. by deleting the node b from the graph in presentation 44. It follows that the ionization energy $I_{\text{crossing}} = 9.1$ eV $= -\mathcal{E}_\pi$ defined by the cross-over in Figure 19 should correspond to the π-ionization energy of bicyclo[2.2.2]octene or bicyclo[3.2.2]non-6-ene, i.e. the monoenes that correspond to the dienes **81** and **92** which bracket the cross-over. That this is indeed the case can be seen from Figure 15.

b. Brief comment on symmetry assignments using a correlation technique. The use of a simple independent electron model — coached in terms of through-space and through-bond interactions — can yield safe assignments if applied to a homologue set of molecules, as was shown above for the two top π-orbitals of bicyclic dienes, a result fully supported by more sophisticated calculations. The question is, whether such an assignment can be obtained if only a single diene is available instead of a homologue series. Using norbornadiene **75** as an example, the relative sequence of its π-orbitals $\varphi_2(B_2)$ and $\varphi_3(A_1)$ can be assessed through a simple correlation technique[209] by letting them interact with a third localized π-orbital of known symmetry behaviour. In the instance of **75** which contains the symmetry equivalent orbitals π_a and π_b as shown at top of Figure 20, we include a third π-orbital π_c by adding an exocyclic double bond in position 7 of **75** to yield, e.g., 7-methylidenenorbornadiene **196**[131] or 7-isopropylidenenorbornadiene **206**[26,77]. The symmetry behaviour of π_c is known to be B_2 under C_{2v}, i.e. antisymmetric with respect to rotation about the twofold axis or with reflection through the x, z plane. This means that π_c can only interact with the antisymmetric π-orbital $b_2 \equiv \varphi_2(B_2)$ containing the linear combination $(\pi_a - \pi_b)/\sqrt{2}$, and not with the symmetric π-orbital $a_1 \equiv \varphi_3(A_1)$ containing $(\pi_a + \pi_b)/\sqrt{2}$. Disregarding small inductive shifts we expect therefore that $\mathcal{E}_3$ will remain the same going from **75** to **196** or **206**, whereas $\mathcal{E}_2$ should experience a significant change. As can be seen from Figure 20, the observed shifts of the π-bands are only compatible with the above deduction if the orbital energy $\mathcal{E}_2$ of the π-orbital $b_2 \equiv \varphi_2(B_2)$ lies above $\mathcal{E}_3$ of $a_1 \equiv \varphi_3(A_1)$. This 'natural' order is in perfect agreement with what we had derived from the correlation diagram of Figure 19 presented in the previous section.

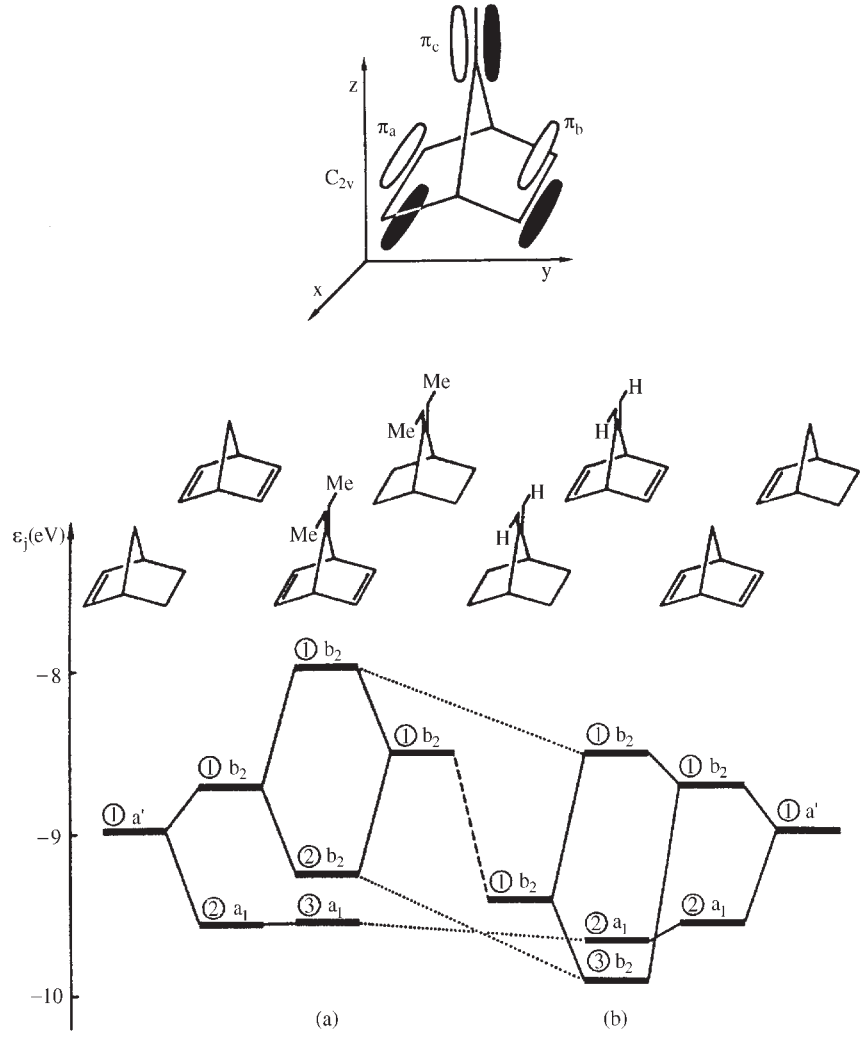
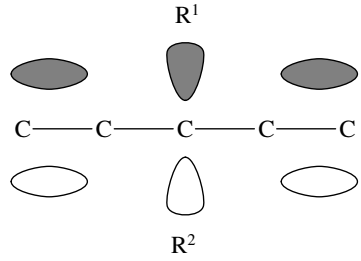


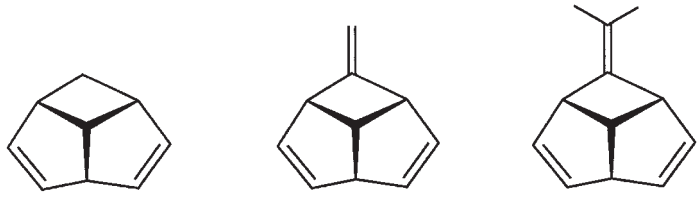
FIGURE 20. Top: Definition of the phase relationship of the three localized basis π-orbitals of a norbornadiene molecule with an exocyclic double bond in position 7. Bottom: Correlation diagram of the 'experimental' orbital energies $\mathcal{E}_j = -I_j^v$ of norbornadiene **75**, 7-methylidenenorbornadiene **196** and 7-isopropylidenenorbornadiene **206**, with those of the corresponding monoenes

c. Homoconjugation. A special case of interaction, known as 'homoconjugation', occurs between the π-orbitals of two double bonds separated by a methylene group, $-CH_2-$, or a $-CR^1R^2-$ group. As before, this situation can be discussed in terms of through-space and through-bond interactions, the special feature being that the 'relay orbital' for the latter type of interaction is now the out-of-phase combination of the two localized CH σ-orbitals of the methylene group, or of the two CC σ-orbitals linking the alkyl groups R^1 and R^2 to the central C atom, as shown in diagram 58.



(58)

A typical example of cyclic homoconjugation is provided by (*Z*, *Z*, *Z*)-cyclonona-1,4,7-triene **189**, which is the prototype of a 'homoaromatic' molecule, a term introduced by Winstein[210]. Its spectrum[26,49] is shown in Figure 21, together with a diagram illustrating the relative contributions of through-space and through-bond interaction. The double band at 8.8 and 9.0 eV in the PE spectrum of **189** corresponds to the ejection of an electron from the degenerate frontier orbital labelled e in Figure 21, yielding the corresponding radical cation in its ^2E ground state. Because of this degeneracy the cation undergoes a Jahn–Teller distortion, which is the cause for the observed double-humped shape of the Franck–Condon envelope. The second feature at 9.8 eV is due to electron ejection from the totally symmetric orbital labelled a. The observed splitting of *ca* 1 eV has, unfortunately, been sometimes quoted as an indication of the 'homoaromaticity' of **189**. However, the interactions manifest in the PE spectrum have no noticeable effect on the ground-state properties of the molecule. A similar observation concerns triquinacene **213**, the PE spectrum of which[136,211] shows again sizeable interactions between the three homoconjugated double-bond π-orbitals, but whose ground-state properties, as shown by Dewar and Holder[212], present no significant effects which could be attributed to 'homoaromaticity'. Finally, the PE spectroscopic investigation of nortriquinacene **289**, methylidenenortriquinacene **290** and isopropylidenenortriquinacene **291** by Houk and his coworkers[213] strongly supports the conclusion that the PE spectroscopic observation of homoconjugative interactions in molecules of this type should not be interpreted as evidence of 'homoaromaticity'.



(289) **(290)** **(291)**

d. Spiroconjugation. We conclude this short list of examples with [4.4]spirononatetraene **247**[63] — a hydrocarbon of D_{2d} symmetry — which is the paradigm of a molecule exhibiting 'spiroconjugation'. Although the interaction between the four localized double-bond π-orbitals π_a, π_b, π_c and π_d across the spiro-centre 5 (see top of Figure 22) can be again discussed in terms of through-bond and through-space interaction, the feature of interest is the important role played by the high symmetry of the system. Indeed, the four π-orbitals π_a, π_b, π_c and π_d yield the symmetry-adapted, normalized linear combinations 59. These

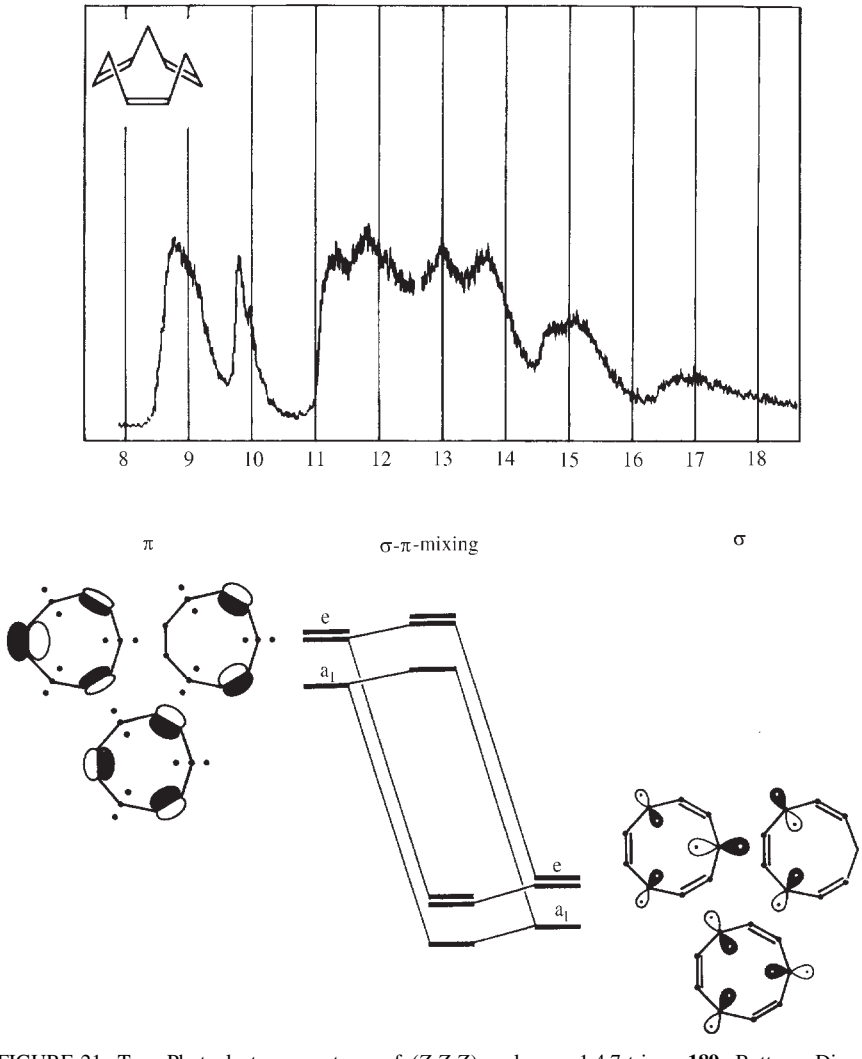


FIGURE 21. Top: Photoelectron spectrum of (*Z*,*Z*,*Z*)-cyclonona-1,4,7-triene **189**. Bottom: Diagram showing the homoconjugative σ/π-interaction between the symmetry-adapted linear combinations of the π- and of the methylene σ-orbitals

$$
\begin{aligned}
1a_2(\pi) &= (\pi_a - \pi_b - \pi_c + \pi_d)/2 \\
1b_1(\pi) &= (\pi_a - \pi_b + \pi_c - \pi_d)/2 \\
7e(\pi) &\begin{cases} = (\pi_a + \pi_b + \pi_c + \pi_d)/2 \\ = (\pi_a + \pi_b - \pi_c - \pi_d)/2 \end{cases}
\end{aligned} \tag{59}
$$

combinations, depicted in Figure 22, which determine the symmetry behaviour of the molecular orbitals to which they contribute. The resulting orbital energy diagram, where

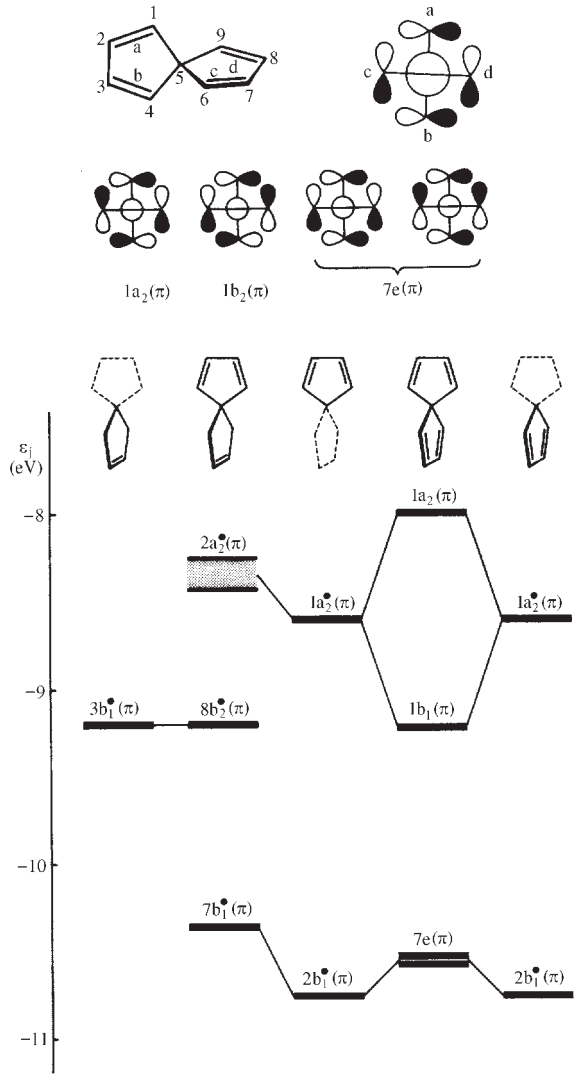


FIGURE 22. Top: Labels of the four localized basis π-orbitals of [4.4]spirononatetraene **247** and Newman projection defining their relative phases. Middle: Newman projections of the four linear combinations $1a_2(\pi)$, $1b_1(\pi)$ and $7e(\pi)$, defined in equation 59. Bottom: Correlation diagram showing the splitting due to spiroconjugation between the butadiene moieties in **247**

the $\mathcal{E}_j$-values are the 'observed' ones assuming the validity of the Koopmans theorem 'in reverse', i.e. $-I_j^{\mathrm{v}} = \mathcal{E}_j$, is shown at the bottom of Figure 22.

Contrary to what is suggested by an independent electron treatment, the energy gap $\Delta I^{\mathrm{v}} = I_2^{\mathrm{v}} - I_1^{\mathrm{v}}$ between the ionization energies corresponding to the first two bands in the PE spectrum of a molecule is not equal to the difference ΔE between the first two

electronic transitions of the neutral molecule. As has been pointed out by Haselbach and Schmelzer[214], the two quantities are related by the equation.

$$\Delta E = \Delta I^{v} - (J_{2,-1} - J_{1,-1}) - 2(K_{1,-1} - K_{2,-1}) \tag{60}$$

where $J_{i,j}$ and $K_{i,j}$ are the coulomb and exchange integrals, respectively, between the molecular orbitals φ_i and φ_j involved in the ionization process and in the electronic transitions. The remarkable feature of the above example is that the high symmetry conditions prevailing in **247** lead to the result that the difference between the (finite) coulomb integrals $J_{i,j}$ in equation 60 becomes vanishingly small and that the individual exchange integrals $K_{i,j}$ are practically zero. As a result the molecule **247** is one of the rare examples where the naive expectation $\Delta E = \Delta I^{v}$ suggested by an independent electron treatment turns out to be true[63].

III. EXCITED STATES OF POLYENE RADICAL CATIONS BY OTHER METHODS

A. Introduction

For many years, investigations on the electronic structure of organic radical cations in general, and of polyenes in particular, were dominated by PE spectroscopy which represented by far the most copious source of data on this subject. Consequently, attention was focussed mainly on those excited states of radical ions which can be formed by direct photoionization. However, promotion of electrons into *virtual* MOs of radical cations is also possible, but as the corresponding excited states cannot be attained by a one-photon process from the neutral molecule they do not manifest themselves in PE spectra. On the other hand, they can be reached by electronic excitation of the radical cations, provided that the corresponding transitions are allowed by electric-dipole selection rules. As will be shown in Section III.C, the description of such states requires an extension of the simple models used in Section II, but before going into this, we would like to discuss them in a qualitative way and give a brief account of experimental techniques used to study them.

Optical absorption spectroscopy of organic radical cations was pioneered by Hoijtink and coworkers[215] and others[216] before the advent of PE spectroscopy, but it was limited for a long time to aromatic amines, polycyclic aromatic hydrocarbons and similar compounds whose radical cations could be generated under stable conditions by chemical oxidation[217]. It was observed that many colourless neutral compounds give rise to intensely coloured radical cations which indicates that excited states of these reactive species lie generally at much lower energy than those of the neutral parent molecules (the most famous example is perhaps Wurster's blue, the radical cation of the colourless tetramethyl-*p*-phenylenediamine).

This agrees with the observation that the energy differences between the first and one of the following bands in the PE spectra often lie in the visible energy range. As pointed out above, the optical spectra of radical ions should show additional bands which can be assigned to excitations into virtual MOs. In many radical cations with planar π-systems, the most prominent band in the electronic absorption (EA) spectrum is essentially due to a HOMO $\rightarrow$ LUMO excitation (we will examine below to what extent this is also true for polyene radical cations). Interestingly, even this excitation occurs at much lower energy than in the corresponding neutrals. In a simple MO picture, this may be viewed as being due to the rise of the HOMO on removal of an electron.

The latter feature leads to the expectation that, in cases where the HOMO $\rightarrow$ LUMO excitation in the neutral occurs in the visible, the corresponding state of the radical cation should turn out to be the lowest one. There are indeed several cases where this was

found to be true, most prominently in the cross-conjugated polyene radical cation of *o*-quinodimethane and in some of its derivatives. As the first excited state is usually the photochemically active one, it is important to know its character.

An interesting aspect of this alternative way of looking at the electronic structure of radical cations concerns the dependence of the excited state energies on *changes in structure*: Whereas the maxima of PE bands correspond to ionic state energies at the *neutral* equilibrium geometry, those of optical bands measure the energies of excited states at the *cation* equilibrium geometries. The occurrence of shifts between the two cases is most easily visualized by juxtaposing PE and EA spectra on the same energy scale, matching the energy origin of the latter with I_1^a (or, if this cannot be discerned, with the onset) of the first PE band, assuming that this represents the energy of the relaxed radical cation.

As every chemical species undergoes *some* change of geometry upon ionization, one would expect that this always entails shifts in the excited state energies. However, in many cases where such comparisons were made (for example in aromatic hydrocarbons) these shifts were found to be insignificant, presumably because the changes in bond lengths upon ionization are too small, due to the stiffness of the σ-frame. However, the same appears to be true in polyene radical cations where significant bond-length changes take place upon ionization. In this case, as will be discussed below, the absence of shifts is due to a cancellation of effects. A group of compounds where a comparison of the PE spectrum of M and the EA spectrum of $M^{+\bullet}$ is particularly interesting are non-conjugated π-systems interacting through-space and/or through-bond, such as those discussed in Section II.E.

Finally, before turning to a brief review of methodological and theoretical aspects, we mention that one of the distinguishing features of planar conjugated polyene radical cations (cf Section II.D) is that their EA spectra reveal a breakdown of the single-configuration picture for ionic excited states which had been used so successfully in interpreting their PE spectra (cf. Section II).

B. Experimental Methods

1. Gas-phase experiments

a. Photodissociation spectroscopy. The first studies of the electronic structure of radical cations which cannot be formed under stable conditions in solution used a technique which takes advantage of the fact that *dissociation* is the predominant deactivation process of electronically excited radical cations in the gas phase. Thus it is possible to monitor the disappearance of a radical cation in an ion beam or an ICR trap (or the appearance of certain fragment ions) as a function of the exciting wavelength. As the quantum yield of fragmentation often shows little dependence on the excitation energy above threshold, the so-called *photodissociation* (PD) *spectra* obtained in this way are usually very similar to the corresponding optical absorption spectra.

This technique, whose analytical application was pioneered by Dunbar and colleagues[218], was mainly used to distinguish isomeric radical cations in the gas phase. It was also used for the investigation of many polyenes, and the efficiency of its high-resolution variant (using a dye laser as excitation source) was demonstrated on the example of hexatriene radical cation (Figure 23). From a spectroscopic point of view, its principal advantage is the possibility to obtain full UV/VIS spectra of radical cations in the absence of solvent. As an example, we show the PD spectrum of hexatriene radical cation[219] and an expanded high-resolution scan of the first band[220].

b. Ion emission spectroscopy. Fluorescence of radical ions is much less common than that of neutral molecules. This is mainly due to the fact that the first excited states of

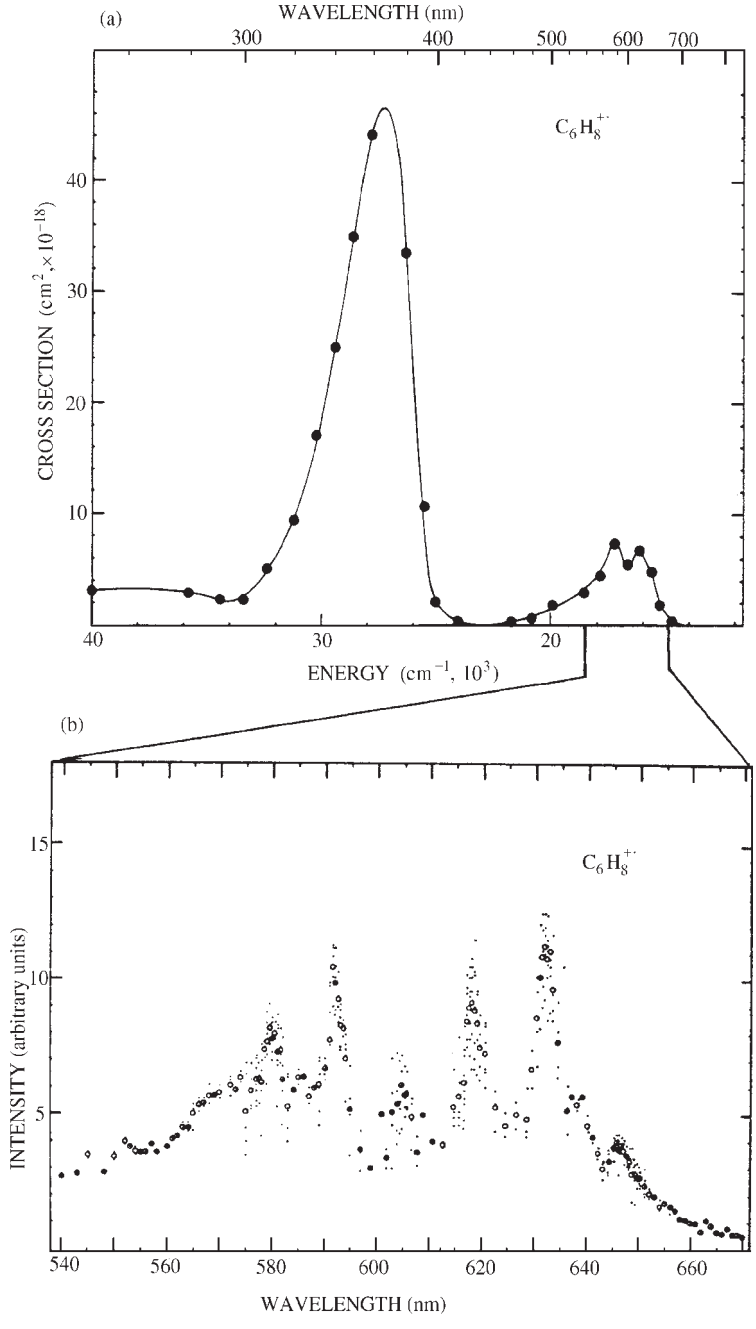


FIGURE 23. Gas-phase photodissociation (PD) spectra of the radical cation of hexatriene (a) at low resolution, (b) expanded scan of the first absorption band at high resolution[219,220]

radical ions are usually at much lower energy, often in the NIR region, so that radiationless internal conversion to the ground state frequently wins out by virtue of the energy-gap law. Most emissive radical cations are either small (oligo)acetylenes and their derivatives, or fluorinated benzene derivatives. Notable exceptions are the radical cations of hexatriene and octatetraene, and therefore a brief discussion of the techniques used to study emission spectra of radical cations seems warranted in the present context[221].

Emission spectra of radical cations are obtained by vacuum UV ionization and subsequent laser excitation in noble-gas matrices (see below), or by electron-impact ionization of a beam of neutral parent molecules at energies above the first ionic excited state. After internal conversion to the first excited state, emission may compete more or less successfully with radiationless deactivation. If the experiment is carried out on a supersonic molecular beam one obtains highly resolved emission spectra which, in the case of small molecules, may contain sufficient information to allow a determination of the molecular structure.

In order to record *excitation spectra*, the radical ions must first be thermalized to the electronic ground state, which happens automatically if they are created in condensed phase (e.g. in noble-gas matrices, see below). In the gas-phase experiments where ionization is effected by collision with excited argon atoms (Penning ionization), the unexcited argon atoms serve as a heat bath which may even be cooled to 77 K if desired. After thermalization, excitation spectra may be obtained by laser-induced fluorescence.

Figure 24 shows as an example the gas-phase emission and excitation spectra of the radical cation of dimethyldiacetylene from the work of Maier and coworkers[222] and Miller and Bondybey[223] who have pioneered these methods. For direct comparison, the bottom part of Figure 24 represents the same spectra taken in neon matrices[223] (see below).

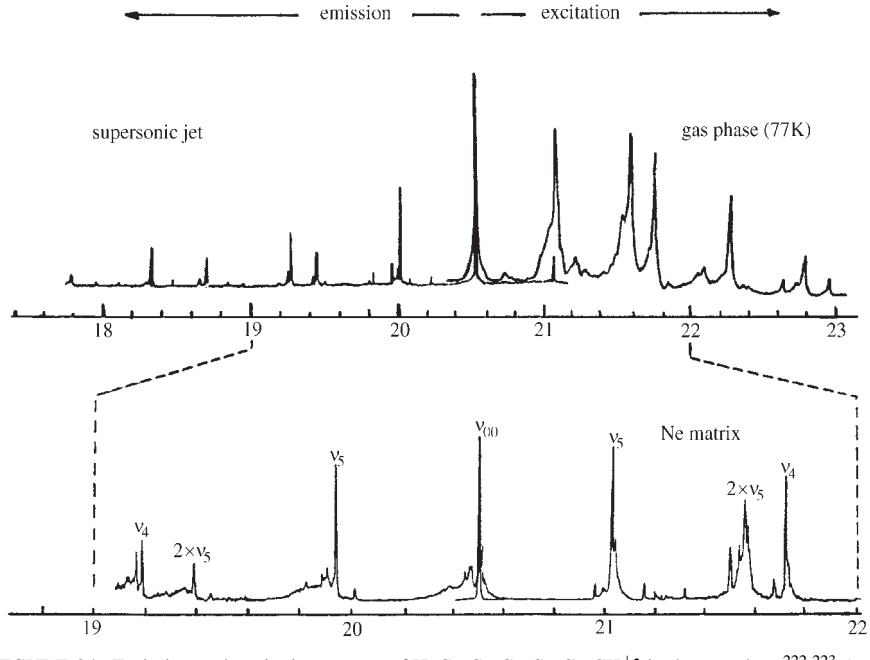


FIGURE 24. Emission and excitation spectra of $H_3C-C\equiv C-C\equiv C-CH_3^{+\bullet}$ in the gas phase[222,223] (top) and in a neon matrix[223] (bottom)

2. Condensed-phase experiments

a. Solution studies. Optical and ESR spectra of radical cations were first obtained on samples subjected to chemical ionization in solution[215]. However, these methods were never applied to dienes and polyenes because their radical cations are too reactive to be observed under such conditions.

Radical cations can also be produced in solution by *photoinduced electron transfer* (PET) in polar solvents. Although this method is widely used to study the processes involved in the formation and decay of ion pairs[224], free radical cations appear only as transients in such experiments.

Finally, radical cations can be generated in solution by different types of *pulse radiolysis*[225]. Like PET, this is inherently a method for transient spectroscopic observations, but it has proved to be invaluable in investigations of dimer cations, e.g of polyenes, which form spontaneously upon diffusion of radical cations in the presence of an excess of the neutral parent compound, but a discussion of the electronic structure of such species is beyond the scope of this review. Pulse radiolysis is of interest in the present context because it allows the observation of large carotenoid radical cations which are difficult to create in solid-state or gas-phase experiments

b. Frozen glasses. Systematic investigations of optical spectra of polyene radical cations in condensed phase had to await the advent of methods allowing their production under conditions which prevent decay through charge recombination or other bimolecular processes. Such methods were pioneered in the 1960s by Hamill and Shida[226] who found that radical ions are formed quite cleanly upon exposure of frozen solutions to ^{60}Co γ-irradiation (1.17 and 1.33 MeV).

Which species are formed in such experiments depends on the solvent, i.e. its capacity to trap either the holes or the electrons which are created in the primary radiolytic step (see Figure 25). Thus, holes are scavenged efficiently by methyltetrahydrofuran, presumably through proton transfer, whereas electrons are trapped by alkyl chlorides which dissociate into alkyl radicals and chloride anions (to the extent that this is possible in rigid matrices). Subsequently, the holes (electrons) travel through the solvent by resonant charge transfer until they encounter a solute of lower ionization energy (higher electron affinity), thus creating radical cations (radical anions) at a distant site from the carrier of the opposite charge. It is important to realize that ionization of the solute occurs actually *by charge transfer from the solvent* and not through interaction with the highly energetic γ-rays to which hydrocarbons are essentially transparent.

For the investigation of radical cations, Shida replaced the initially used solvent CCl_4 by a mixture of *n*-butyl chloride and isopentane which forms a transparent glass upon freezing. Later, Grimison and Simpson[227a] found that a mixture of two freons, $CFCl_3$ and CF_2BrCF_2Br, which had originally been proposed for low-temperature studies by Sandorfy[227b] because of its glass-forming quality, represented an even better medium, due to the absence of C−H vibrational overtones in the NIR region. This proved to be very important, especially in studies of dimer cations which show characteristic absorptions in this range. In 1979 it was found — somewhat surprisingly — that it was also possible to record reasonably well resolved ESR spectra of radical cations in certain freons[228]. This led to many important investigations of radical cations which cannot be generated under stable conditions by chemical oxidation[229].

The first systematic studies of *polyene radical cations* were carried out by Shida and coworkers[230] using the above methods. In this connection an important feature of these species was discovered, namely that they exist in the form of multiple rotamers which do not interconvert easily due to the partial double-bond character which all polyene C−C bonds attain upon ionization (see below).

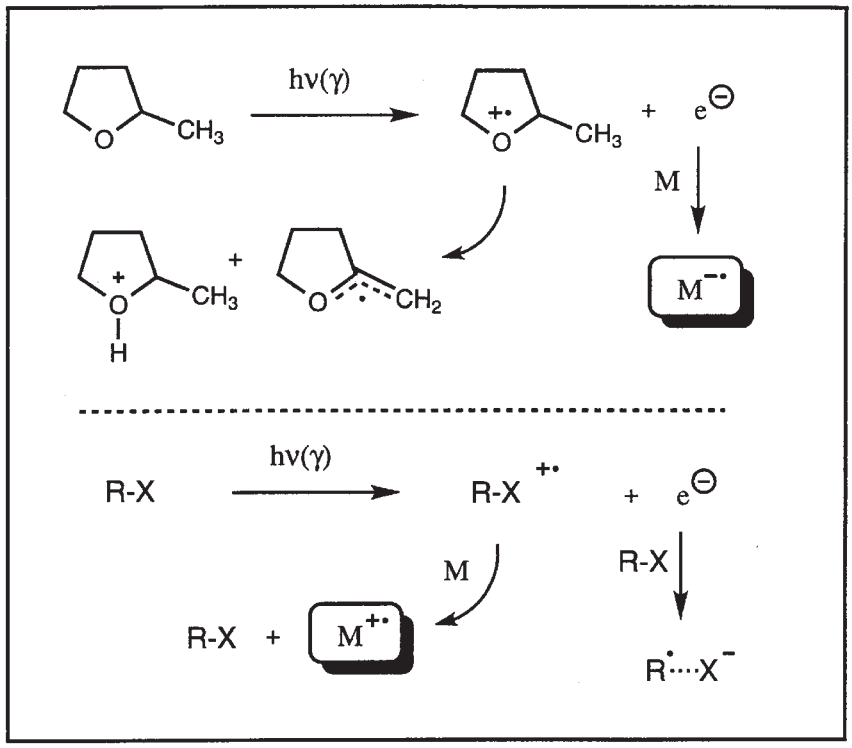


FIGURE 25. Mechanism of formation of radical anions $M^{-\bullet}$ and cations $M^{+\bullet}$ in frozen glasses of methyltetrahydrofuran (top) and alkyl chlorides (bottom), respectively

c. Matrix isolation experiments. The methods mentioned above suffer from several disadvantages: (a) solutes tend to form aggregates upon cooling the solution, (b) the halogenated solvents may undergo chemical interactions with some of the more reactive radical cations and (c) these solvents are not transparent below 300 nm and in the IR region, especially after γ-irradiation. Therefore, attempts were made in several laboratories to find suitable conditions for the creation of radical ions in solid *noble gases*, applying techniques of *matrix isolation* elaborated in the 1950s by Pimentel and others[231].

First successes were reported by Andrews and coworkers, who tried various methods to produce radical ions in the gas phase for subsequent trapping at 10 K. A particularly fruitful strategy involved excitation of the argon used for matrix isolation in a microwave discharge[232]. Although it was never determined unambiguously how ionization of the substrate occurred under these conditions (Penning ionization or photolysis through light emitted by the excited argon atoms), the method proved quite generally applicable and was used in many studies of radical cations, in particular those of polyenes. The main disadvantage of the method is that it does not permit the recording of difference spectra which would yield the spectra of the radical cations unperturbed by those of the parent neutral.

At the same time, studies of *emission spectra* of matrix isolated radical cations were undertaken by Miller and Bondybey at Bell Laboratories[233] and by Maier and coworkers

in Basel[234]. In these studies, the radical cations were created by FUV photolysis of the neutral molecules isolated in neon matrices, without adding an electron scavenger (see below). The yield of radical cations is quite low and side products are unavoidably formed under these conditions, but through choice of suitable excitation wavelengths and by virtue of the zero-background nature of the experiment, very clean and extremely well resolved spectra of many emissive radical cations were reported (see e.g. Figure 24).

In the early 1980s, one of the authors of this chapter began to study argon matrix isolation of radical cations[235] by applying the radiolytic techniques elaborated by Hamill and Shida. A central factor was the addition of an *electron scavenger* to the matrix which was expected to increase the yield of radical cations and the selectivity of the method. For practical reasons, X-rays replaced γ-rays as a radiolytic source and argon was chosen as a matrix material because of its substantial cross section for interaction with keV photons (which presumably effect resonant core ionization of Ar). Due to the temporal separation of the process of matrix isolation of the neutral molecules and their ionization, it was possible to obtain difference spectra which show exclusively the bands of the radical cations.

This method proved quite generally applicable, in particular for the study of the electronic structure of several polyene radical cations and, more recently, for investigations of

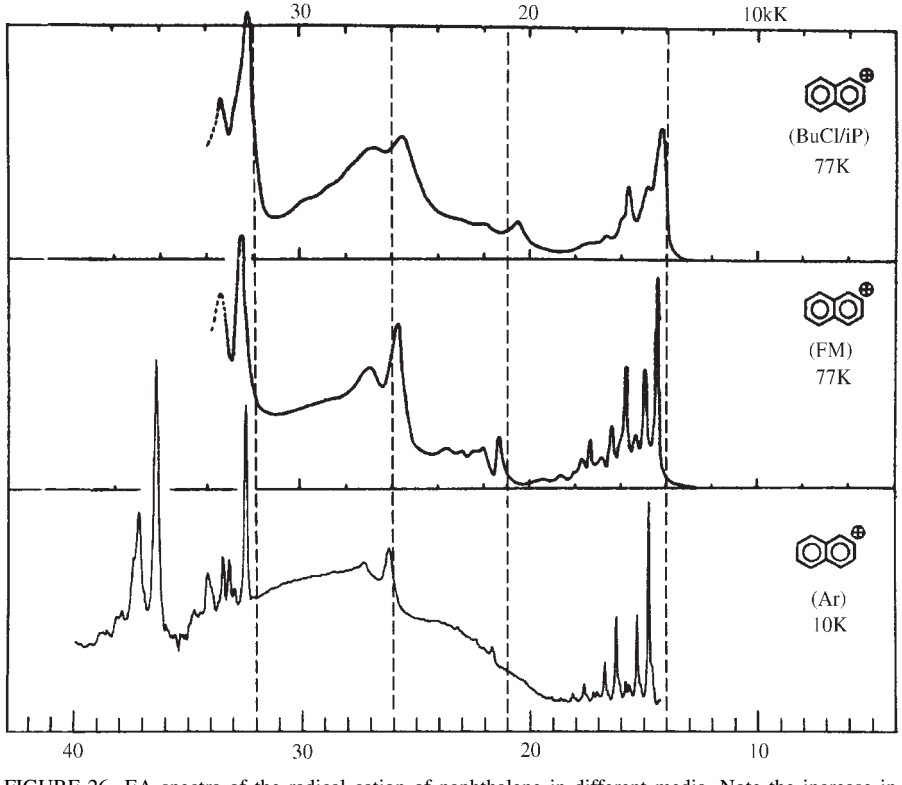
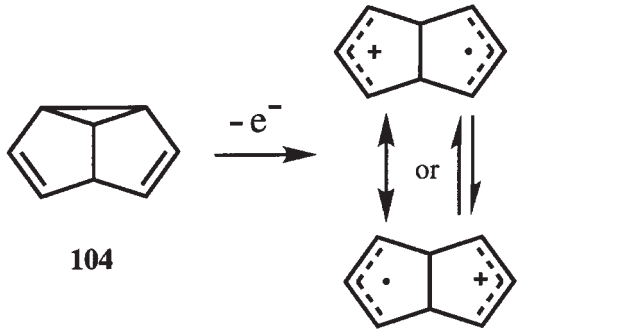


FIGURE 26. EA spectra of the radical cation of naphthalene in different media. Note the increase in resolution and optical range in argon matrices

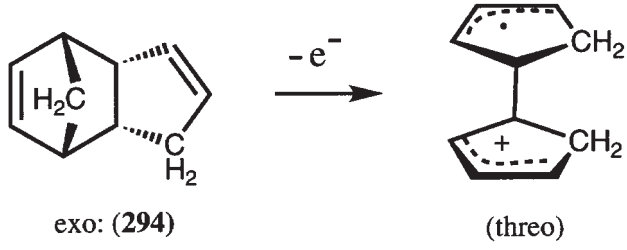
their vibrational structure by IR spectroscopy. The main disadvantage is that the charge transfer from ionized argon is exothermic by several eV and that the excess energy imparted to the radical cations is only slowly dissipated by the argon lattice. Therefore, primary cations on occasion undergo partial rearrangement, sometimes to the extent that they are no longer observable. Unfortunately, attempts to circumvent this problem by addition of 'hole moderators' (matrix components of lower ionization energy than argon) or 'energy dissipators' (species capable of taking up excess vibrational energy) have so far met with limited success.

As an example of the application of the solid-state methods described above, we show the spectra of the naphthalene radical cation in different media[236] (Figure 26). Note the increase in spectroscopic resolution and the extension of the range of observation into the UV when using argon matrices.

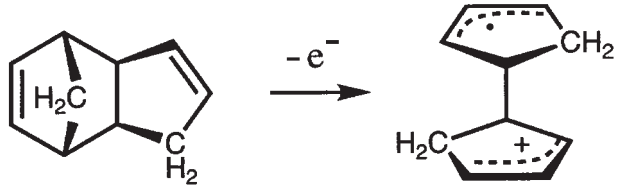
Table 3 lists all polyenes whose radical cations have been investigated by one or other of the above-described techniques and some of the structures listed are shown below the table. Note that some nonconjugated dienes do not retain their structure upon ionization [e.g. semibullvalene **104** (equation 61) or the cyclopentadiene dimers **126** and **294** (equation 62)] but break a bond to form a bisallylic radical cation, a rather common tendency of radical cations that have this possibility.



104 (61)



exo: (**294**) (threo) (62)



endo: (**116**) (meso)

TABLE 3. Electronic spectra of dienes and polyenes C_nH_m
$m = 2(n - d - r + 1)$ where d = number of double bonds and r = number of rings

r	n	m	No.	Name	References (Method)[a]
Dienes: $d = 2$					
0	3	4	**1**	Allene	237 (PD)
	4	6	**2**	1,3-Butadiene	238 (PD) 239, 240 (AS) 241, 242 (AM)
	5	8	**3**	(3*E*)-1,3-Pentadiene (1-Methylbutadiene)	240 (AS), 243 (PD)
			5	2-Methylbutadiene (Isoprene)	240 (AS)
	6	10	**10**	Hexa-2,4-diene	24 (PD)
			11	2,3-Dimethylbuta-1,3-diene	240 (AS)
			16	(3*E*)-Hexa-1,3-diene	233, 238, 244 (PD)
	7	12	**292**	(2*E*,4*E*)-Hepta-2,4-diene	245 (PD)
	8	14	**24**	(3*E*)-Octa-1,3-diene	245 (PD)
			25	2,5-Dimethylhexa-2,4-diene	238 (PD), 240 (AS)
	12	22	**293**	1,4-Di-*t*-butylbuta-1,3-diene	246 (AS)
1	5	6	**37**	Cyclopentadiene	240 (AS), 247 (AS, AM)
	6	8	**44**	Cyclohexa-1,3-diene	245, 248 (PD) 249 (AS) 250, 251 (AM)
			45	Cyclohexa-1,4-diene	240, 249 (AS)
	7	10	**49**	Cyclohepta-1,3-diene	249 (AS), 252 (PD) 253 (AM)
	8	12	**57**	Cycloocta-1,3-diene	238, 245 (PD), 250 (AM)
2	6	5	**71**	Dewar benzene (Bicyclo[2.2.0]hexa-2,5-diene)	254 (AS)
	7	8	**75**	Norbornadiene (Bicyclo[2.2.1]hepta-2,5-diene)	252 (PD) 255 (AM) 256 (AS)
	8	10	**79**	Bicyclo[4.2.0]octa-2,4-diene	257 (AS)
			81	Bicylo[2.2.2]octadiene	258 (AS)
3	8	8	**104**	Semibullvalene	259, 260 (AS)
	10	12	**116**	*endo*-Dicyclopentadiene	261, 262 (AS), 263, 264 (AM)
			294	*exo*-Dicyclopentadiene	261, 262 (AS)
4	12	14	**139**	*endo, endo*-1,4,4*a*,5,8,8*a*-Hexahydro-1,4:5,8-dimethanonaphthalene	265, 266 (AS, AM)
10	20	20	**156**	Pagodiene	265, 266 (AS, AM)
12	20	16	**296**	Dodecahedradiene	266 (AM)
Trienes: $d = 3$					
0	6	8	**161**	(3*E*)-Hexa-1,3,5-triene	240 (AS), 241, 250 (AM) 267 (PD), 268 (EG) 269 (EM)
			162	(3*Z*)-Hexa-1,3,5-triene	249 (AS), 268 (EG) 270 (AM)
	14	24	**297**	1,6-Di-*t*-butylhexa-1,3,5-triene	246 (AS)
1	6	6	**173**	[3]Radialene	271 (AS)
			298	5-Methylidenecyclohexa-1,3-diene	272 (PD), 254, 273 (AM)
			174	3,4-Dimethylidenecyclobutene	274 (PD)
	7	8	**179**	Cyclohepta-1,3,5-triene	240 (AS), 252 (PD), 253, 255 (AM)

TABLE 3. (*continued*)

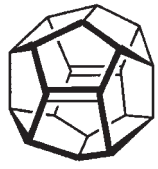
r	*n*	*m*	No.	Name	References (Method)[a]
Trienes: $d = 3$					
	8	10	**184**	Cycloocta-1,3,5-triene	240, 257 (AS), 263, 264, 275 (AM)
			299	7-Methylcyclohepta-1,3,5-triene	276 (AM)
			300	(*E*/*Z*)-5-Ethylidenecyclohexa-1,3-diene	276, 277 (AM)
			301	2-Methyl-5-methylidenecyclohexa-1,3-diene	276 (AM)
			302	5-Vinylcyclohexa-1,3-diene	258 (AS)
			303	2-Vinylcyclohexa-1,3-diene	279 (AS)
	9	12	**304**	2-Ethyl-5-methylidenecyclohexa-1,3-diene	277 (AM)
			305	5-*n*-Propylidenecyclohexa-1,3-diene	277 (AM)
			306	5-Isopropylidencyclohexa-1,3-diene	277 (AM)
	10	14	**307**	5-n-Butylidenecyclohexa-1,3-diene	277 (AM)
			308	2-Isopropyl-5-methylidenecyclohexa-1,3-diene	277 (AM)
			309	2-Ethyl-5-ethylidenecyclohexa-1,3-diene	277 (AM)
			310	2-Methyl-5-isopropylidenecyclohexa-1,3-diene	277 (AM)
2	8	8	**197**	Barrelene	273 (AS)
			198	1,2-Dihydropentalene	278 (AS,AM)
			199	1,4-Dihydropentalene	278 (AS,AM)
			200	1,5-Dihydropentalene	278 (AS,AM)
			311	1,6-Dihydropentalene	278 (AS,AM)
			312	1,6*a*-Dihydropentalene	278 (AS,AM)
	10	10	**313**	Bicyclo[6.2.0]deca-2,4,6-triene	285 (AM)
	10	12	**314**	1,2,3,5-Tetrahydronaphthalene	277 (AM)
Tetraenes: $d = 4$					
0	8	10	**234**	Octa-1,3,5,7-tetraene (different rotamers)	240, 258 (AS), 241, 263, 264, 275, 279 (AM), 280 (EG)
	16	26	**315**	1,8-Di-*t*-butylocta-1,3,5,7-tetraene	246 (AS)
1	8	8	**239**	Cyclooctatetraene	281 (PD), 240, 260, 282 (AS)
			316	*o*-Quinodimethane	283 (AM)
	11	12	**250**	2,2-Dimethyl(2*H*)indene	284 (AS)
Polyenes: $d \geqslant 5$					
$d = 5$					
1	10	12	**317**	Deca-1,3,5,7,9-pentaene	261 (AS), 285 (AM)
	18	28	**318**	1,10-Di-*t*-butyldeca-1,3,5,7,9-pentaene	246 (AS)
2	16	20	**319**	Bis(3,3-dimethylcyclohexa-1,4-dienylidene)	286 (AS)
$d = 6$					
0	20	30	**320**	1,12-Di-*t*-butyldodeca-1,3,5,7,9,11-hexaene	246 (AS)
$d = 7$					
0	22	32	**321**	1,14-Di-*t*-butyltetradecaheptaene	246 (AS)
$d = 8$					
0	24	34	**322**	1,16-Di-*t*-butylhexadecaoctaene	246 (AS)
$d = 9$					
0	26	36	**323**	1,18-Di-*t*-butyloctadecanonaene	246 (AS)
	40	64	**324**	Phytoene (*cis* and *trans*)	287 (PR)
2	35	50	**325**	Septapreno-β-carotene	287 (PR)

(*continued overleaf*)

TABLE 3. (*continued*)

r	*n*	*m*	No.	Name	References (Method)[a]
$d = 10$					
0	28	38	**326**	1,20-Di-*t*-butyleicosadecaene	246 (AS)
2	40	58	**327**	7,7′-Dihydro-β-carotene	287 (PR)
$d = 11$					
0	30	40	**328**	1,22-Di-*t*-butyldocosaundecaene	246 (AS)
2	40	56	**279**	β-Carotene	287 (PR)
			280	(15*Z*) − β-Carotene	287 (PR)
$d = 13$					
0	40	56	**329**	Lycopene (all-*trans*)	287 (PR)
$d = 15$					
2	50	68	**330**	Decapreno-β-carotene	287 (PR)
$d = 19$					
2	60	70	**331**	Dodecapreno-β-carotene	287 (PR)

[a]PD, photodissociation; AS, absorption in frozen solvent; AM, absorption in Ar matrix; EG, gas-phase emission; EM, emission in neon matrix; PR, pulse radiolysis.



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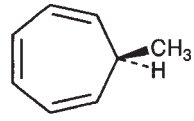

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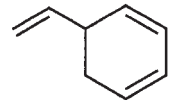

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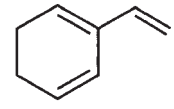

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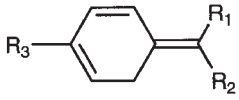
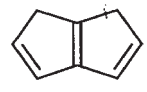


	R_1	R_2	R_3
298	H	H	H
300	Me	H	H
301	H	H	Me
304	H	H	Et
305	Et	H	H
306	Me	Me	H
307	n-Pr	H	H
308	H	H	i-Pr
309	Me	H	Et
310	Me	Me	Me



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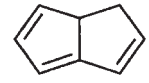

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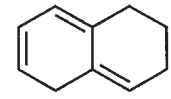

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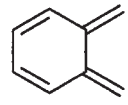

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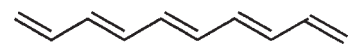

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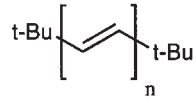
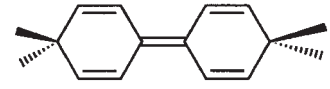


n= 2 3 4 5 6
293 297 315 318 320
7 8 9 10 11
321 322 323 326 328



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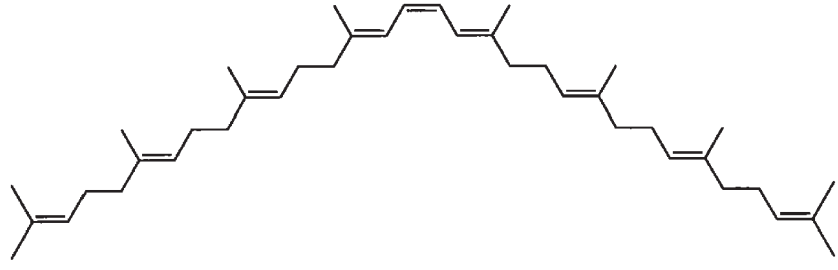

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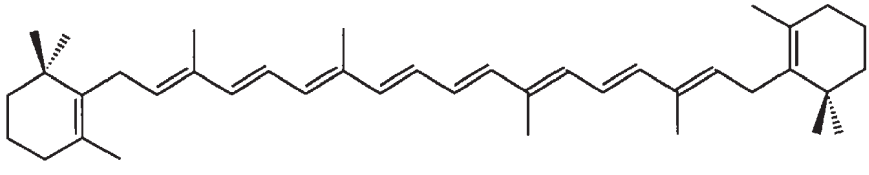

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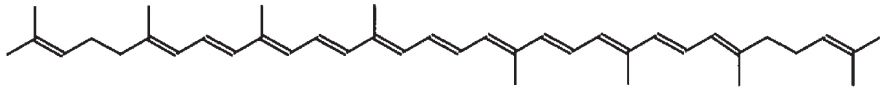

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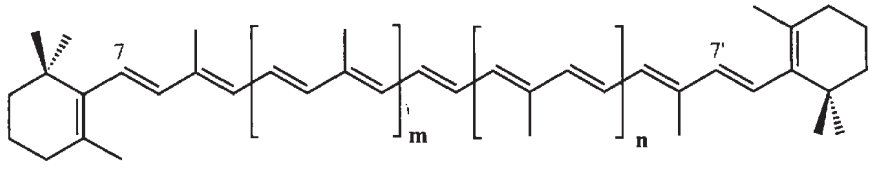


m	n		
1	0	Septapreno-β-carotene	**325**
1	1	β-carotene	**279**
2	2	decapreno-β-carotene	**330**
3	3	dodecapreno-β-carotene	**331**

C. Theoretical Methods

1. Koopmans and non-Koopmans states

In Section II.C (equations 7–10 and Figure 3) it was explained how electronic states of $M^{+\bullet}$ that give rise to PE bands can be related directly to orbital energies $\mathcal{E}_j$ from Hückel or Hartree–Fock type calculations. In the present context it becomes necessary to extend this picture by taking into account excited configurations which arise through promotion of electrons into *virtual orbitals*. Excited states of $M^{+\bullet}$ described by such configurations cannot be related to orbital energies $\mathcal{E}_j$ by the Koopmans theorem, and therefore it has become customary to call such states *non-Koopmans* states (as opposed to Koopmans states which are seen in PE spectra).

Figure 27 shows how different types of excited configurations can be formed from the ground configuration $^2\tilde{\Phi}_0$ of a radical cation $M^{+\bullet}$: electron promotion from doubly occupied MOs ϕ_{n-j} to the singly occupied HOMO ϕ_n give rise to Koopmans configurations $^2\tilde{\Phi}_1$ and $^2\tilde{\Phi}_2$, which are also called A-type configurations. Excitation from the HOMO into virtual MOs ϕ_{n+j} yields B-type configurations whereas promotion of electrons from doubly occupied into virtual MOs gives C-type configurations. The latter always come in pairs which correspond to promotion of α or β electrons (termed C_α and C_β, respectively). Due to differences in electron repulsion between α and β electrons, the corresponding excited states $^2\tilde{\Psi}_j$ ($M^{+\bullet}$) lie at different energies† and are also associated with different transition moments, a phenomenon which is unique to open-shell systems such as radical ions.

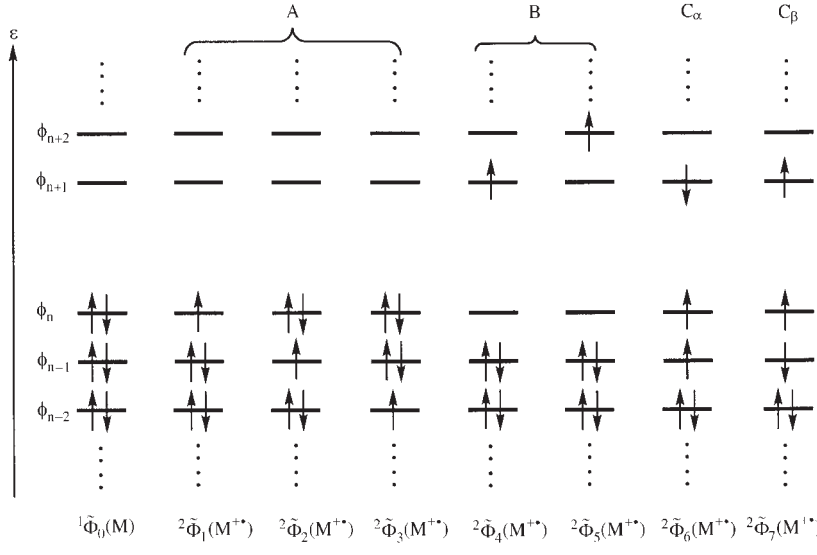


FIGURE 27. Different types of configurations of radical cations (the numbering does not imply an energetic ordering). A-type are Koopmans, B- and C-type are non-Koopmans configurations

† In actual fact, the three configurations corresponding to spin arrangements $\alpha/\alpha/\beta$, $\alpha/\beta/\alpha$ and $\beta/\alpha/\alpha$ (or the corresponding ones with two β and one α electron) are not eigenfunctions of the S^2 operator. Upon proper combination, they give rise to three spectroscopic states, two doublets and one of the components of a quartet.

2. Limitations and extension of single-determinant models

Although in many cases, particularly in PE spectroscopy, *single* configurations or Slater determinants ${}^2\tilde{\Phi}_j(M^{+\bullet})$ were shown to yield heuristically useful descriptions of the corresponding spectroscopic states ${}^2\tilde{\Psi}_j(M^{+\bullet})$, this is not generally true because the independent particle approximation (which implies that a many-electron wavefunction ${}^2\tilde{\Psi}_j$ can be approximated by a single product of one-electron wavefunctions, i.e. MOs ϕ, as represented by a Slater determinant ${}^2\tilde{\Phi}_j$) may break down in some cases. As this becomes particularly evident in polyene radical cations, it seems appropriate to briefly elaborate on methods which allow one to overcome the limitations of single-determinant models.

This can be achieved, for example, by introducing an additional degree of flexibility into the wavefunction through *mixing of different configurations* ${}^2\tilde{\Phi}_j(M^{+\bullet})$. It can be shown that by doing so one allows for a degree of correlation between the motions of different electrons which is suppressed in single-determinant MO models[†]. In the present context we will, however, not be concerned with the application of this so-called *Configuration Interaction* (CI) method for attempting a full recovery of electron correlation, but rather with its application to very simple cases (such as excited states of polyene radical cations) where only a few configurations must be considered in order to gain a qualitatively correct description of excited states[‡].

In analogy to using a linear combination of atomic orbitals to form MOs, a variational procedure is used to construct many-electron wavefunctions $\tilde{\Psi}_k$ from a set of N Slater determinants $\tilde{\Phi}_j$, i.e. one sets up a $N \times N$ matrix of elements $H_{ij} = \langle\tilde{\Phi}_i|\mathbf{H}|\tilde{\Phi}_j\rangle$ which, upon diagonalization, yields state energies E_k and associated vectors of coefficients a_{ki} used to define $\tilde{\Psi}_k$ as a linear combination of $N\tilde{\Phi}_i$s:

$$\tilde{\Psi}_k = \sum_i^N a_{ki}\tilde{\Phi}_i \tag{63}$$

This is usually sufficient for a *qualitatively* correct description of electronically excited states of $M^{+\bullet}$, even though electron correlation is not well accounted for if N is small.

Unfortunately, the dynamic correlation energy[¶] is not constant for a given molecule but may vary considerably between different electronic states. Thus, any procedure geared towards *quantitative* accuracy in predicting excited-state energies must in some way account for these variations. The most economical way to achieve this is to introduce a number of parameters into the model. By scaling those to a set of experimental data

[†] In single-determinant models each electron is considered to be moving in the *average* field of the other electrons and the nuclei. Consequently, the different electrons cannot maximize their average distance at any moment by correlating their movements, which is what they do in reality. Allowing for electron correlation invariably leads to a lowering of the total energy of a molecule, by the so-called 'correlation energy'.

[‡] Note that only configurations of the same symmetry can interact. In radical ions (and, generally, open-shell systems) the symmetry of a configuration is obtained as the direct product of the irreducible representations of all singly occupied MOs. If there is only one of these, as is the case in all A- and B-type configurations of radical ions, this corresponds to the irreducible representation of that MO.

[¶] It has become customary in quantum chemistry to subdivide electron correlation effects into two classes according to the methods used to account for them. The first are termed 'non-dynamic' and they can be recovered by the above type of small CI. On the other hand, all deficiencies which remain once these 'non-dynamic' effects are taken care of are attributed to 'dynamic' correlation.

one hopes to 'absorb' all deficiencies of the model, including correlation effects. In these so-called 'semiempirical' methods, different kinds of experimental data usually require different parameters, in analogy to the simple HMO model where the values for β used to predict thermochemical or spectroscopic properties vary by almost a factor of two[288].

In *ab initio* methods (which, by definiton, should not contain empirical parameters), the dynamic correlation energy must be recovered by a true extension of the (single configuration or small CI) model. This can be done by using a very large basis of configurations, but there are more economical methods based on many-body perturbation theory which allow one to circumvent the expensive (and often impracticable) large variational CI calculation. Due to their importance in calculations of polyene radical ion excited states, these will be briefly described in Section 4.

3. Semiempirical CI methods

As conjugated polyenes are often (essentially) planar molecules, their electronic structure can be described quite satisfactorily in terms of their π-electrons alone. Thus, models involving CI between singly excited π-configurations were developed already in the early days of computational quantum chemistry. The Hückel MOs used originally[289] were soon replaced by those obtained from semiempirical π-SCF procedures as in the popular PPP method[290], which was adapted and tested for open-shell systems by Zahradník and Čársky in the late 1960s[291]. Such models are usually adequate for a qualitatively correct interpretation of the spectra of the radical ions of planar π-systems, including those of polyenes, and continue to be used successfully for this purpose.

Analogous to the PPP method for planar π-systems, semiempirical *all-valence* methods can be and were extended to include CI, thus giving rise to a family of procedures based on the CNDO[292], INDO[293] and NDDO[294] variants of the zero-differential overlap (ZDO) approximation, many of which were applied also to the discussion of CI effects in radical cations. Due to the parametric incorporation of dynamic correlation effects, such procedures often yield rather accurate predictions of excited-state energies and they continue to be the methods of choice for treating very large chromophores which are not amenable to *ab initio* calculations.

Because of the inherent limitations of such semiempirical procedures, they can only be relied upon for yielding predictions for a limited set of data, the range of which includes the set of experimental data used for their parametrization. As such data are less abundant for open-shell species, such as radical ions, it is not surprising that there are examples of dramatic failures of semiempirical methods in predicting their electronic spectra, some of which will be discussed later. *Ab initio* methods are not burdened by these limitations but, as mentioned above, they require additional computations to account for dynamic electron correlation.

4. Many-body perturbation methods

Due to the size of the variational problem, a large CI is usually not a practicable method for recovering dynamic correlation. Instead, one usually resorts to some form of treatment based on many-body perturbation theory where an explicit calculation of all off-diagonal CI matrix elements (and the diagonalization of the matrix) are avoided. For a detailed description of such methods, which is beyond the scope of this review, the reader is referred to appropriate textbooks[295]. For the present purpose, it suffices to mention two important aspects.

Firstly, such methods, for example the popular Møller–Plesset (MP) or the more recent coupled cluster (CC) or quadratic CI (QCI) procedures, are implemented in several standard quantum-chemistry packages such as Gaussian, Gamess or Cadpac. Their application

is therefore quite straightforward, at least as long as single-determinant wavefunctions offer a qualitatively correct description of the system.

However, if this is not the case, the perturbations are large and perturbation theory is no longer appropriate. In other words, perturbation methods based on single-determinant wavefunctions cannot be used to recover non-dynamic correlation effects in cases where more than one configuration is needed to obtain a reasonable approximation to the true many-electron wavefunction. This represents a serious impediment to the calculation of well-correlated wavefunctions for excited states which is only possible by means of cumbersome and computationally expensive multi-reference CI methods.

Luckily, this impasse was removed through the recent introduction of the CASPT2 model, which combines a powerful procedure for treating cases of strong non-dynamic correlation (CASSCF)[†] with a very economical one for treating dynamic correlation[296]. As will be shown below, the CASPT2 method works very well for polyene radical cations.

D. Linear Conjugated Polyenes

Electronic spectra of linear conjugated polyene radical cations are of interest for several reasons. Firstly, such species occur as intermediates in different processes of biological relevance, e.g. the protection of the photosynthetic reaction centre[297], the charge transfer processes in membranes[298] or in model studies for photoinduced charge separation[299]. Secondly, they may be involved in the formation of solitons upon doping or photoexcitation of polyacetylene[300], and finally, they are of theoretical interest because their interpretation requires models which account for non-dynamic correlation.

1. The minimal CI model

To illustrate the latter point, consider the butadiene radical cation ($BD^{+\bullet}$). On the basis of Hückel theory (or any single-determinant Hartree–Fock model) one would expect this cation to show two closely spaced absorption bands of very similar intensity, due to $\pi_1 \rightarrow \pi_2$ and $\pi_2 \rightarrow \pi_3$ excitation (denoted by subscripts a and v in Figure 28), which are associated with transition moments μ_a and μ_v of similar magnitude and orientation. Using the approximation $\beta_{HMO} \approx -3$ eV[288] the expected spacing amounts to about 0.7 eV.

Actually, two bands of quite different intensity separated by nearly 2 eV are observed! Whereas the positions of the two bands could possibly be accommodated by appropriate parametrization, this is not possible for the band intensities which reveals the limitations inherent in the single-configuration approximation.

Fortunately, a qualitatively correct modelling of the $BD^{+\bullet}$ spectrum requires only a single further step, i.e. taking into account the interaction between the first two excited configurations $^2\tilde{\Phi}_a$ and $^2\tilde{\Phi}_v$ which are of the same ^2A_u symmetry. Solving this simple 2×2 problem leads to two states

$$^2\tilde{\Psi}_+ = {}^2\tilde{\Phi}_v + \Delta \cdot {}^2\tilde{\Phi}_a \text{ and } {}^2\tilde{\Psi}_- = {}^2\tilde{\Phi}_a - \Delta \cdot {}^2\tilde{\Phi}_v \tag{64}$$

where Δ measures the degree of mixing between $^2\tilde{\Phi}_a$ and $^2\tilde{\Phi}_v$. The actual value of Δ depends on the Hamiltonian $\mathbf{H}$ used to compute the integral $H_{av} = \langle {}^2\tilde{\Phi}_a|\mathbf{H}|{}^2\tilde{\Phi}_v\rangle$ but falls

[†] This procedure corresponds to a full CI (i.e. including all possible excitations) within a restricted set of occupied and virtual MOs (called the 'active space', hence the CAS acronym). In addition, the AO coefficients in the one-electron MOs are simultaneously optimized, such that these eventually represent an optimal basis set for the given CI.

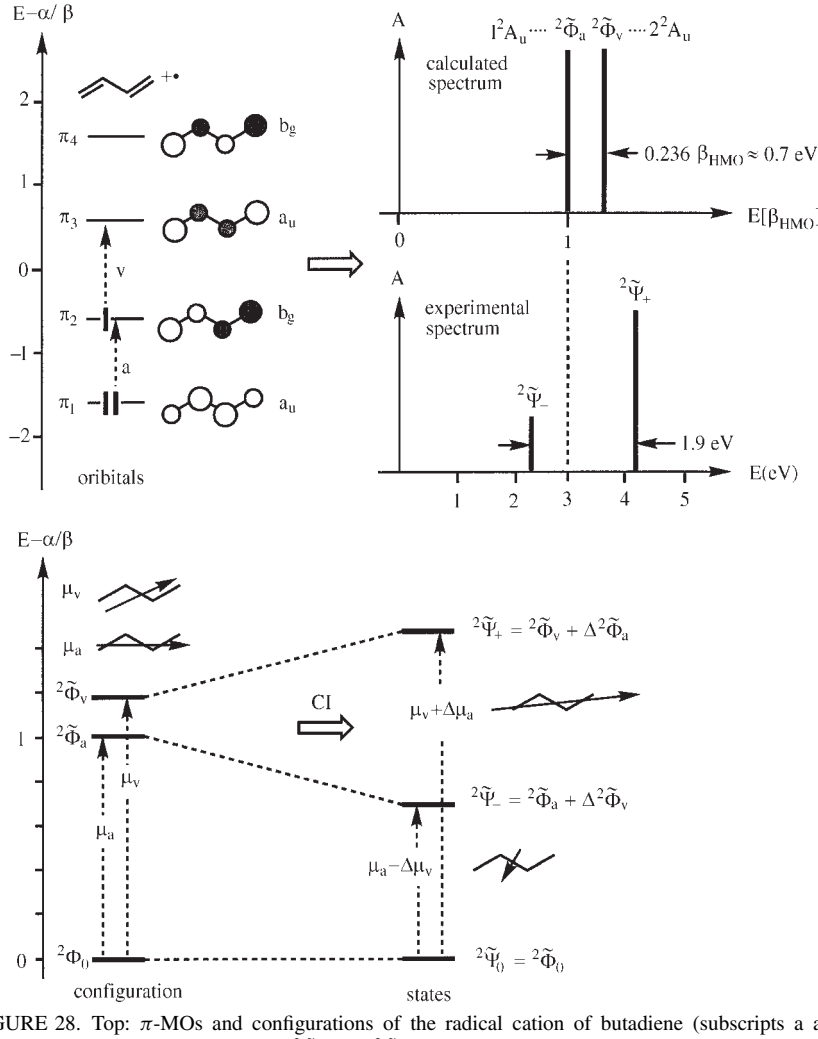


FIGURE 28. Top: π-MOs and configurations of the radical cation of butadiene (subscripts a and v correspond to excitations leading to $^2\tilde{\Phi}_a$ and $^2\tilde{\Phi}_v$, respectively). The resulting calculated spectrum is compared to the experimental one on the right. Bottom: The effect of a simple CI between $^2\tilde{\Phi}_a$ and $^2\tilde{\Phi}_v$ on excitation energies and on the transition moments μ_a and μ_v

generally in the range of 0.15 to 0.35. With regard to transition moments, the above 2×2 CI leads to a reduction due to partial cancellation of μ_a and μ_v in the first transition $^2\tilde{\Psi}_0 \rightarrow {}^2\tilde{\Psi}_-$ whereas the two reinforce each other in the higher-energy $^2\tilde{\Psi}_0 \rightarrow {}^2\tilde{\Psi}_+$ excitation[†], thus explaining the observed disparity in band intensities. Concurrently, the

[†] Due to the nature of the off-diagonal elements in a 2×2 CI matrix, the *negative* combination of determinants gets to lie below the positive combination, in contrast to the situation which prevails for interacting MOs.

energy separation between the two states increases, which naturally accounts for the larger spacing between the two bands.

The same treatment can be applied to longer polyenes, except that higher-lying π-excited configurations $^2\tilde{\Phi}_i$ will come into play. However, by virtue of the alternating a_u/b_g symmetries of polyene π-MOs, those immediately above $^2\tilde{\Phi}_a$ and $^2\tilde{\Phi}_v$ are usually of the same symmetry as $^2\tilde{\Phi}_0$ and therefore electronic excitation into the corresponding states $^2\tilde{\Psi}_i$ is dipole-forbidden within C_{2h} symmetry. Consequently, these configurations can be ignored when discussing EA spectra of polyene radical cations. The next π-excited states of the same symmetry as $^2\tilde{\Psi}_+$ and $^2\tilde{\Psi}_-$ as well as the σ-excited states are usually higher in energy than the first excited states of the neutral polyenes. They are associated with small transition moments and thus very difficult to detect in the presence of an excess of the neutral polyene, as is usual in EA experiments.

The EA spectra of linear conjugated polyene radical cations which have been observed so far conform well with the picture that emerges from the 2×2 CI model, i.e. they all show a weak low-energy and an often very intense high-energy band. In accord with qualitative expectations, both bands move to lower energies as the number of conjugated double bonds increases whereas their splitting decreases. This is due to the fact that the first two excited configurations move closer in energy as the chains grow longer and that the off-diagonal matrix element H_{av} which determines their splitting becomes smaller. This is shown schematically in Figure 29 where the energies of the first two excited states of the radical cations t-Bu$-$(CH=CH)$_n-$Bu-$t^{+\bullet}$[246] are plotted against $1/n$ (in addition, the energies corresponding to the second, intense EA band of some carotenoid radical cations observed in pulse radiolysis experiments[287] have been included in Figure 29).

The literature records numerous, more or less successful, attempts to predict the energies of the first two excited states in linear conjugated polyene radical cations by semiempirical or *ab initio* methods. Some of these endeavours were reviewed elsewhere[241] whereas a more recent publication[242] gives an account of the difficulties met in predicting the energy of the second state accurately by *ab initio* CI procedures. However, it was recently shown that the CASSCF/CASPT2 model mentioned in Section III.C is capable of reproducing both excited-state energies of polyene cations H$-$(CH=CH)$_n-$H$^{+\bullet}$ ($n = 2$ to 4) within 0.25 eV[301]. Thus, a model has finally become available which appears to provide reliable predictions of the energies of such excited states.

2. Long polyenes: Towards the polaron

Figure 29 raises the question of how the energies of these two excited states evolve as one goes to longer polyene chains, in analogy to those found in polyacetylenes which become conductive upon oxidative doping (= ionization) or photoexcitation.

The regression curves in Figure 29 tend to approach linearity for $n > 4$, which seems to suggest that a linear extrapolation to infinity ($1/n \rightarrow 0$) is appropriate. However, this is certainly not true because the charge and spin are not distributed evenly over the entire polyene cation chain. Consequently, longer polyene radical cations undergo a characteristic distortion leading to a localization of charge and spin around the centre of the chains. In solid state physics this distorted conjugated system, associated with a spin of 1/2 and a single charge, is called a *polaron*, in analogy to the structure of odd-alternant radicals or cations where the single electron or the charge also accumulate about the centre (a *soliton* in solid state physics language). These charge-carrying polarons and solitons can move rather easily along chains of conjugated systems under the influence of an external electric field, an effect which is thought to be one of the reasons for the high conductivity of doped conjugated polymers such as polyacetylene.

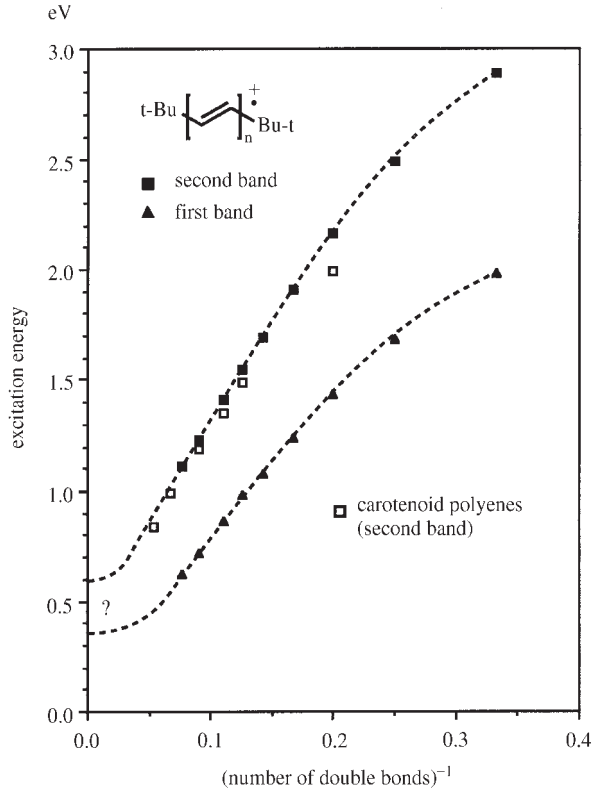


FIGURE 29. Energies of first (triangles) and second transition (squares) of radical cations t-Bu$-$(CH=CH)$_n-$Bu-t (filled symbols) and some carotenoid polyenes (open symbols) as a function of $1/n$

Because the extension of the polaron in polyene radical cations is finite (10–20 double bonds depending on the type of calculation), its electronic structure is independent of the number of double bonds attached to either side of it, so that the two lines in Figure 29 *must* bend at some point to meet the abscissa horizontally, as indicated by the dashed curves. Apparently, the point of inflection has not been reached for $n = 15$, but it is of interest that the curve for the first excited state could well extrapolate to 0.35 eV, which happens to be where the absorption of a polaron in polyacetylene has been observed[300]. If this is true, a second, more intense absorption band should occur between 0.5 and 0.7 eV, but the corresponding experiments have not yet been carried out.

3. Geometry dependence of excited-state energies

The realization of the polaronic nature of polyene radical cations leads naturally to the question, to what extent the pronounced relaxation of polyenes upon ionization affects their excited-state energies. Such changes can be assessed by comparing the ionization energy differences $I_i^v - I_1^v$ obtained from PE spectra with the positions of the band maxima in the radical cation's EA spectra which measure the same quantities at the radical cation

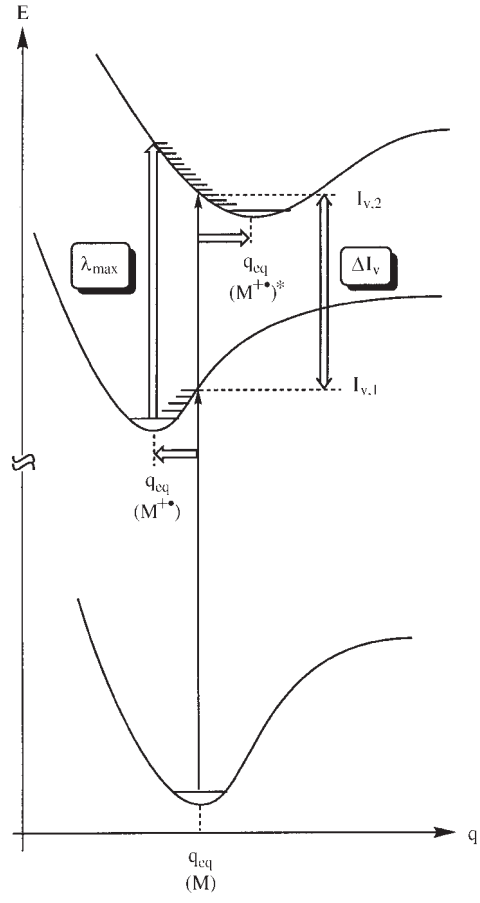


FIGURE 30. Potential energy curves for a neutral molecule M, and its radical cation $M^{+\bullet}$ in the ground and first excited state (q_{eq} are the equilibrium distances with respect to an arbitrary coordinate q along which the three geometries differ). Note the shift in the $M^{+\bullet}/(M^{+\bullet})^*$ energy difference ΔE on going from q_{eq} of M ($\Delta E = \Delta I_v$ from the PE spectrum of M) to q_{eq} of $M^{+\bullet}$ (ΔE corresponds to λ_{max} from the EA spectrum of $M^{+\bullet}$)

equilibrium geometries, as illustrated schematically in Figure 30. A juxtaposition of PE and EA spectra for the first three members of the polyene radical cations shows that these changes are very small for the first π-excited state and perhaps somewhat larger for the second, which cannot be observed unambiguously in the PE spectra. This is surprising in view of the pronounced bond length changes which accompany the ionization of these polyenes and the corresponding ground-state relaxation energies which amount to several tenths of an eV. Indeed, the energies of the excited *configurations* $^2\tilde{\Phi}_a$ and $^2\tilde{\Phi}_v$ are very much affected by these changes, in accord with expectations from the nodal properties of the MOs involved. However, it was recently shown[301] that these effects are strongly attenuated in the corresponding excited *states* $^2\tilde{\Psi}_+$ and $^2\tilde{\Psi}_-$, i.e. that they are almost entirely washed out by dynamic correlation effects, at least for the first excited state. This

is, however, not generally true, as in the case of dihydropentalenes, where pronounced mismatches were observed between PE- and EA-band positions[278].

4. Conformational isomerism in linear conjugated polyene radical cations

In neutral polyenes a clear distinction can be made between essential single bonds (which can be twisted fairly easily) and double bonds (which offer much more resistance to rotation). It has become customary to distinguish stable *isomers* (classified *E*/*Z* with regard to the configuration around the double bonds) and easily interconvertible *conformers* (classified as s-*cis*, s-*trans* or *gauche* with regard to the substituents on the essential single bonds) in polyenes.

Due to the fact that polyene HOMOs are invariably bonding along the double bonds and antibonding along the single bonds, removal of an electron from the HOMO entails a weakening of the former and a strengthening of the latter, i.e. a trend towards equalization of bond lengths[301], force constants[302,303] and rotational barriers[303] upon ionization. Eventually, a distinction between double and single bonds is no longer meaningful in polyene radical ions because all rotational isomers (rotamers) are stable in the sense that they do not readily interconvert.

In their first study on triene radical cations, Shida and coworkers found that irradiation of ionized hexatriene in frozen glasses yields a multitude of species with similar EA spectra, which could be selectively interconverted by narrow-band photolysis[249]. They assigned the observed band systems to four different rotamers of the hexatriene radical cation. Allan and Maier found that (3*E*)- and (3*Z*)-hexatriene gave distinct gas-phase emission spectra in agreement with the earlier PE findings[20]. However, the two isomers could not be distinguished by photodissociation spectroscopy[267].

In subsequent argon matrix isolation studies, similar bands were found when hexatriene or cyclohexadiene are ionized[250,270], and eventually, five of the six possible rotamers of hexatriene radical cation were identified by selective, wavelength-specific interconversions[270]. Similar results were later obtained for octatetraene[264,275,279,285], where six of the twenty possible rotamers are formed on ionization in argon (Figure 31) which could be interconverted and identified by selective photolysis[275,279]. Interestingly, in the case of the butadiene radical cation the s-*cis* rotamer could not be detected, even if the diene radical cation was formed from the cyclobutene radical cation[304]. In contrast, in a recent resonance Raman study, some weak bands were detected and assigned to the s-*cis*-butadiene radical cation which might have escaped detection in the earlier ESR and EA experiments[303].

One distinctive feature of polyene radical cations (especially of the long ones) is their great photosensitivity. For example, exposure of a sample of matrix isolated all-*trans* octatetraene radical cation to diffuse daylight leads, within about an hour, to a new photostationary equilibrium containing at least six rotamers. It is by virtue of this sensitivity, which is in part due to the very large absorptivities of the second EA bands, that a highly selective rotamer interconversion can be achieved, using a very narrow bandwidth[270,279].

In a recent comprehensive study at the CASSCF level of *ab initio* theory, Cave and Johnson have carried out calculations for all six rotamers of the hexatriene radical cation. In agreement with experiment they found that the first excited state is hardly affected by the additional interactions which prevail in partially *cis*-configurated rotamers, whereas the energy of the second excited states decreases as the number of those *cis*-interactions increases. On this basis, they were able to confirm some of the original assignments of the observed spectra[305] but proposed revisions for some of the others.

It was generally found that the all-*trans* rotamers always yield the shortest-wavelength second EA bands whereas *cis*-interactions result in bathochromic shifts, perhaps due to

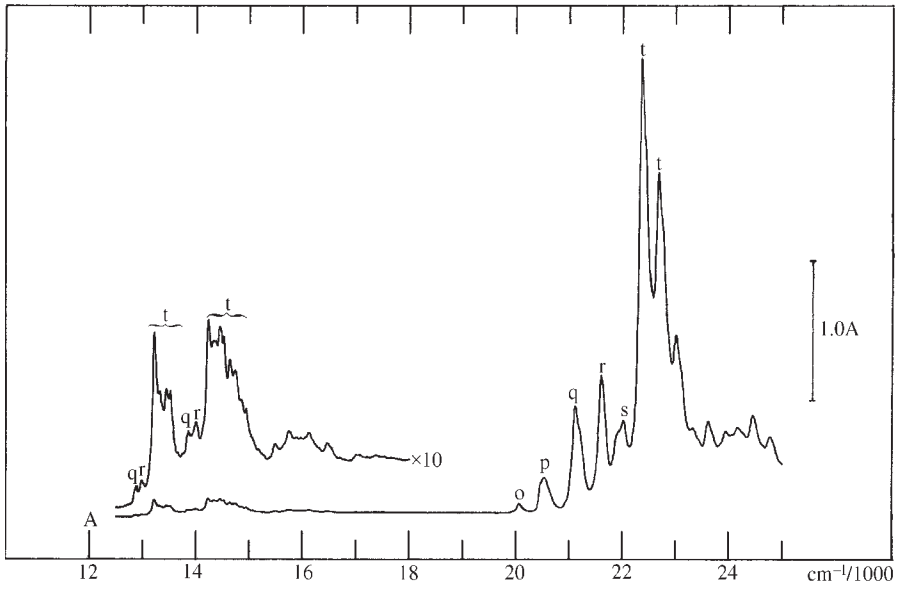


FIGURE 31. Spectrum obtained after ionizaton of all-*trans* octatetraene in argon. Note the occurrence of different rotamers (labelled **o** to **t**). The fine structure in the first absorption band of the **t** rotamer is due to site splittings[279]

slight deviations from planarity. Although this is difficult to prove in the absence of definitive assignments, these shifts appear to be roughly additive in the number of *cis*-configurated bonds. With increasing red shift, the strong second absorption loses much of its intensity. When one goes to longer polyenes, the spread in the λ_{max} values of this band becomes smaller, perhaps due to a restriction in the number of *cis*-configurated rotamers in rigid media[246].

5. Alkylated and cyclic conjugated dienes and trienes

In the early days of PD spectroscopy, many alkylated polyenes were investigated because it was found that this method allows one to distinguish between isomers[238]. However, no systematic attempts were made to explain the band shifts due to the alkyl groups, as had been done for the corresponding PE spectra. Generally, the first excited state is affected only weakly by alkyl substituents, whereas the second excited state undergoes a more substantial shift which decreases as the polyene chain grows longer.

Several cyclic conjugated polyenes have been investigated[238,240,245,247,250,252,257,285], in part as independent sources of *cis*-configurated conjugated open-chain polyenes. Although they retain the general feature of a weak low-energy and an intense high-energy band, the former sometimes appears only as a shoulder in diene spectra. Most of them readily undergo photochemical ring-opening to open-chain conjugated polyenes whereas the reverse reaction, i.e. cyclization, has never been observed in radical cations.

It is possible in principle to deduce from the position of the first absorption band the twisting angle between the double bonds in cyclic conjugated polyenes, e.g. on the basis of a simple LCBO model[50]. This has been attempted for cycloocta-1,3,5-triene **184**[257] and cyclooctatetraene **239**[260]. For the former it was deduced that the π-system becomes

essentially planar upon ionization whereas the tetraene radical cation retains a significant puckering. This is in contrast to the radical anion, which is planar[306]. From the point of view of its electronic structure, the cyclooctatetraene radical cation is an interesting case because excitation occurs to the second, degenerate excited state where a very pronounced Jahn–Teller distortion prevents the relaxation into the first excited state and causes the interesting photochemistry of this compound which takes place in violation of Kasha's rule[260,278].

6. Cross-conjugated polyenes

In spite of the continued interest in cross-conjugated polyenes ('dendralenes'), of which more than 100 are known[307], surprisingly few of these have been investigated by PE or radical ion spectroscopy†.

A special case are the radical cations of *o*- and *p*-quinodimethane which have low-lying non-Koopmans excited states. Due to mixing between A- and B-type configurations (cf Figure 27) these states sometimes show up as additional weak bands (so-called satellite bands) in the PE spectra[148,150,283] and thus represent rare examples of cases where the number of PE bands exceeds the number of occupied MOs in the range of π-ionizations. In the case of *o*-quinodimethane and derivatives, the positions of these states were confirmed by the EA spectra of the corresponding radical cations[283,284] whereas the same was not done for *p*-quinodimethanes.

Otherwise, not much can be said about this class of compounds, except that they share with their linear conjugated homologues the feature, that their excited-state energies appears to be hardly affected by the substantial bond length changes which accompany ionization[278].

E. Interaction Between Non-conjugated π-Orbitals

We mentioned in Section III.A that one of the unique features of radical ion optical spectroscopy is that it allows one to measure excited-state energies of a molecule at two different geometries, namely that of the neutral species (I_i^v in PE spectra) and that of the relaxed radical cation (λ_{max} of the EA bands). In many cases this feature is of little relevance because either the geometry changes upon ionization are too small to lead to noticeable effects (e.g. in aromatic hydrocarbons), or because such effects are obscured, due to the invisibility of the states in one or other of the two experiments (i.e. strong σ-ionizations in the PE spectrum) or because of the near-cancellation of opposing effects (as in the case of linear conjugated polyene radical cations).

However, one class of molecules not affected by the above limiting factors, and where much can be learned from a comparison of PE and EA spectra, are those which contain non-conjugated π-systems interacting through-space and/or through-bond. The radical cation of a simple model system consisting of a pair of ethylene moieties with facing π-MOs, π_a and π_b, will show a characteristic so-called 'charge resonance' absorption which corresponds to promotion of an electron from the bonding combination of π MOs $\pi_+ = N_+(\pi_a + \pi_b)$ to the antibonding combination $\pi_- = N_-(\pi_a - \pi_b)$. The energy E_{CR} of this transition is a measure of their energy splitting which, in a first approximation, is proportional to the overlap $S_{ab} = \langle \pi_a / \pi_b \rangle$ as discussed in Section II.E.1.

At the distance R between π_a and π_b which prevails in the neutral molecule (Figure 32), E_{CR} corresponds to $\Delta I_v = I_v(\pi_+) - I_v(\pi_-)$ which is used as a measure of the

† If we disregard the special class of pentafulvenes, these are the molecules **173, 174, 180, 194, 200, 237–241, 246, 250, 268, 277, 303, 314** and **318** in Tables 2 and 3.

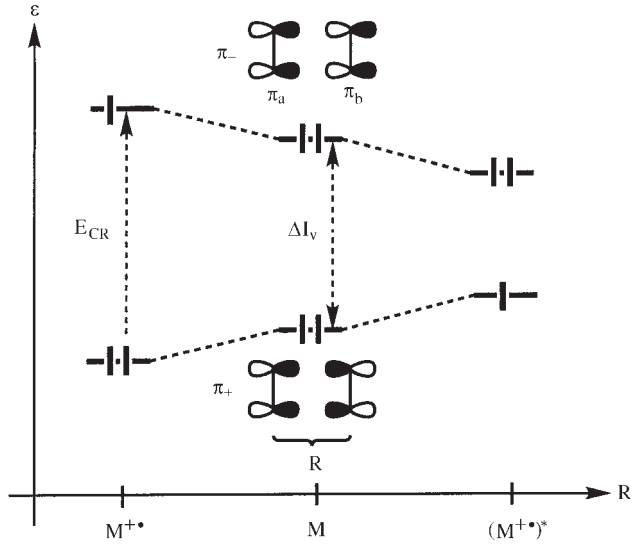


FIGURE 32. Schematic representation of the geometry changes of a hypothetical model of two facing π-systems with HOMOs π_a and π_b. The neutral molecule is represented in the centre. Upon ionization (removal of an electron from the HOMO π_-), the antibonding interactions which prevail in π_- are reduced, and the distance R decreases. As a consequence, the π_+/π_- overlap and E_{CR} increase. Conversely, upon electron ejection from π_+ (or on $\pi_+ \rightarrow \pi_-$ excitation), the bonding interaction in π_+ is diminished, which has the opposite effect on R and E_{CR} as described above

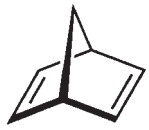
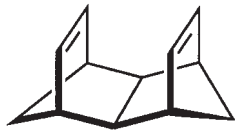
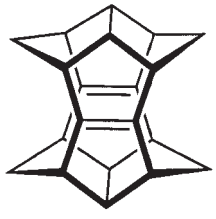
through-space interaction between π_a and π_b. At the geometry of the radical cation, E_{CR} is often significantly higher because the removal of an electron from π_-, decreases the antibonding interaction between π_a and π_b, thus allowing the two π-systems to come closer. This increases S_{ab} and leads to an overall stabilization of the system. The extent of this geometry change, and hence the change in E_{CR}, is limited by repulsive interactions between the interacting π-systems and by the stiffness of the σ-frame which connects them.

Such CR bands, which have been observed for many radical cations, usually manifest themselves by intense, broad bands in the visible or NIR part of the spectrum. The reason for the broadness is that, upon excitation of an electron from π_+ to π_-, the antibonding interaction is greatly enhanced. Consequently, the equilibrium distance of the π-systems in the excited state is significantly larger than in the ground state of the radical cation (or that of the neutral molecule) which results in a Franck–Condon envelope for the EA band which may be even broader than that for the corresponding PE band.

The above features can be illustrated by the molecules in Table 4, where the difference between the first and second ionization energy is compared to E_{CR} from the ion's optical spectra. The molecules are arranged in order of decreasing flexibility to show how this influences the difference between E_{CR} and ΔI_v.

In norbornadiene **75**, with its rather flexible σ-frame, the change in E_{CR} on going from the neutral molecule to the radical cation is more than 1 eV. In the more rigid dimethanonaphthalene derivative **139** it decreases to 0.84 eV, whereas in the already rather stiff pagodiene **295**, the change is only 0.54 eV. Finally, in the very strained dodecahedradiene **296**, E_{CR}, is nearly the same at the neutral molecule's and at the radical cation's geometry. As it happens, the geometry change upon electronic excitation in **296**$^{+\bullet}$ coincides almost

TABLE 4. Change in E_{CR} and ΔI_v between neutral and cation geometry for a series of selected non-conjugated diene radical cations

No.	Compound	R (pm)[a]	ΔI_v (eV)[b]	E_{CR} (eV)[c]	Δ (eV)[d]
75		225	0.85[45]	1.94	1.09
139		280[308]	1.26[105]	2.10[265]	0.84
156		280[309]	1.91[310]	2.43[265]	0.52
296		350[310]	0.68[310]	0.75[266]	0.07

[a]Distance between the double bonds.
[b]$I_{v,2} - I_{v,1}$ from PE spectra.
[c]From EA spectra of radical cations.
[d]Increase in E_{CR} on going from the neutral to the radical cation's equilibrium geometry.

perfectly with an excited-state normal mode involving mainly a change in the distance between the double bonds. Therefore, the first EA band shows a single, well-resolved vibrational progression, a feature which is atypical for a charge resonance band.

The above considerations neglect the possible influence of through-bond interaction. That this must be very important becomes evident if one compares the dimethanonaphthalene derivative **139** with the pagodiene **156**: both have similar distances between perfectly facing double bonds, and yet E_{CR} is much larger in the latter due to an interaction via four single bonds which reinforces the through-space splitting. It is fair to assume that the magnitude of the through-bond interaction via the real σ-MOs does not change significantly with the geometry changes upon ionization, and that the change of E_{CR} is dictated mainly by the through-space term. Unfortunately, an attempt to assess the relative influence of the two effects by a study of the *syn*- and *anti*-dimers of cyclobutadiene (compounds **102** and **103**) failed because of the rapid rearrangement of the corresponding radical cations under the conditions of the EA experiment.

As shown in Section II.E, such through-bond interactions can be explained on the basis of a simple three-centre model involving the two interacting π-MOs and the intervening σ-MO. Of course, such models can also be applied to the changes in E_{CR} upon ionization, but all that can be learned from them in this context is that $B = \langle \pi_a | \mathbf{H} | \pi_b \rangle$ increases. If

one wants to relate this change to changes in geometry, one must resort to some quantum-chemical calculation. As it happens, through-space interactions which occur typically over distances of the order of van der Waals radii of the atoms involved, are difficult to assess by semiempirical methods because these often do not account properly for the fall-off in electron density at such distances.

This situation is exemplified in Figure 33, where the π_+/π_- splitting for a pair of ethylene molecules with facing π-MOs is plotted as a function of their distance for two popular semiempirical methods and an *ab initio* SCF method (for the latter, the splittings obtained with the 3-21G and 6-31G* basis set are indistinguishable). Whereas the *ab initio* model (if applied to the molecules in Table 4) gives roughly correct results, the INDO/S method largely *overestimates* the effect of through-space interaction at all distances, although it shows the correct limiting behaviour. Conversely, AM1 strongly *underestimates* this effect, even at large distances. Consequently, the charge resonance absorptions of the first three cations in Table 4 are predicted to occur in the UV by INDO/S and in the IR by AM1 whereas they actually all occur in the visible range (500–630 nm), as predicted correctly by the *ab initio* models. Thus, caution should be exercised when

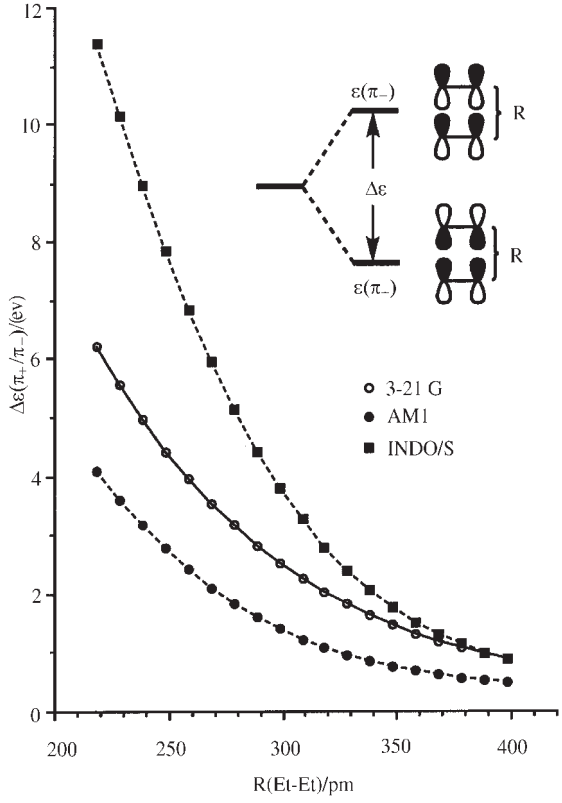


FIGURE 33. Energy difference $\Delta\mathcal{E}$ between MOs π_+ and π_- of two ethylene molecules as a function of their distance R as calculated by an *ab initio* method (using the 3-21G basis set), by AM1 and by INDO/S. Note the strong underestimation of the through-space interaction by AM1 at all distances and the overestimation by INDO/S which diminishes, however, for large R

applying semiempirical methods for a quantitative prediction of E_{CR} values of π-systems interacting through space.

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CHAPTER **7**

The photochemistry of dienes and polyenes: Application to the synthesis of complex molecules

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I. INTRODUCTION

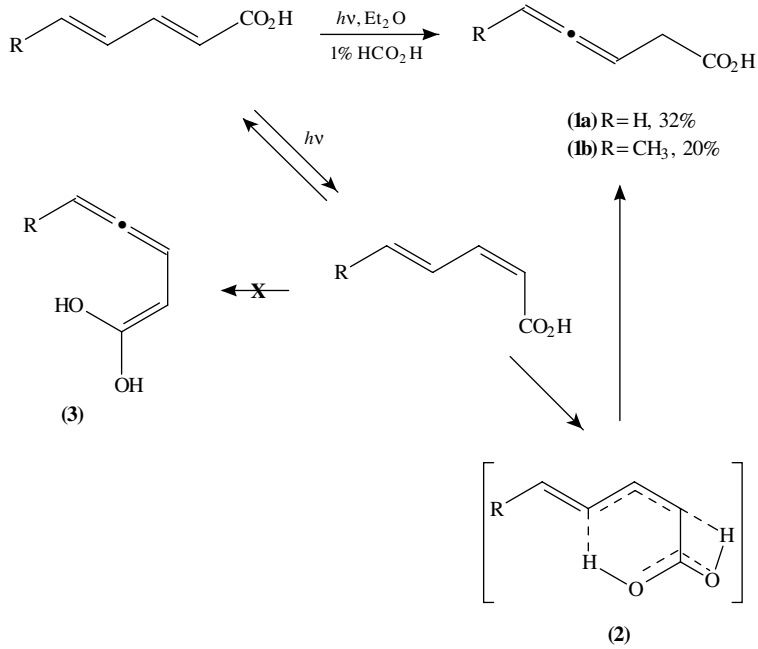
Organic photochemistry has typically been approached from a physical/mechanistic perspective, rather than a synthetic one. This may result from a certain reluctance on the part of synthetic chemists to employ reactions which often produce many products. Nonetheless, careful design of substrates can lead to high levels of chemoselectivity. In fact, there have been many recent examples of the successful application of photochemical reactions to the synthesis of complex targets[1]. In many cases, these processes provide access to unique modes of reactivity, or offer unrivaled increases in molecular complexity[2].

The literature of diene and polyene photochemistry provides many cases of synthetically useful reactions. As a result, certain arbitrary decisions have been made regarding what is covered in this chapter. For example, intramolecular [2 + 2]-photocycloaddition reactions of α,ω-dienes can be formally included under the general rubric of diene photochemistry. However, we have chosen to restrict our discussion to dienes and polyenes which constitute a self-contained chromophore, viz. conjugated, cross-conjugated and 1,4-diene systems. Likewise, arene-olefin photocycloadditions will not be considered. These two broad classes of photoreactions have been applied extensively in synthesis, and have been the subject of recent reviews[3,4].

II. PHOTOREARRANGEMENTS OF DIENES AND POLYENES

A. Bond Migration

Photoenolization is a frequently encountered process for aromatic and α,β-unsaturated carbonyl compounds[5]. Typically, an allylic or benzylic γ-hydrogen is abstracted by the

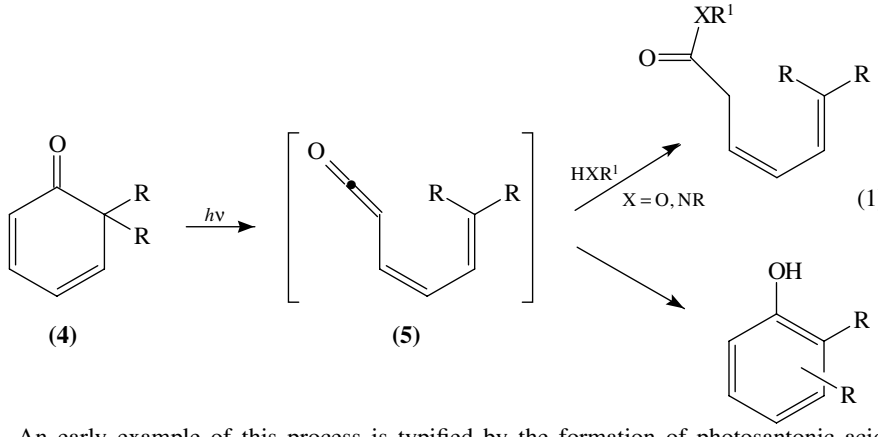


SCHEME 1

oxygen of the photochemically excited carbonyl. In contrast to their saturated counterparts, which produce a 1,4-diradical capable of either fragmentation or closure to cyclobutanol, these systems lead to dienols, also referred to as photoenols. These intermediates can then undergo ketonization to give the isomeric β,γ-unsaturated carbonyls, or take part as diene partners in Diels-Alder cycloadditions. In the case of $\alpha,\beta,\gamma,\delta$-unsaturated carbonyls, the vinylic γ-hydrogen is presumably somewhat less reactive. However, Crowley reported that irradiation of sorbic acid or 2,4-pentadienoic acid in the presence of formic acid furnishes **1**, presumably involving prior photochemical *cis/trans* isomerization of the C-2/C-3 alkene (Scheme 1)[6]. This leads to a net deconjugation of the unsaturated carbonyl, with concomitant creation of an allene. This process does not occur with the corresponding carboxylate salts, and only in low yields with methyl sorbate. To explain these differences, a transition state **(2)** involving simultaneous transfer of the γ- and carboxyl hydrogens was invoked, rather than photoenolization to give **3**, followed by tautomerization.

B. Electrocyclic Ring Opening of Cyclic Dienes

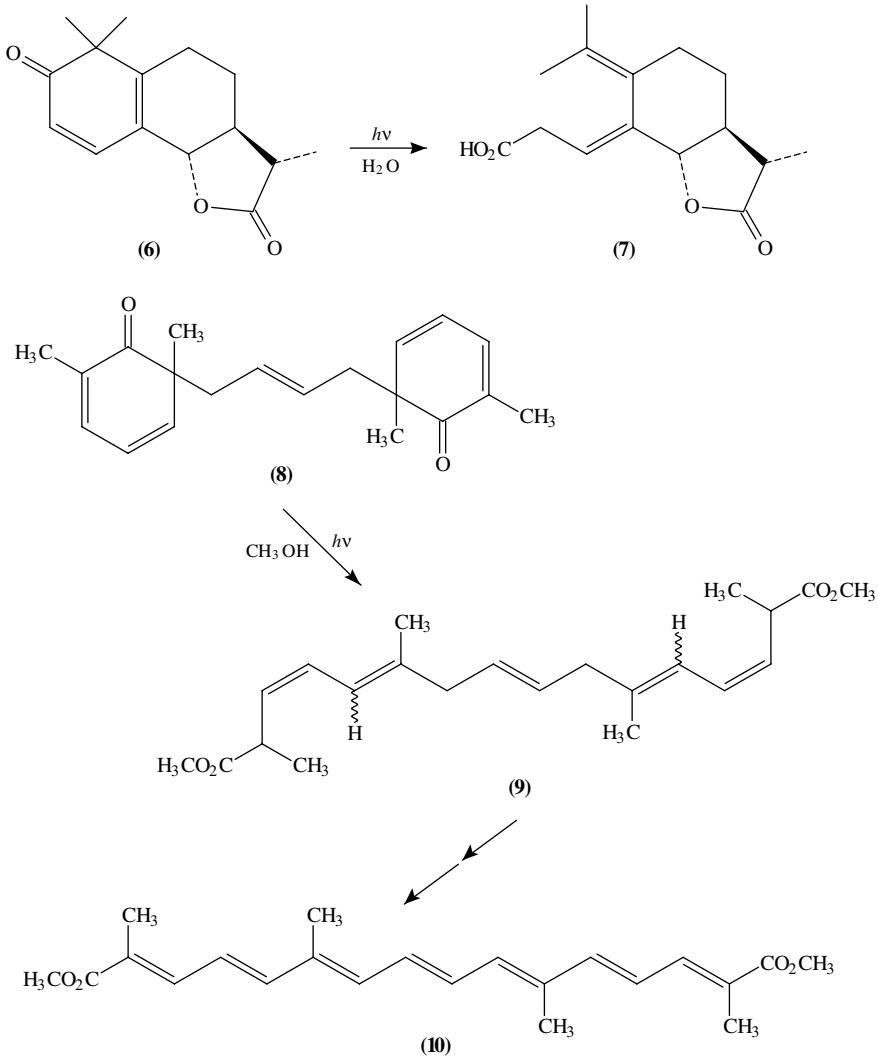
The photochemistry of linearly conjugated 2,4-cyclohexadiene-1-ones (e.g. **4**) has been studied extensively[7]. These linearly conjugated systems generally photorearrange to a (*Z*)-dienylketene **5** (equation 1); this process is usually reversible, so that in the absence of a nucleophile little change is observed. In the presence of amines or alcohols, however, amides and esters are typically isolated. In the presence of weaker nucleophiles a slow formation of phenol derived products is usually observed.



(4) **(5)** (1)

An early example of this process is typified by the formation of photosantonic acid **7**, isolated in high yield when **6** is irradiated in aqueous solution (Scheme 2)[8]. Barton and Quinkert have also utilized this ring opening/trapping process in the synthesis of dimethylcrocetin, **10**, as well as other derivatives of this diapocarotenoid[9]. Double C-alkylation of the 2,6-dimethylphenol with 1,4-dibromobut-2-ene affords the requisite (bis)cyclohexadieneone **8** in modest yield. Irradiation of **8** in methanol affords a mixture of isomeric dimethyltetrahydrocrocetins (**9**), which on dehydrogenation with DDQ leads to a mixture of compounds from which the naturally occurring dimethylcrocetin **10** can be isolated.

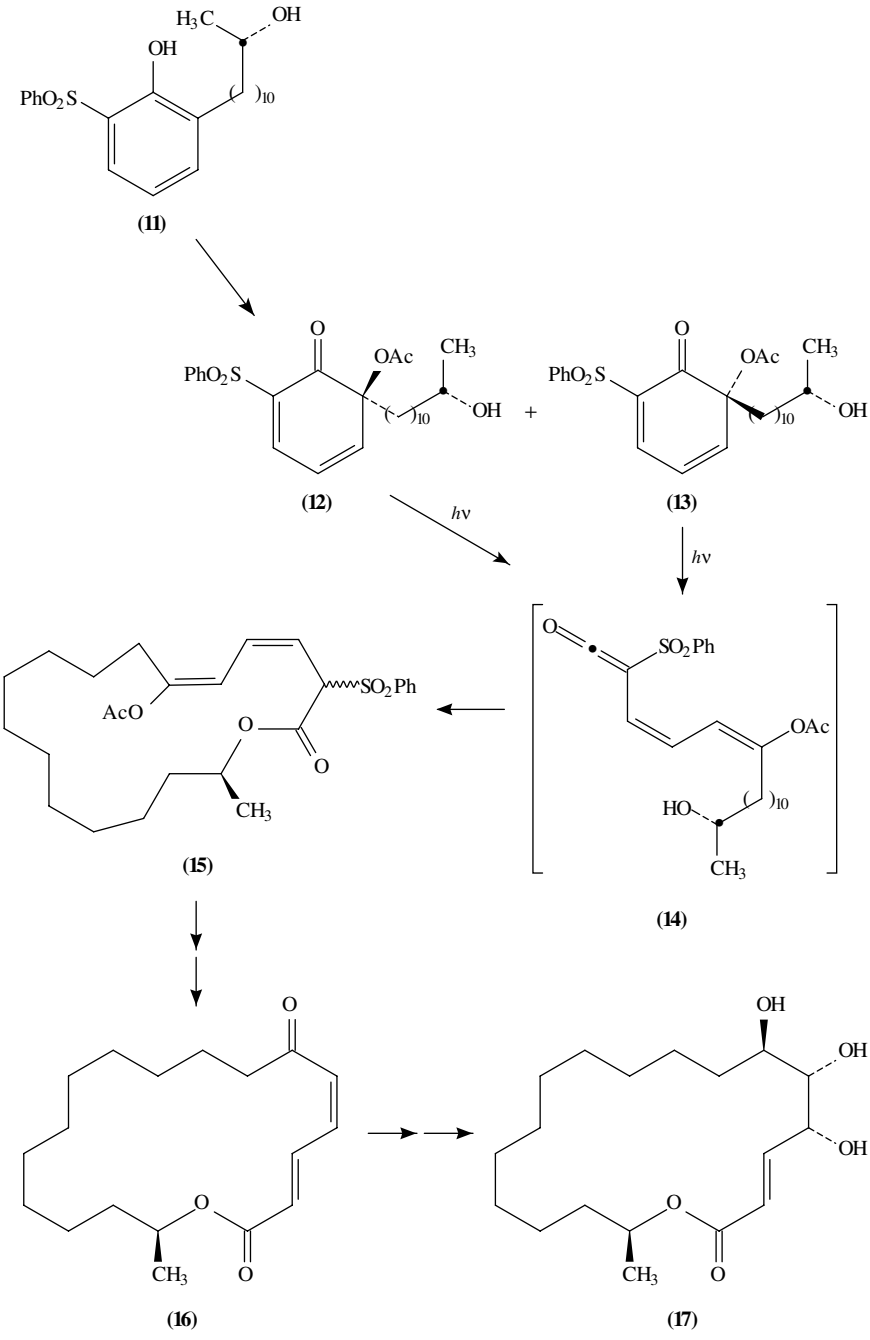
Quinkert and coworkers have also described a clever synthesis of the lichen macrolide (+)-aspicilin **(17)** using this ring opening/trapping strategy in which the trapping is done intramolecularly by a remote hydroxyl functionality, affording a macrolide product



SCHEME 2

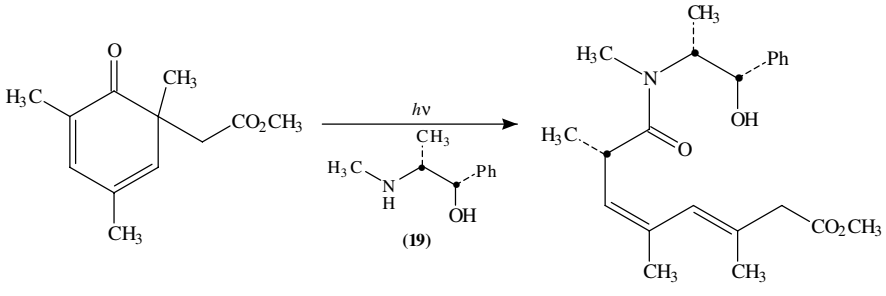
(Scheme 3)[10]. Indeed, independent photolysis of 2,4-cyclohexadien-1-ones **12** and **13** afforded the macrolides **15**. These reactions likely proceed via a common intermediate, in this case dienylketene **14**, which is trapped intramolecularly by the pendant hydroxyl group. Adjustment of the oxidation level and functional group interconversion then led efficiently to the desired macrolide **17**. The sulfonyl group was used for two reasons: first, to easily transform lactones **15** into dienyl lactones **16** needed for **17**, and secondly, to control the regiochemistry of the Wessely oxidation of phenolic precursor needed to produce the photolysis substrates **12** and **13**.

Schultz and Kulkarni have explored the possibilities of using this process in asymmetric synthesis by trapping the ketene generated from these photochemical ring-opening


H3C
OH
OH
PhO2S
)10
(11)
O
OAc
CH3
PhO2S
)10
OH
+
(12)
(13)
hν
hν
O
SO2Ph
OAc
HO
)10
CH3
(14)
AcO
SO2Ph
O
O
CH3
(15)
O
O
CH3
O
(16)
OH
OH
OH
O
CH3
O
(17)

SCHEME 3

reactions with a chiral, nonracemic amine or alcohol (Scheme 4)[11]. Preliminary studies indicated that irradiation of **18** in the presence of a chiral, nonracemic amine (or amino alcohol) led to only moderate yields of the amide or ester products. The best chiral modifier in this case is the (D)-ephedrine, **19**, which gave a *ca* 70:30 ratio of diastereomers. The authors did show, however, that this method is preparatively useful, as multigram quantities of optically pure **20** can be produced easily.



(18) **(19)** **(20)**

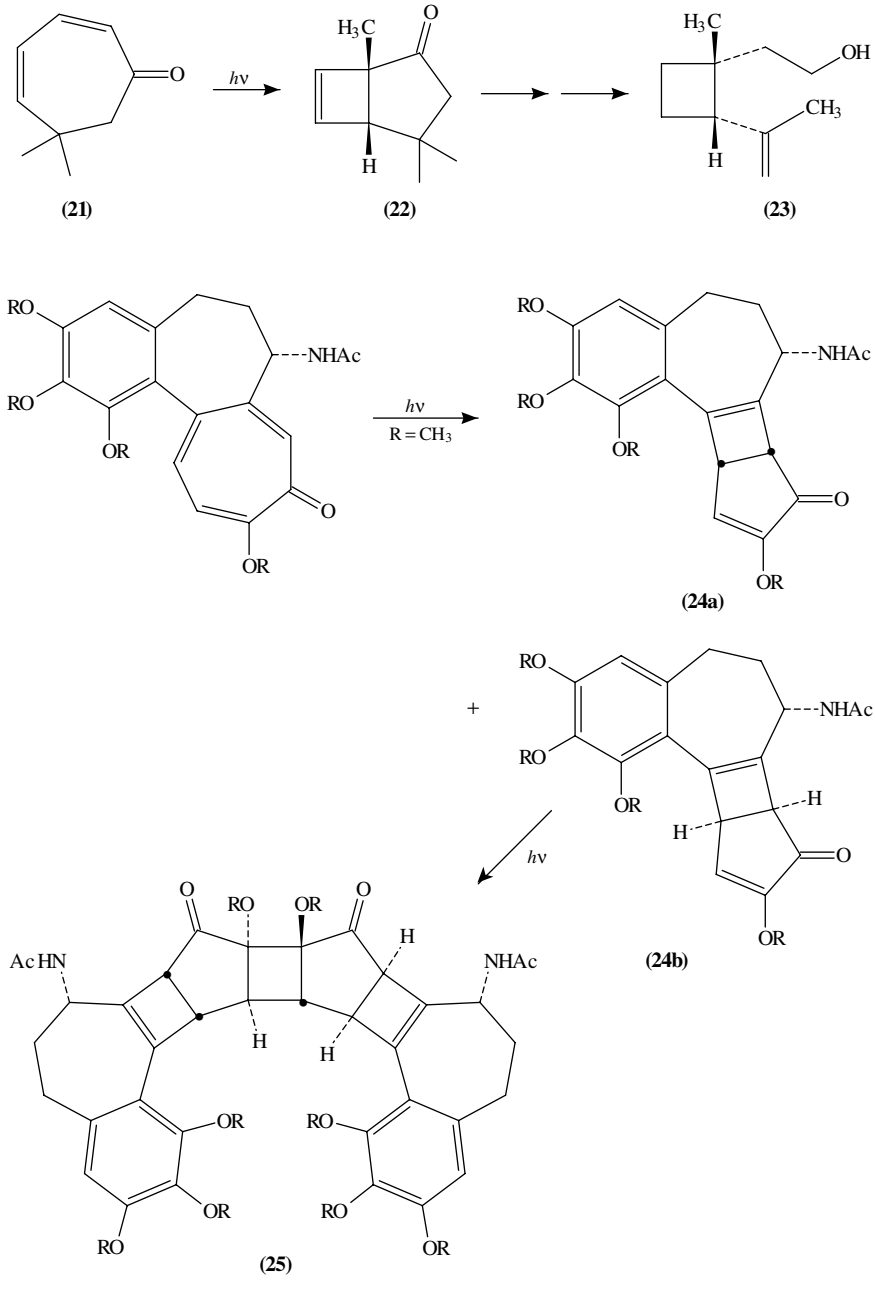
SCHEME 4

C. Electrocyclic Closure of Dienes and Trienes

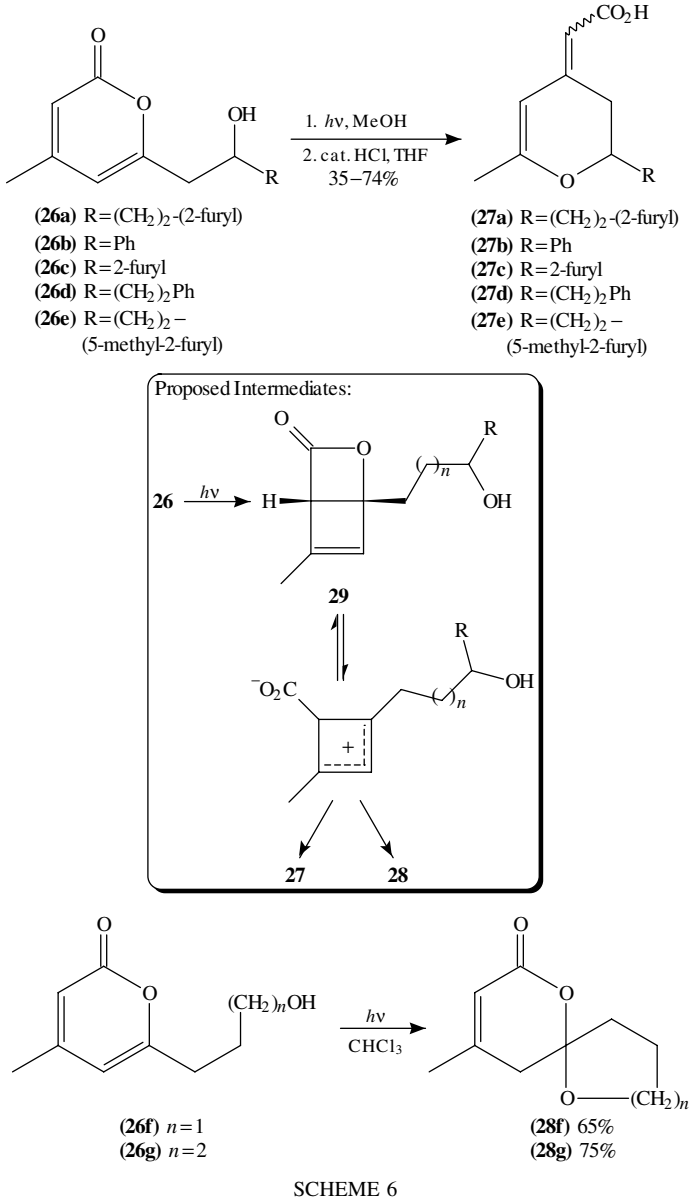
Electrocyclic closure of butadiene units encased within cycloheptane rings has been used to obtain bicyclo[3.2.0]heptene systems (Scheme 5)[12]. For example, irradiation of eucarvone **21** led to the formation of adduct **22** in 52% yield via a disrotatory ring closure[12a]. This adduct was used as a key intermediate in the synthesis of the pheromone grandisol, **23**, which proceeded in 20% overall yield from **22**. In their synthesis of α-lumicolchicine, Chapman and coworkers utilized a photochemically initiated four-electron disrotatory photocyclization of colchicine to produce β-lumicolchicine **24a** and its γ-isomer **24b** in a 2:1 ratio[12b]. These adducts were then converted, in a second photochemical step, to the *anti* head-to-head dimer α-lumicolchicine **25**.

In conjunction with studies probing [4 + 4]-photocycloaddition chemistry of 2-pyrones (*vide infra*), West and coworkers recently reported observations regarding alternative rearrangement pathways[13]. Irradiation of 6-hydroxyethylpyran-2-ones **26** furnished novel dihydropyrans **27** (Scheme 6). Although the details of the mechanism are not available, initial closure to bicyclic 'Dewar pyrone' **29** is considered to be a likely pathway[14]. When the length of the tether connecting the pendant alcohol to the 2-pyrone was increased, spirocyclic products **28** were formed instead.

The hexatriene/cyclohexadiene isomerization has been extensively studied and has been the topic of numerous reviews and monographs[15]; this section will attempt to deal only with applications of these reactions to synthesis, and in particular the use of these reactions for the synthesis of natural products. Much of the early work in this area was done by Havinga and coworkers during the course of their detailed work on the stereochemical consequences of the thermal and photochemical conversions in the vitamin D field[16]; this work provided much of the impetus for the development and elaboration of the Woodward–Hoffman rules (Scheme 7)[17]. The reversible photochemical ring opening of provitamin **30** to precalciferol **(31)** and the photochemical ring closure of **31** to lumisterol **32** can be explained by consecutive photochemically allowed conrotatory processes[16].


O
hν
H3C
O
H
H3C
OH
CH3
H
(21)
(22)
(23)
RO
RO
OR
NHAc
O
OR
hν
R = CH3
RO
RO
OR
NHAc
O
OR
(24a)
+
RO
RO
OR
NHAc
H
H
O
OR
(24b)
hν
O
RO
OR
O
H
AcHN
NHAc
H
H
OR
RO
OR
RO
RO
OR
(25)

SCHEME 5



(26a) R=$(CH_2)_2$-(2-furyl)
(26b) R=Ph
(26c) R=2-furyl
(26d) R=$(CH_2)_2$Ph
(26e) R=$(CH_2)_2$–(5-methyl-2-furyl)

(27a) R=$(CH_2)_2$-(2-furyl)
(27b) R=Ph
(27c) R=2-furyl
(27d) R=$(CH_2)_2$Ph
(27e) R=$(CH_2)_2$–(5-methyl-2-furyl)

29

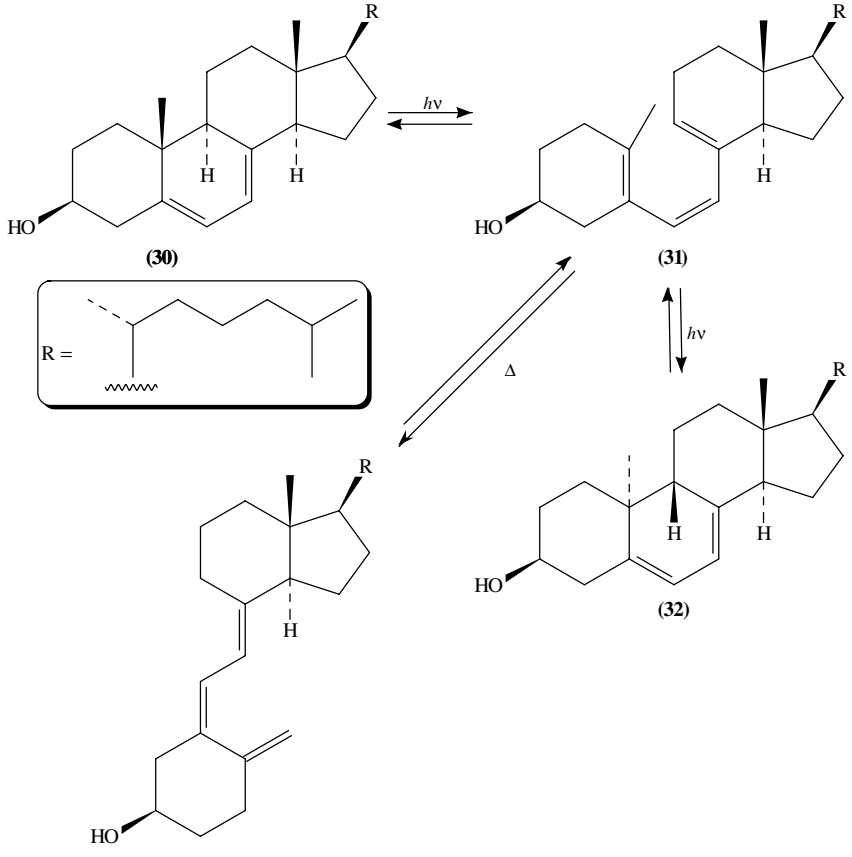
27 **28**

(26f) $n=1$
(26g) $n=2$

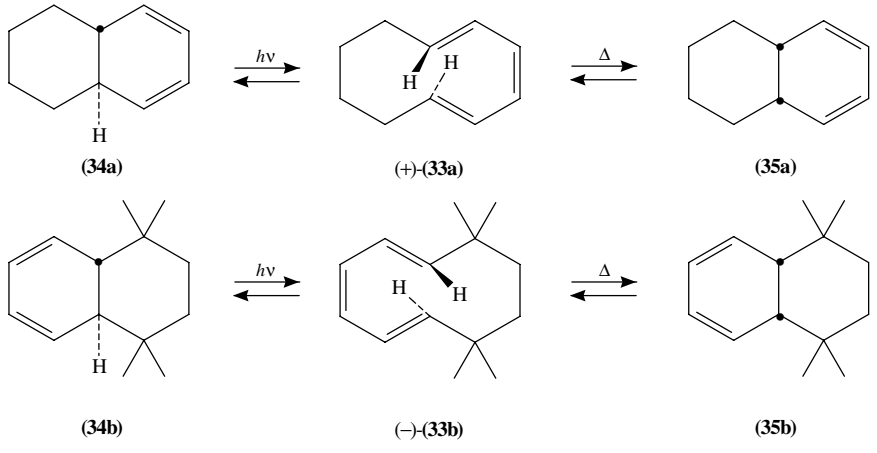
(28f) 65%
(28g) 75%

SCHEME 6

In an interesting illustration of these reactions, the two disymmetric trienes (+)-**33a** and (−)-**33b** were found to preserve their chirality upon photolysis at 193 K and provide cyclohexadienes **34a** and **34b**, respectively (Scheme 8)[18]. Upon warming above 205 K, however, they lose their chiral integrity by competitive disrotatory cyclization to the achiral dienes **35a** and **35b**. The thermal disrotatory closure to the *cis*-fused ring isomer is generally found to be extremely facile in these systems.

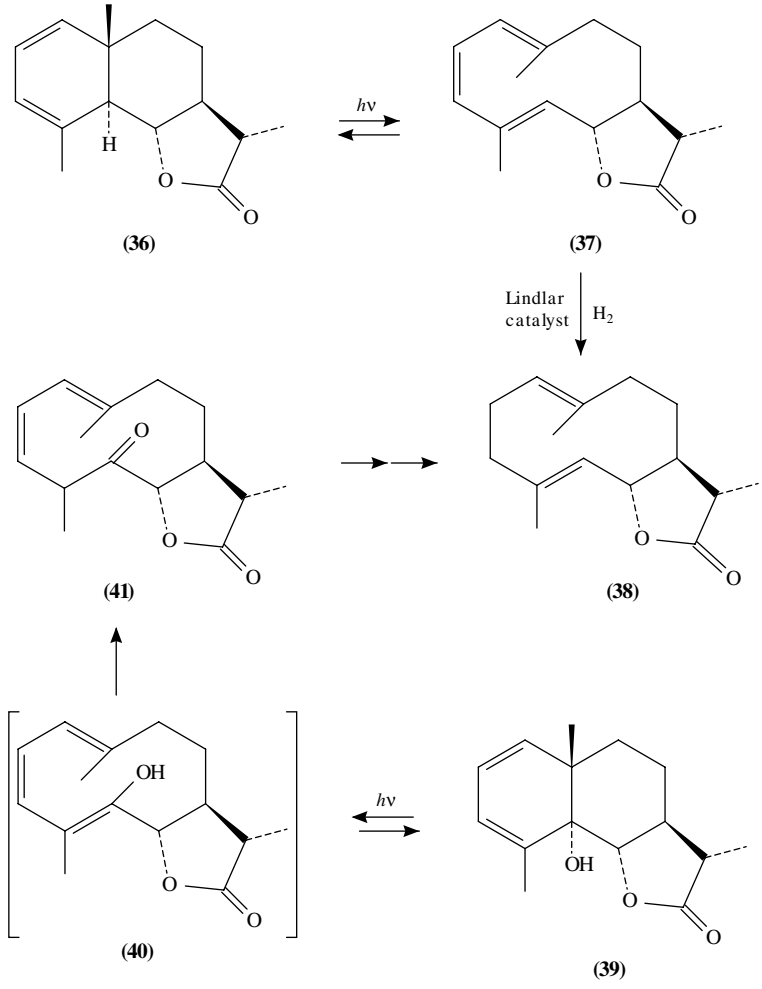


SCHEME 7



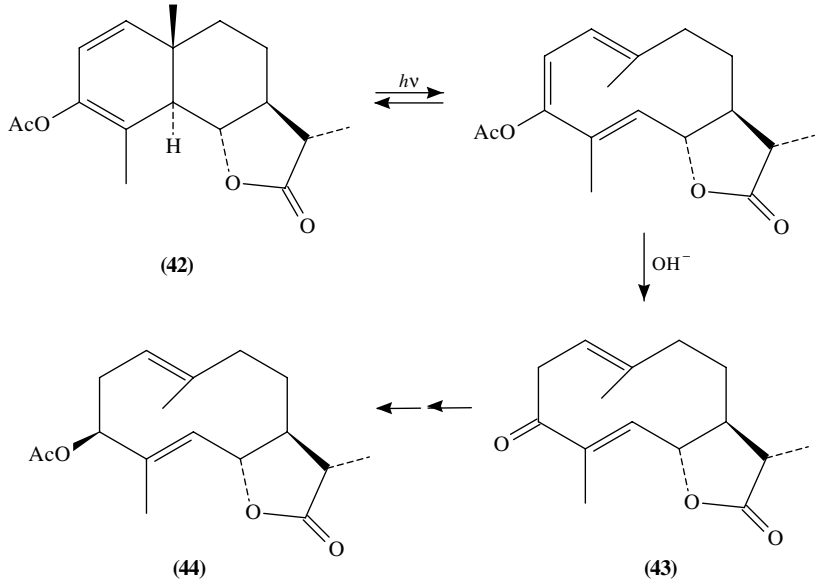
SCHEME 8

In one of the earliest applications of this type of process to complex molecule synthesis, Corey and Hortmann, in their synthesis of dihydrocostunolide **38**, found that photolysis of **36** afforded a photostationary state of **36** and **37** (Scheme 9)[19]. Hydrogenation of this mixture then gave **38**. A recent modification of this synthesis, which avoids the photostationary equilibrium between eudesmane **(36)** and germacrane **(37)** forms, was realized using a modified substrate, **39**[20]. Irradiation of **39** provided a 77% yield of a mixture of diastereomeric ketones **41**; these are produced via tautomerization of the intially produced trienol **40**. Dienone **41** was then easily converted to **38** via a series of conventional steps (Scheme 9).



SCHEME 9

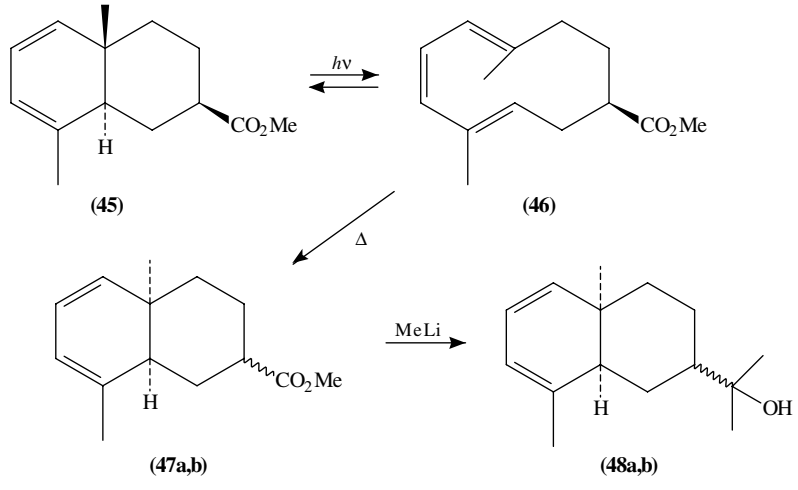
A similar strategy has been employed in a clever synthesis of the sesquiterpene dihydronovanin **(44)**[21]. Enol acetate **42** was irradiated in cold methanol to prevent thermal closure to the *cis*-fused system via a facile disrotatory electrocyclization (Scheme 10).



SCHEME 10

This was followed by immediate saponification of the enol ester to afford dieneone **43**, which could be easily elaborated to **44**.

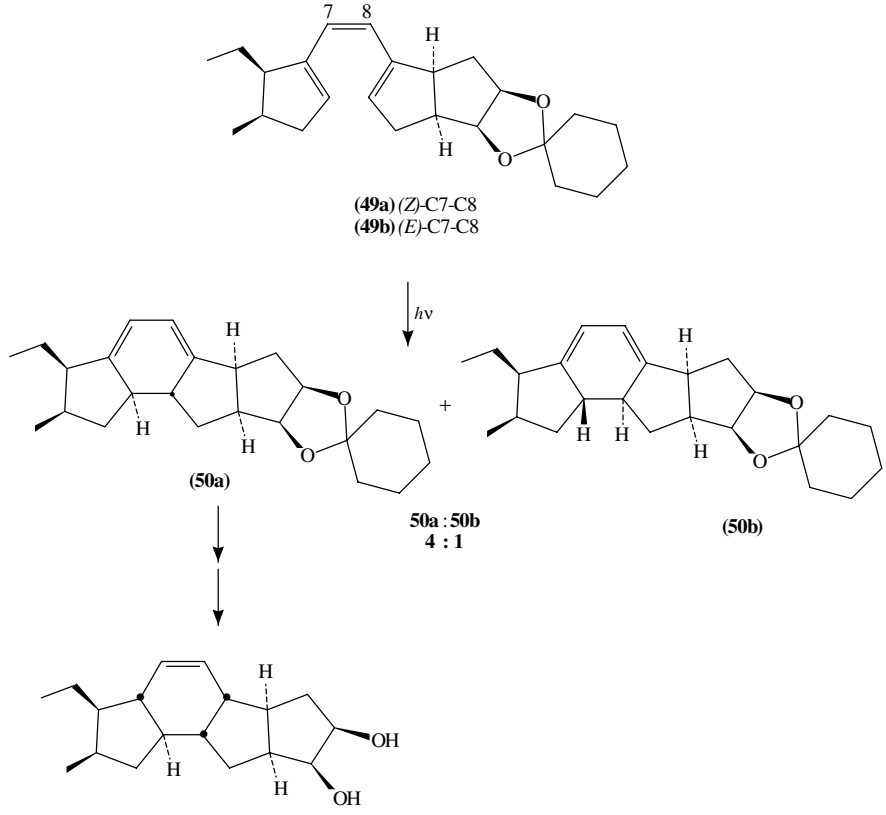
The *trans*–*cis* isomerization process observed in the eudesmane/germacrane ring system has been utilized for the synthesis of the *cis*-fused sesquiterpene occidentalol, **48a**, and its 7-epi isomer, **48b** (Scheme 11)[22]. Photolysis of the *trans*-fused diene **45** at −78 °C afforded triene **46**, which upon warming underwent disrotatory electrocyclization to give **47a** and **47b** as a 1:2 mixture of diastereomers. Apparently, the carboalkoxy group imparts



SCHEME 11

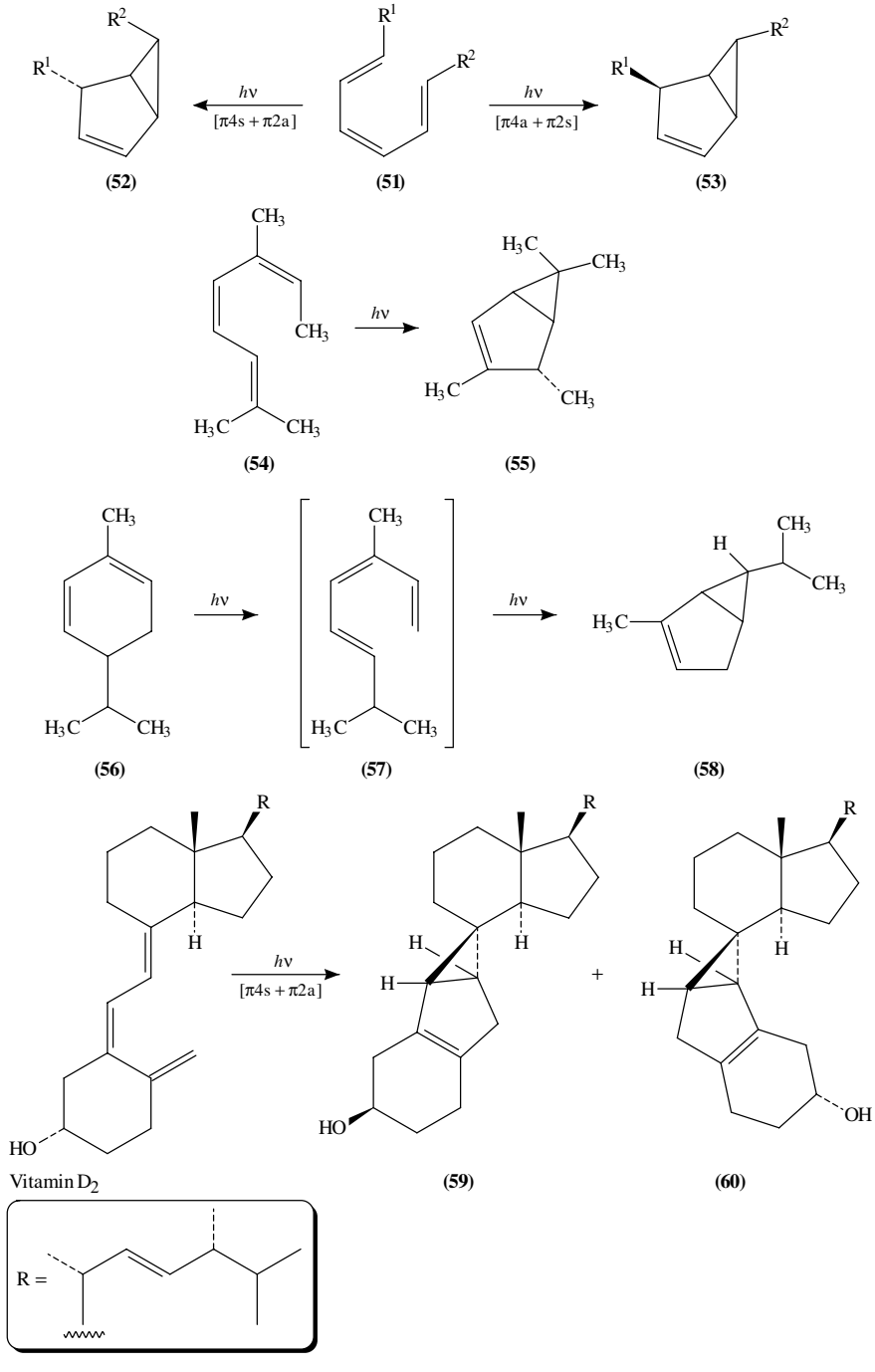
little stereoinduction in the electrocyclization of triene **46**. These diastereomers could be separated and they reacted with methyllithium to afford **48a** and **48b** in good yield.

Whitesell and Minton have reported an ingenous synthesis of the antimicrobial and amoebicidal agent ikarugamycin which utilizes a photochemically initiated conrotatory electrocyclization as its critical step (Scheme 12)[23]. These workers found that photolysis of a *ca* 2:1 mixture of the trienes **49a** and **49b** led to a 4:1 mixture of the two possible conrotatory closure products **50a** and **50b** in near-quantitative yield. This product ratio most likely reflects the conformational bias in the ground state of the (*Z*)-triene **49a**, as it is likely that one conformer reacts to give **50a** while the other conformer reacts to give **50b**. Triene **49b** is assumed to photochemically equilibrate with **49a**, followed by conversion to **50a** and **50b**. Glycol **50a** functioned as a key intermediate in the synthesis of the target compound.



SCHEME 12

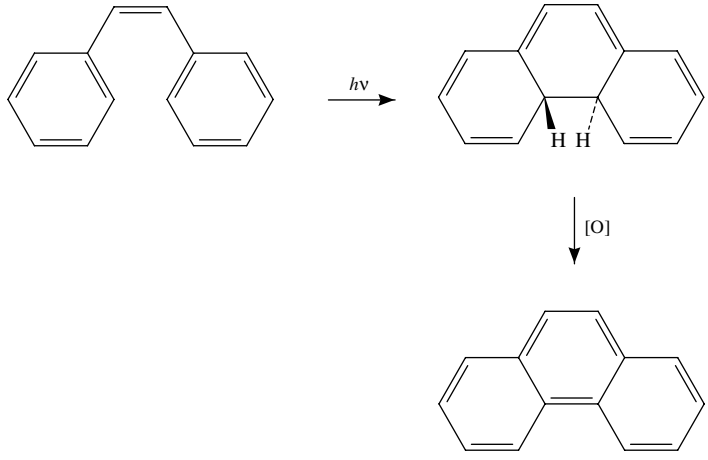
Irradiation of conjugated trienes such as **51** can also lead to the formation of bicyclo[3.1.0]hexanes (**52** or **53**) via a process that can be considered as a formal [π4s + π2a] or [π4a + π2s] cycloaddition (Scheme 13)[17,24]. Thus, triene **51** affords **52** and **53** via symmetry-allowed processes[17]. For example, allocimene **54** gave **55** (with other photoproducts)[25], while α-phellandrene **(56)** gave **57**, which upon further irradiation afforded **58**[26]. These reactions would be of little interest were it not for the observation


R2
R1
hν
[π4s + π2a]
R1
R2
hν
[π4a + π2s]
R1
R2
(52)
(51)
(53)
CH3
CH3
H3C
CH3
hν
H3C
CH3
H3C
CH3
(54)
(55)
CH3
hν
CH3
H3C
CH3
hν
H
CH3
CH3
H3C
(56)
(57)
(58)
R
H
hν
[π4s + π2a]
H
H
H
HO
+
H
H
H
OH
Vitamin D2
(59)
(60)
R =

SCHEME 13

that upon irradiation Vitamin D_2 (calciferol) undergoes photocyclization to afford suprasterols **59** and **60**[27]. The formation of these adducts, and their stereochemistry, can be nicely rationalized by a [π4s + π2a] process.

The photocyclization of stilbenes to phenanthrene derivatives and related conjugated arylalkenes to polycyclic aromatic derivatives constitutes one of the most widely used applications of organic photochemistry to organic synthesis, owing primarily to the plethora of natural products containing a phenanthrene unit[28]. This reaction, in accordance with the accepted mechanism, starts from the excited state of the stilbene, which undergoes a six-electron, conrotatory electrocyclization to afford the dihydrophenanthrene (Scheme 14). In the majority of cases, however, this dihydrophenanthrene is unstable and undergoes either oxidation to the aromatic system (in the presence of oxygen or an oxidant such as iodine) or, less commonly, converts to the isomeric 9,10-dihydrophenanthrene by a hydrogen shift. Though somewhat outside the scope of the present discussion, this type of cyclization has been utilized effectively for the synthesis of a wide variety of complex systems; the reader is referred to numerous excellent review articles for further discussions of this subject[28].

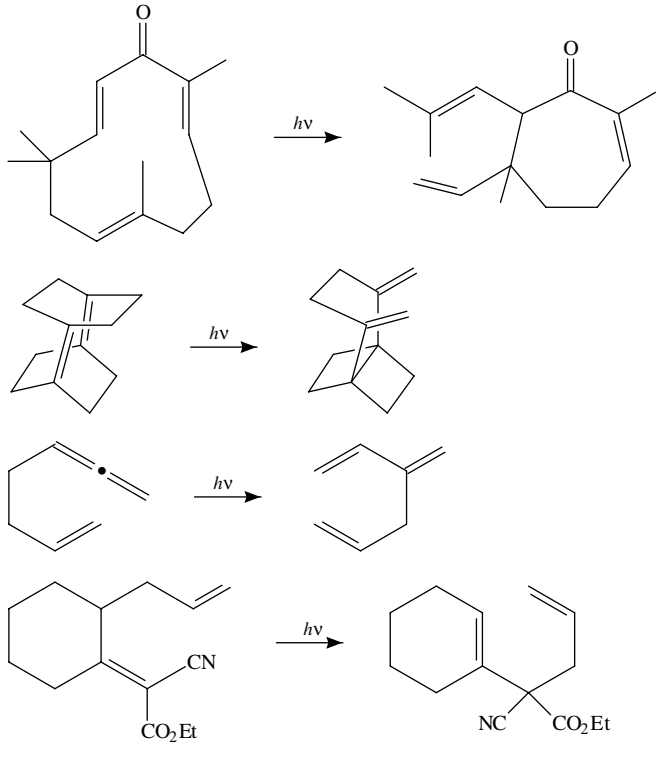


SCHEME 14

D. Sigmatropic Rearrangements

The Cope and Claisen rearrangements are the most widely utilized sigmatropic rearrangements from the standpoint of complex molecule synthesis. It has been found that the Cope rearrangement is frequently subject to great rate enhancements in the presence of catalysts; these most frequently have been either metal salts or acids[29]. However, there are several examples of the use of light to catalyze the [3,3] sigmatropic rearrangement of a 1,5-diene[30]. Some of these are shown in Scheme 15. The examples reported to date are a fairly random collection and it is not clear what factors facilitate the observed photochemical rearrangements, but it should be noted that in at least one case (**61** to **62**) photolysis reverses the normal equilibrium[30d].

In what is one of the few examples of utilization of a higher order sigmatropic hydrogen shift in the synthesis of complex molecules, Eschenmoser, in studies directed toward the synthesis of Vitamin B_{12}, found that an antarafacial [1,16] H-shift could be utilized to effect closure of secocorrin **63** to corrin **65** (Scheme 16)[31]. An intermediate biradical



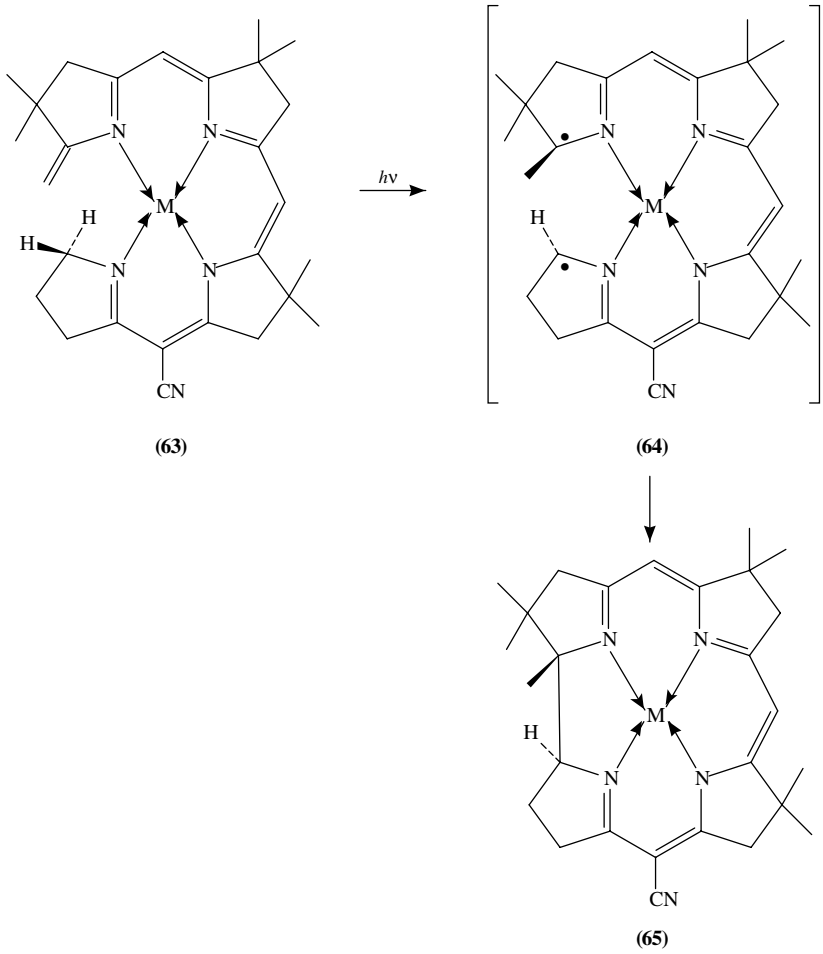
(61) **(62)**

SCHEME 15

64 is formed following the photochemically allowed H-shift. This then undergoes an antarafacial electrocyclic closure to form the desired product **65**. The process has been found to be dependent upon the metal ion used, as reaction occurred with Li, Na, Mg, Ca, Zn, Cd, Pd or Pt ion present but failed to proceed with Co, Ni or Cu ion as the chelating agent.

E. Di-π-methane Rearrangements

While not formally conjugated, the electronic nature of 1,4-dienes is such that they participate in a wide variety of photochemical reactions and have a rich photochemical history. In particular, the photochemical rearrangement of a 1,4-diene to a vinylcyclopropane (**66** to **67**), the so-called di-π-methane (DPM) rearrangement, is one of the most extensively studied photochemical rearrangements (Scheme 17)[32]. This process could be viewed as a formal 1,2-shift of a vinyl group with inversion of configuration of the migrating carbon atom[32a]. In reality, the mechanism is quite complex and has been investigated in exhaustive detail; the reader is referred to other articles for a detailed discussion of these aspects of this reaction. While this rearrangement has been utilized for the synthesis of a wide variety of unusual nonnaturally occurring ring systems, in particular the semibullvalenes and related compounds (e.g. **68** to **69**)[33], its use in the synthesis of natural products has been quite limited. In fact, it is quite surprising, given the level at which the di-π-methane rearrangement has been studied and is understood, that this reaction has not



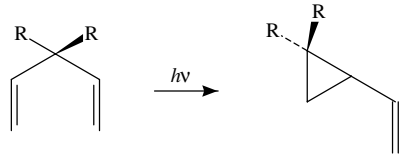
(63) **(64)** **(65)**

SCHEME 16

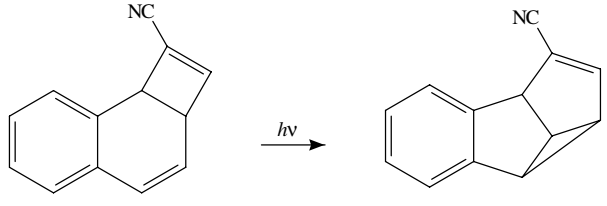
been utilized more in complex molecule synthesis, especially given that the products of this rearrangement, namely vinylcyclopropanes, are quite valuable synthetic commodities[34].

The first reported use of the DPM rearrangement in natural product synthesis can be found in the synthesis of methyl chrysanthemate, **71**, reported by Pattenden and Whybrow (Scheme 18)[35]. This is produced directly by photolysis of 1,4-diene **70**. While it should be noted that this reaction gave **71** in only 12% yield, it did furnish the desired product in a single step, with the correct relative stereochemistry. Bullivant and Pattenden also used a DPM rearrangement to form an advanced intermediate in the synthesis of the dideoxy derivative of the sesquiterpene taylorione, **74**[36]. Irradiation of **72** afforded **73** in 45% isolated yield; this was then simply converted to **74** using standard transformations.

Armesto, Horspool and coworkers have extensively studied the related rearrangement of β,γ-unsaturated imine derivatives, the so-called aza-di-π-methane rearrangement[37]. A particularly interesting example is seen by the rearrangement of **75** to **76** (Scheme 19). Adduct **76** furnished chrysanthemic acid following a simple series of steps. It has been

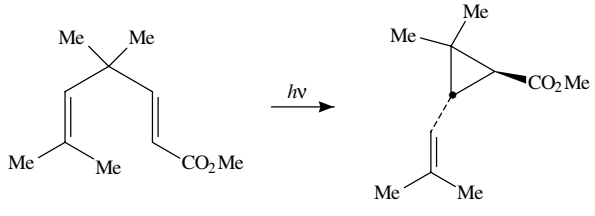


(66) **(67)**

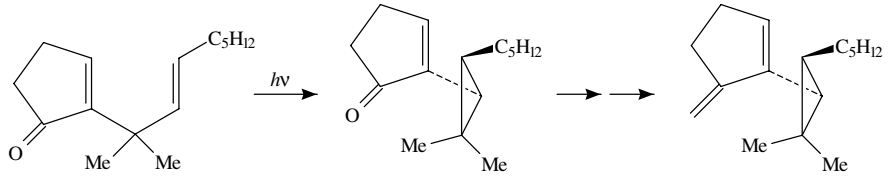


(68) **(69)**

SCHEME 17



(70) **(71)**

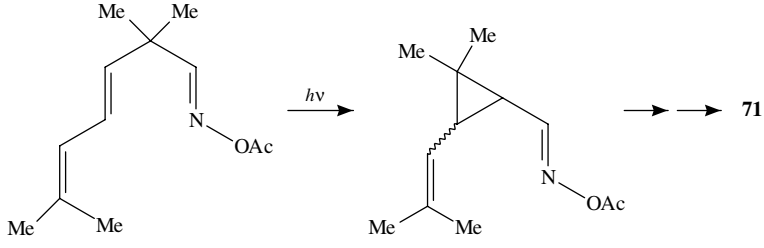


(72) **(73)** **(74)**

SCHEME 18

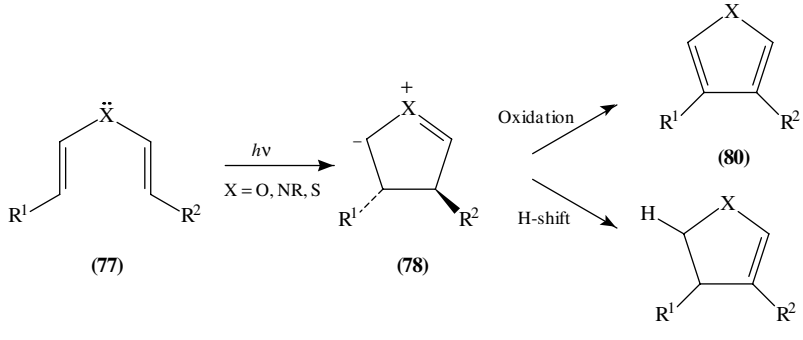
found that, in general, oxime derivatives undergo this rearrangement much more efficiently than do the corresponding imine or hydrazone derivatives.

Electrocyclization of 1,4-dienes is an efficient process when a heteroatom with a lone pair of electrons is placed in the 3-position, as in **77** (Scheme 20)[38]. Photoexcitation of these systems generally results in efficient formation of a C−C bond via 6e conrotatory cyclization to afford the ylide **78**. These reactive intermediates can undergo a variety of processes, including H-transfer (via a suprafacial 1,4-H transfer) to **79** or oxidation to **80**. In a spectacular example of reaction, and the potential it holds for complex molecule synthesis, Dittami and coworkers found that the zwitterion formed by photolysis of divinyl ether **81** could be efficiently trapped in an intramolecular [3 + 2] cycloaddition by the

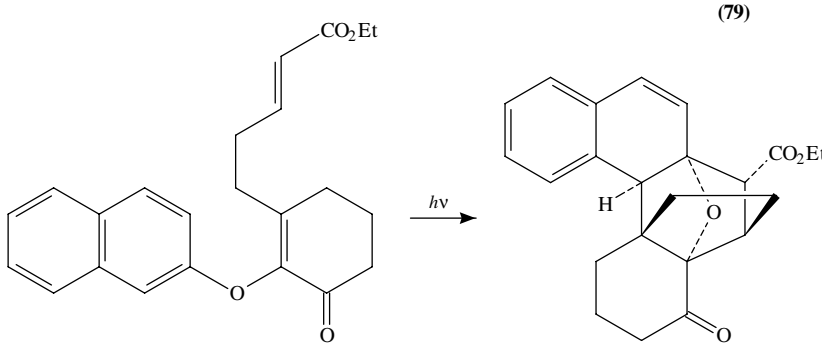


(75) **(76)**

SCHEME 19



(77) **(78)** **(80)** **(79)**



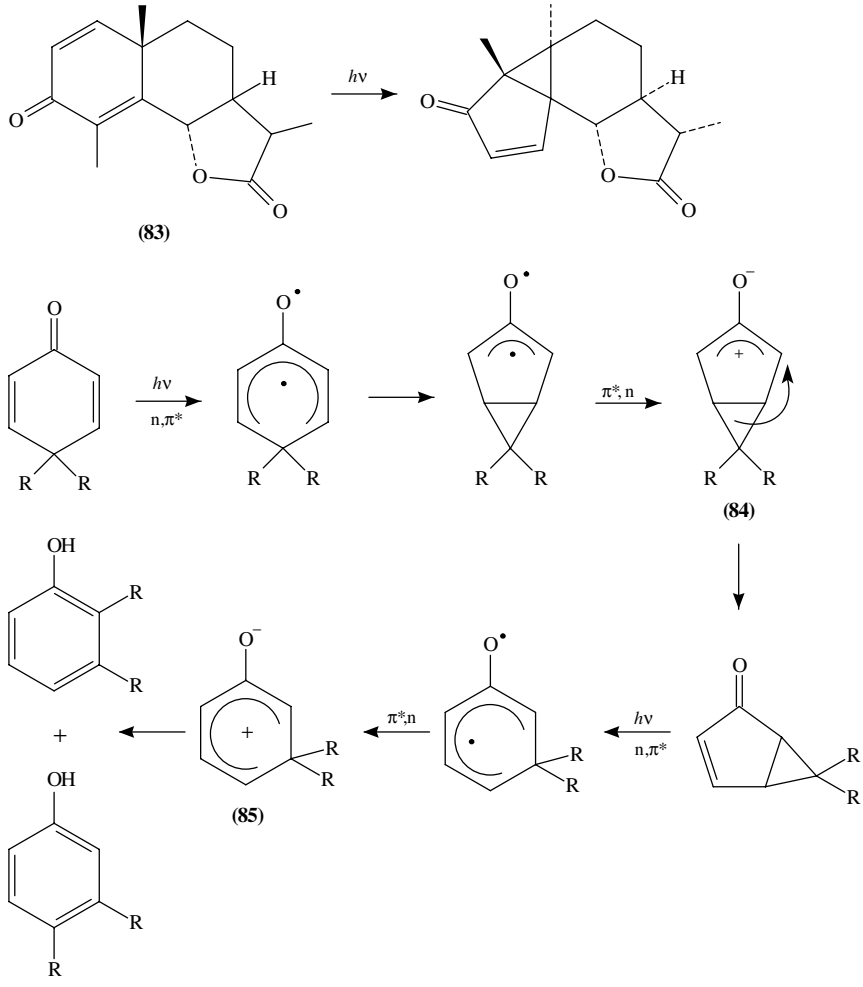
(81) **(82)**

SCHEME 20

pendant acrylate to afford **82** in 85% yield[39]. In general, these electrocyclizations are quite efficient and have been extensively utilized for the synthesis of a variety of complex molecules.

F. Rearrangements of Cross-conjugated Dienones

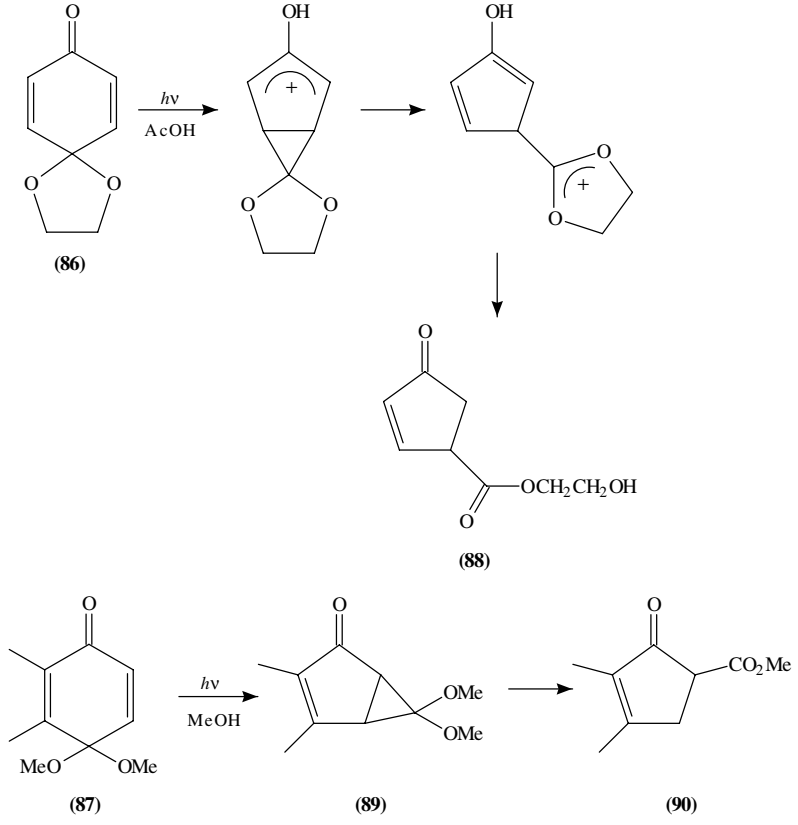
The mechanistic photochemistry of cross-conjugated 2,5-cyclohexadienones has been comprehensively examined (Scheme 21). The photochemical isomerization of the



SCHEME 21

sesquiterpene santonin **83** was first noted more than a century ago. It was later found that these systems undergo photochemical rearrangement to 'lumiketones', with a net extrusion of C-4 and concomitant formation of a new cyclopropane ring[40]. The generally accepted mechanism for this rearrangement[41,42] involves singlet n,π^* excitation, intersystem crossing to the longer-lived triplet state, bonding of the β-carbons of the dienone system, electron demotion to a high-energy zwitterionic ground state and thermal [1,4]-rearrangement of the bicyclic zwitterion. Irradiation of the primary photoproduct gives phenolic secondary photoproducts. This appears to occur via fission of the ring-fusing cyclopropane bond to give a second, conjugated oxyallyl zwitterion **85**, which then suffers [1,2]-migration of one of the substituents on the quaternary carbon. Evidence for 1,5-zwitterion **85** includes formation of the same products following its independent generation under non-photochemical conditions[43].

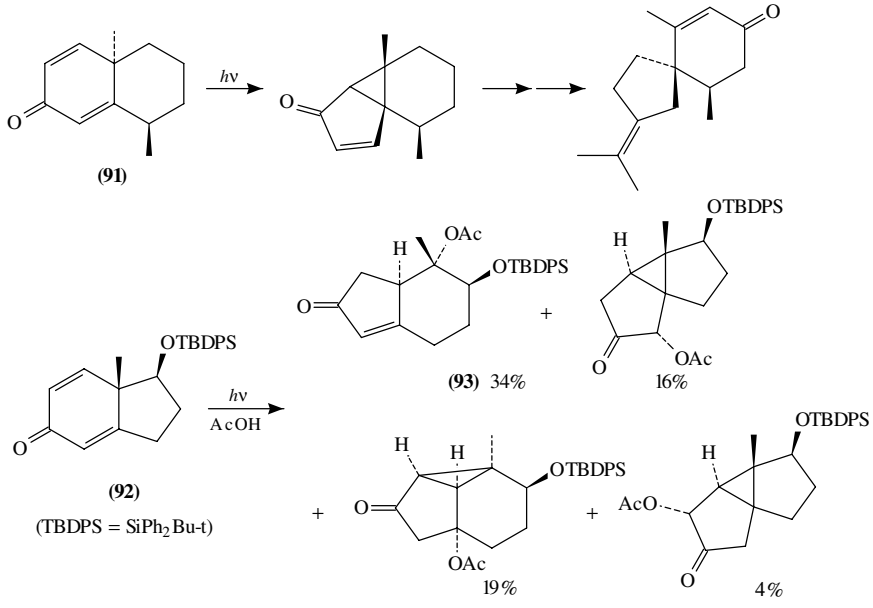
With the considerable degree of bond reorganization inherent in this rearrangement, it is not surprising that several laboratories have sought to exploit dienone photochemistry in synthesis. Simple, readily accessible quinone monoketals **86** and **87**, which possess the cross-conjugated dienone chomophore, have been examined (Scheme 22)[44]. Upon irradiation, substrate **86** rearranged via the bicyclic oxyallyl intermediate to give the ethylene glycol monoester **88** of cyclopentenone-4-carboxylic acid[44a]. The presence of the electron-rich ketal unit allows for facile fragmentation of the cyclopropane ring of the intermediate. On the other hand, the corresponding dimethyl ketal **87** underwent photochemical conversion to 5-methoxycarbonylcyclopentenones **90**, suggesting the intermediacy of dimethoxycyclopropane **89**[44b].



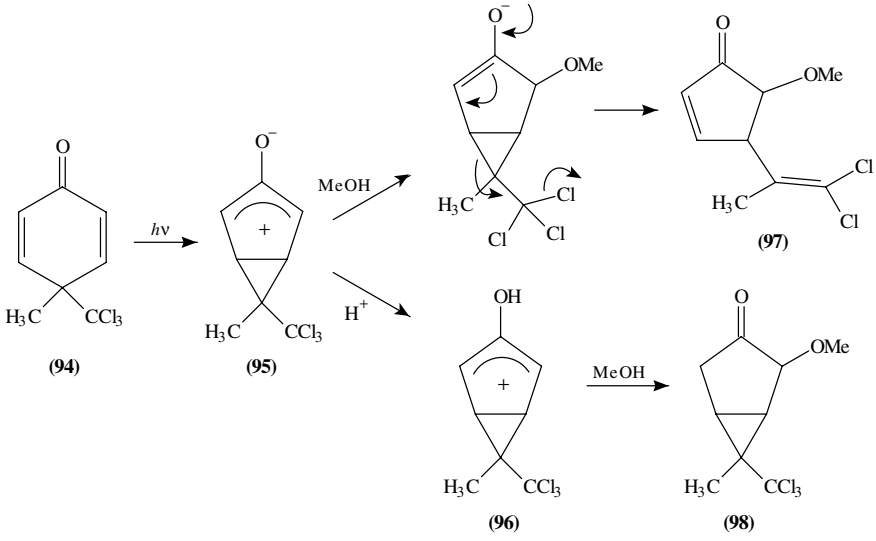
(86) **(88)** **(87)** **(89)** **(90)**

SCHEME 22

In the 1960s, Kropp showed that fused bicyclic dienones structurally related to santonin could potentially serve as synthetically useful precursors to either spirocyclic skeletons or hydroazulenones[45]. One of these cases, **91**, was successfully used by Marshall and Johnson as the starting point in an elegant synthesis of the spirocyclic sesquiterpene β-vetivone (Scheme 23)[46]. More recently, a variety of bicyclic cyclohexadienones have been studied by Caine and coworkers. For example, bicyclic dienone **92** could be photochemically rearranged to the oxygenated bicyclo[4.3.0]nonenone system **93**, along with other rearrangement products, via acetic acid solvolysis of the cyclopropyl ketone intermediate[47].

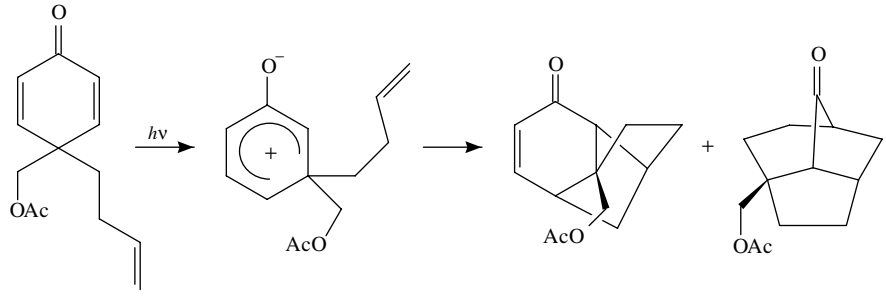


SCHEME 23

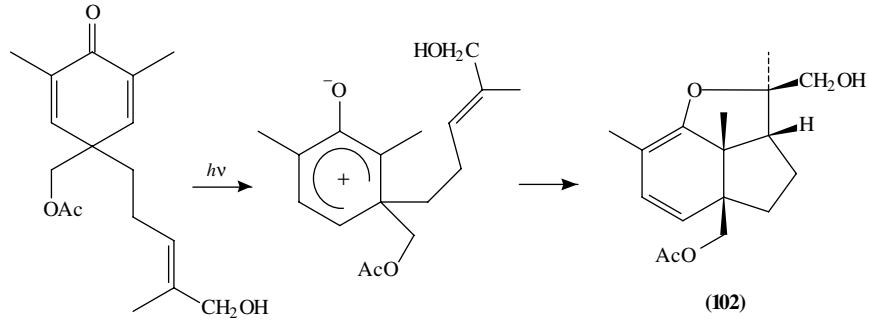


SCHEME 24

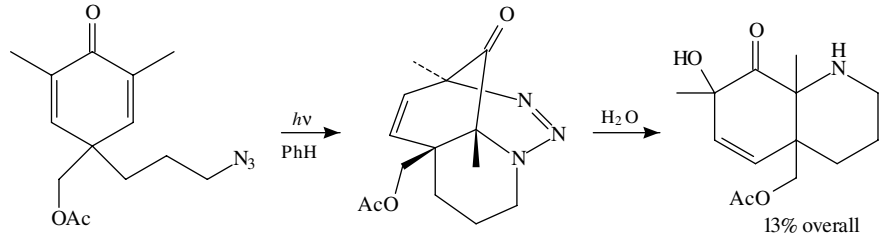
Direct interception of the initially formed bicyclic oxyallyl zwitterion derived from cyclohexadienones is difficult, due to its facile rearrangement to cyclopropyl ketone. One notable exception is the observation that 4-trichloromethyl-substituted dienone **94** gave solvent adduct **97** when irradiated in methanol, and both **97** and **98** upon irradiation in acidic methanol (Scheme 24)[48]. It was proposed that **97** arises either from a facile



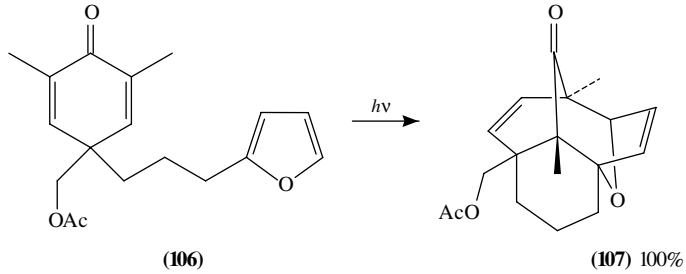
(99a) **(100)** **(101)**



(99b) **(102)**



(103) **(104)** **(105)** 13% overall



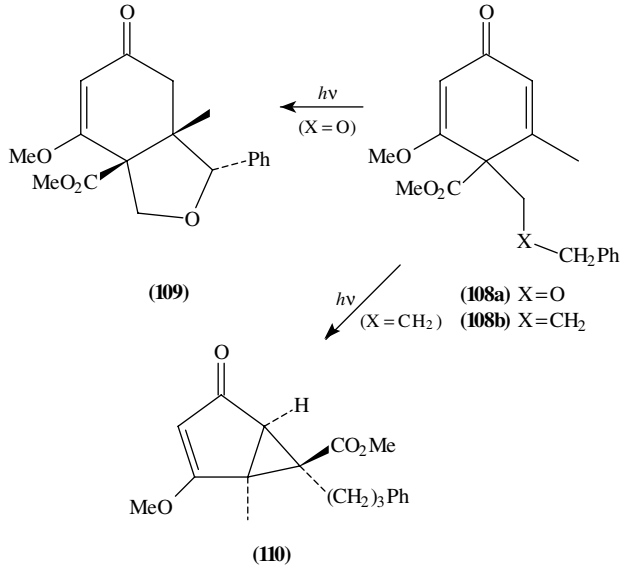
(106) **(107)** 100%

SCHEME 25

fragmentation pathway available to the zwitterion **95**, or by solvent capture of **95** followed by fragmentation. Irradiation in an acidic medium would likely involve hydroxyallyl cation **96**, which would undergo solvent capture without fragmentation to give **98**.

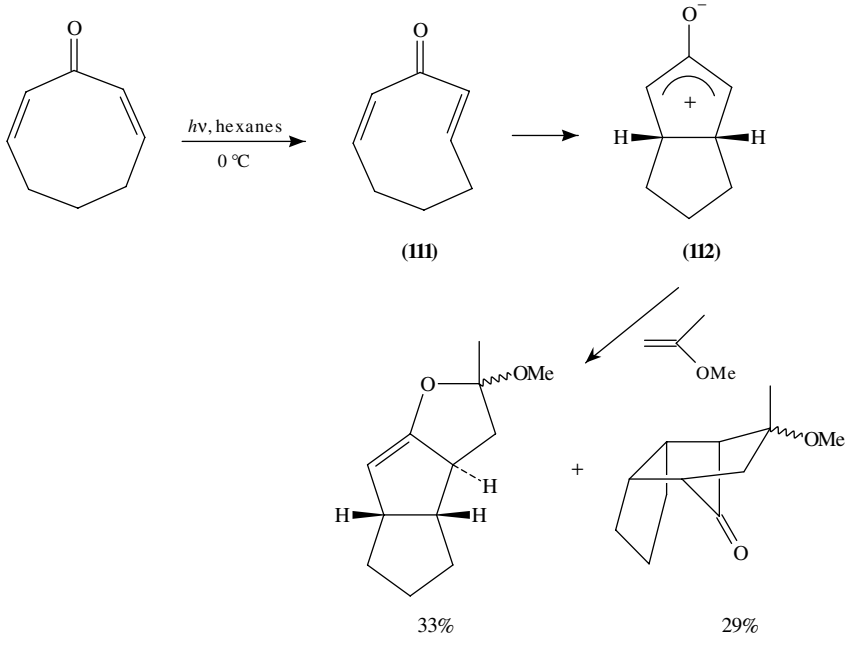
Given the typically rapid rearrangement of the first zwitterion, Schultz and coworkers have focused on trapping processes involving the 1,5-zwitterion arising from secondary photochemistry of the initially formed cyclopropyl ketone (Scheme 25)[49]. Pendant alkenes, as exemplified by substrates **99a** and **99b**, can intercept the zwitterion in a variety of modes, leading to both bridged and fused polycyclic products **100–102**[49c]. Formal 3 + 2 cycloadducts **101** and **102** almost certainly arise from a stepwise pathway with initial cationic cyclization, followed by ring closure with either C−O or C−C bond formation. Pendant 4π traps can also be used to capture the zwitterion in a concerted cycloaddition process. For example, azide **103** could be converted to the highly functionalized triazine **104**, which underwent an unusual, water-mediated loss of dinitrogen to furnish hexahydroquinolone **105**[49a]. Likewise, furan-containing substrate **106** gave [4 + 3]-adduct **107** in excellent yield.

More recently, Schultz and coworkers have reported competing hydrogen abstraction chemistry for dienone substrates containing a 4-alkoxymethylene substituent[50]. For example, benzyl ether **108a** was efficiently converted into bicyclic ether **109** as a single diastereomer (Scheme 26). This presumably proceeds through transfer of a benzylic hydrogen to the α-position of the excited dienone, followed by collapse of the resulting biradical. In contrast, dienone **108b**, containing an all-carbon side-chain, underwent typical dienone photochemistry to produce **110**.



SCHEME 26

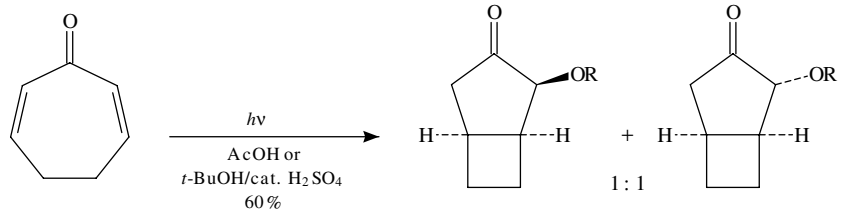
Analogous olefin trapping chemistry employing 2,7-cyclooctadienone has been investigated[51]. With this substrate, the oxyallyl zwitterion **112** could be intercepted intermolecularly with simple alkenes in a (presumably stepwise) 3 + 2 manner (Scheme 27). Importantly, intermediate **112** differs from 2,5-cyclohexadienone-derived zwitterions in terms of its lack of a facile rearrangement pathway. An interesting side-issue



(111) **(112)**

33% 29%

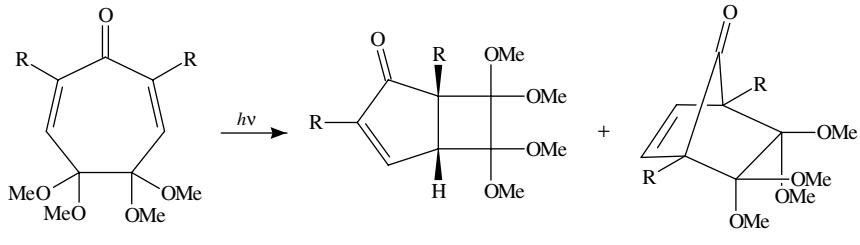
SCHEME 27



(113)

(114a) **R**=Ac
(114b) R=*t*-Bu

(115a) R=Ac
(115b) R=*t*-Bu



47 – 50% 4 – 10%

(116a) R=H
(116b) R=Me
(116c) R=Pr

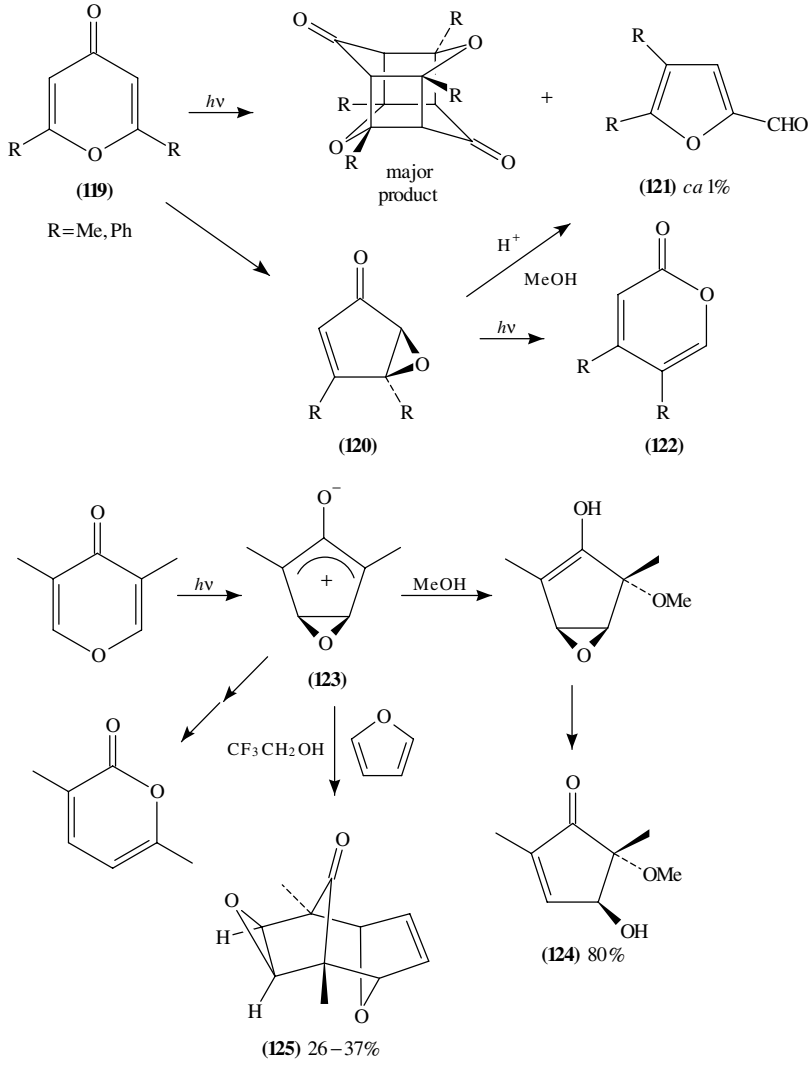
(117a) R=H
(117b) R=Me
(117c) R=Pr

(118a) R=H
(118b) R=Me
(118c) R=Pr

SCHEME 28

concerns the mechanism by which **112** is generated, which may differ from the pathway described above (Scheme 21). The authors report evidence for the prior formation of a short-lived, ground-state intermediate at low temperature, which then rearranges to **112** upon warming, and propose highly strained *E*,*Z*-dienone **111** as a candidate for this intermediate.

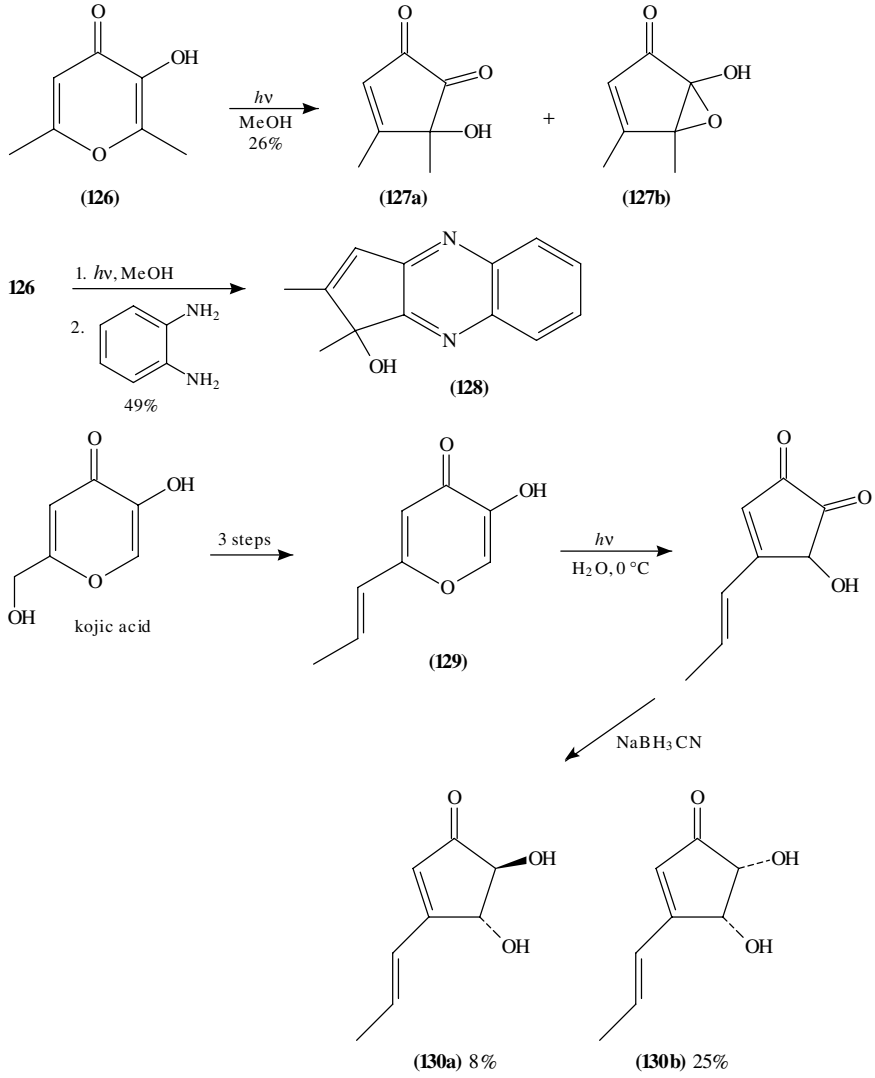
The analogous 2,6-cycloheptadien-1-ones display zwitterion-derived reactivity as well[52,53]. For example, the parent compound **113**, upon irradiation in either acetic acid or *t*-butanol, gave diastereomeric solvent adducts **114** and **115** (Scheme 28)[52a]. On the other hand, tetramethoxy derivatives **116** furnished rearranged products **117**, which are equivalent to the cyclopropyl ketone 1,4-shift products seen with cyclohexadienones[52b].



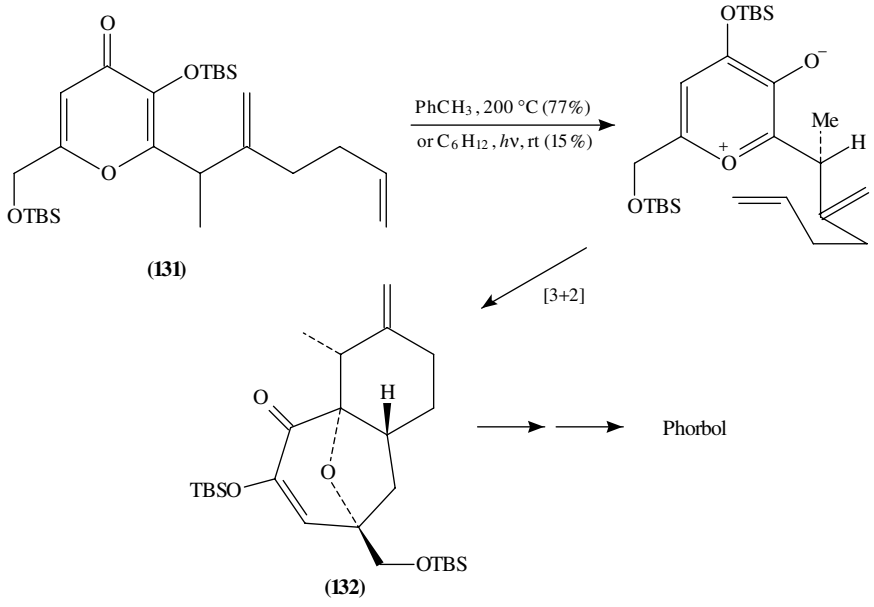
SCHEME 29

In addition to **117**, varying amounts of 7-norbornenones **118** were also isolated, apparently resulting from the 1,3-shift of **117**.

Pyran-4-ones bear an obvious structural similarity to the all-carbon cyclohexadienones discussed above. However, the original studies of their photochemical behavior revealed only dimerization processes to produce a cage product resulting from two successive head-to-tail [2 + 2]-photocycloadditions (Scheme 29)[54]. Much later, small amounts of substituted furfural **121** were observed during the irradiation of **119**[55a]. It was speculated that **121** could arise from bicyclic epoxide **120**, an intermediate analogous to those formed in cyclohexadienone photochemistry. Subsequent reports noted that further irradiation of



SCHEME 30



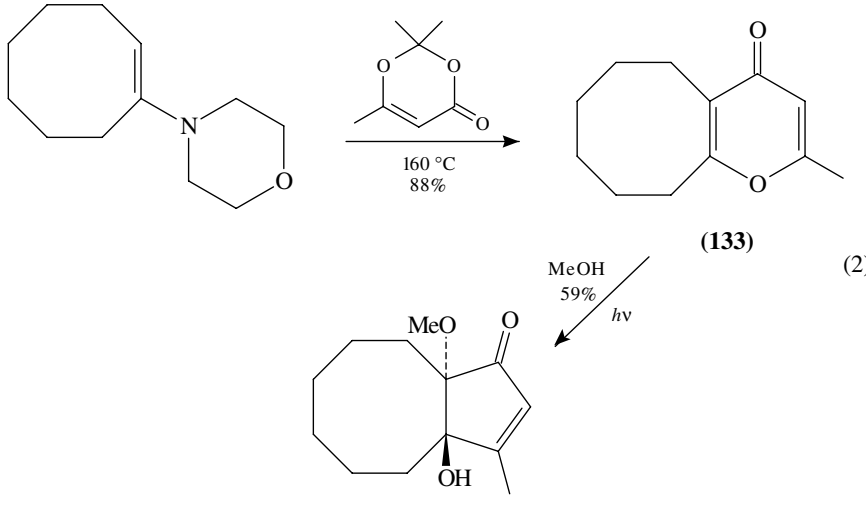
SCHEME 30. (*continued*)

120 led to 2-pyrone **122**, while exposure of **120** to acidic methanol furnished **121**[55b,c]. The photochemical behavior of 4-pyrones in dilute solutions of polar solvents has been examined in detail[56–58]. Rearrangement from 4- to 2-pyrones was found to be a major pathway, and the disposition of the ring substituents suggested the intermediacy of bicyclic zwitterion **123**. The isolation of solvent adducts **124** provided strong evidence for this intermediate. In addition, irradiation in the presence of excess furan led to photoadduct **125**, via a thermally allowed [4 + 3]-cycloaddition of the oxyallyl zwitterion and the diene[58]. Analogous rearrangement of 4-hydroxypyrylium ions to 2-hydroxypyrylium salts was also reported[59].

Substitution with a 3-hydroxy group permits an alternative rearrangement pathway for the zwitterion via deprotonation (Scheme 30). For example, 2,6-dimethyl-3-hydroxy-4-pyrone **126** was converted photochemically to a mixture of hydroxy dione **127a** and epoxy hemiketal **127b**[60a]. Irradiation in the presence of phenylenediamine allowed for an improved yield via *in situ* trapping of the dione to give **128**. A similar transformation was reported involving 3-hydroxy-6-propenyl-4-pyrone **129**, prepared in three steps from readily available kojic acid[60b]. *In situ* reduction gave both the natural product terrein **130a** and its diastereomer **130b**. Use of a 3-silyloxy substituent led to the intervention of an entirely different mechanism. Kojic acid derivative **131**, with a pendant olefin trap, underwent either photochemical or thermal silatropic shift to give a 4-silyloxy-3-oxidopyrylium salt. This intermediate underwent an intramolecular [3 + 2]-cycloaddition to give **132**, which was used in the total synthesis of phorbol[61].

A 2-step route to oxygenated bicyclo[n.3.0]alkanes via bicyclic 4-pyrones such as **133** has been reported (equation 2)[62]. Irradiation in hydroxylic solvents caused ring contraction to the zwitterion, followed by solvent incorporation to give fused bicyclic cyclopentenone **134**. Good regioselectivity in favor of solvent capture at the more substituted oxyallyl terminus was seen in differentially substituted examples, presumably due to increased

charge density at that carbon. Attack by solvent was typically *anti* to the zwitterion epoxide, resulting in a *trans* ring-fusion.

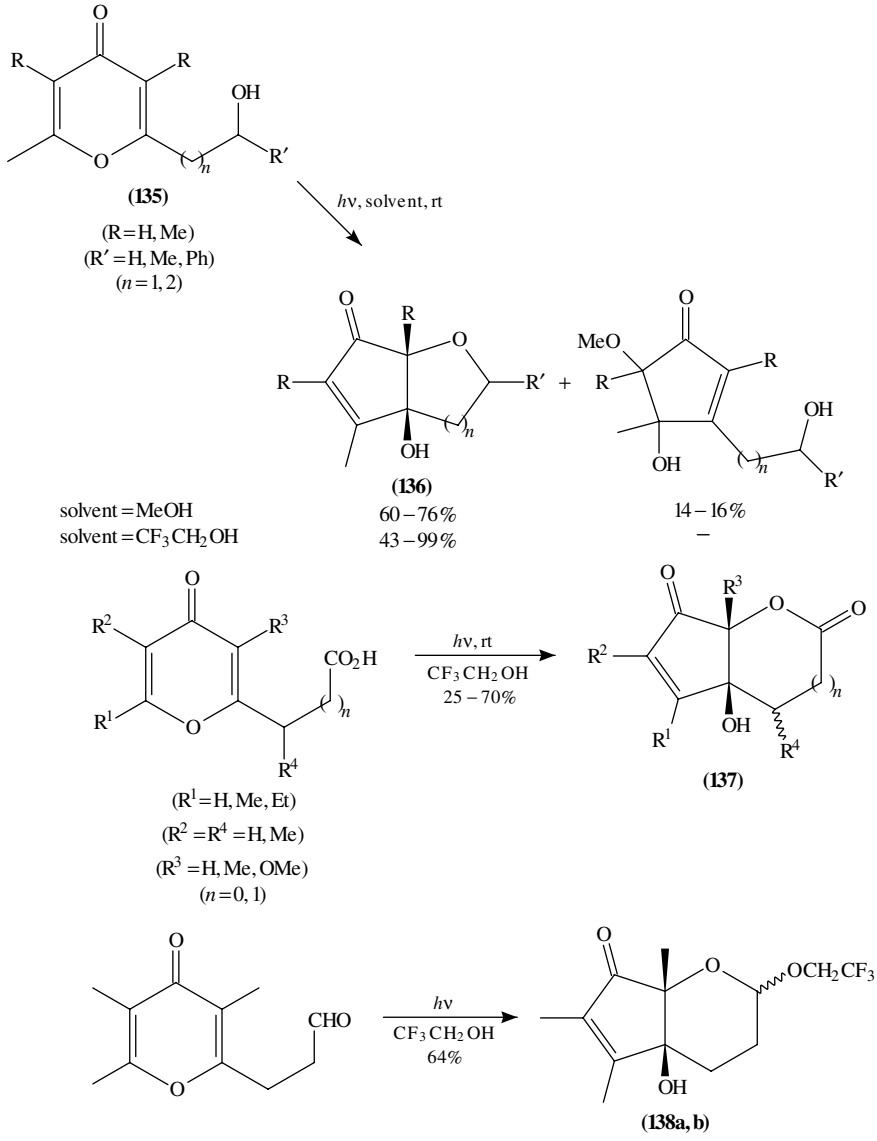


(133) (2)

(134)

The efficiency of the nucleophilic trapping process could be improved by rendering it unimolecular, permitting a wider range of traps. A polar, protic solvent was necessary for efficient photochemical conversion, consistent with the intervention of a π,π^* excited state. This requirement permits a possible competition between the desired intramolecular reaction and intermolecular trapping. 2-Hydroxyalkyl-4-pyrones **135** furnished good yields of intramolecular trapping products **136** in methanol, and only minor amounts of the corresponding solvent adducts (Scheme 31)[63]. Solvent capture could be suppressed completely by use of the less nucleophilic trifluoroethanol. Pendant carboxylic acids were also used as internal traps, giving lactone-fused cyclopentenones **137**[64]. Prior proton transfer to generate a more reactive electrophile/nucleophile pair was deemed a likely possibility in this process. Preliminary studies indicate that a benzyl ether can intercept the zwitterion, with subsequent debenzylation, to give a bicyclic ether identical to that obtained from irradiation of the corresponding free alcohol[65]. Aldehydes were also found to trap through oxygen, giving epimeric bicyclic mixed acetals **138** after solvent addition to the resulting oxocarbenium ion[65].

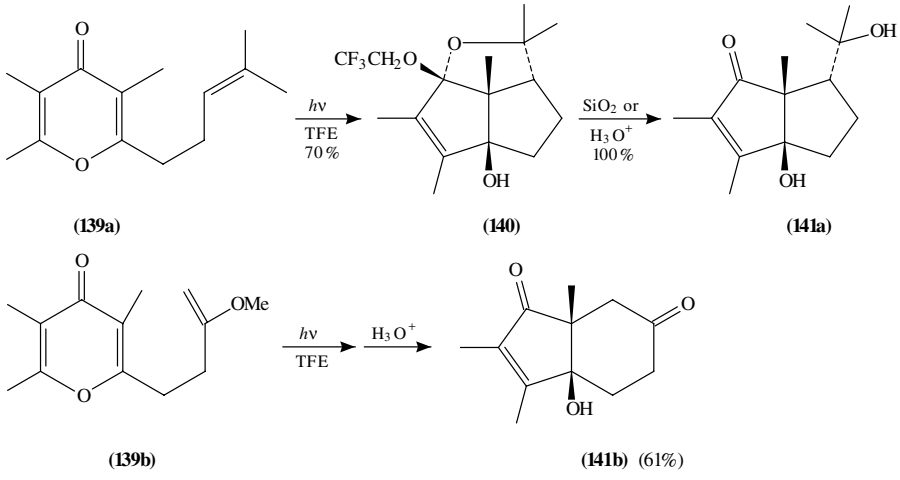
Neutral, π-rich carbon nucleophiles also served as effective internal traps[66]. Irradiation of **139a** in trifluoroethanol at room temperature led to rapid consumption of the starting 4-pyrone and formation of one principal new product, tricyclic mixed ketal **140** (Scheme 32). A second compound, determined to be hydrolysis product **141a**, was formed in trace quantities during chromatography, and could be obtained quantitatively from **140** by treatment with dilute acid. Notably, two new carbon–carbon bonds were formed and three new stereocenters were set with complete control in this process. By varying the olefin substitution pattern (e.g. **139b**), the cationic cyclization step could be switched from a 5-*exo* to a 6-*endo* mode. Substitution at C-3 had a pronounced effect on the stereoselectivity of the cyclization. In those cases bearing only hydrogen at C-3, a mixture of products was obtained, arising from unselective closure to a mixture of epimeric tertiary carbocations. On the other hand, complete diastereoselectivity in favor of an *endo*-oriented carbocation (the product of a compact transition state) was observed in



SCHEME 31

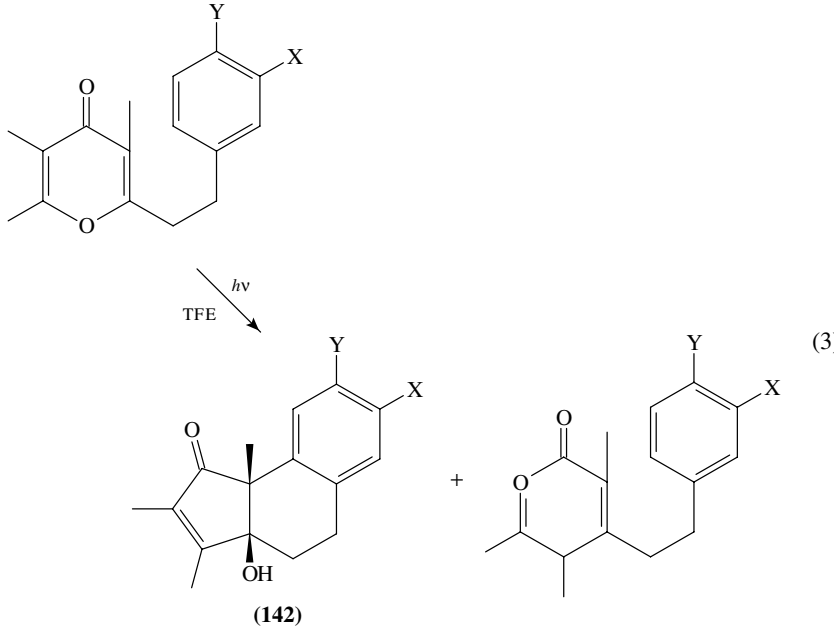
those cases with a nonhydrogen group at C-3. This may result from a destabilizing interaction in the extended transition state leading to the *exo*-disposed carbocation. Schultz and coworkers noted comparable diastereoselectivity in the 5-*exo* cationic cyclizations of 1,5-zwitterions[49c].

Intramolecular electrophilic aromatic substitution to give tricyclic products **142** is also a viable process, with trapping efficiency related to the electron density of the arene trap (equation 3)[67]. With a simple phenyl group pendant, rearrangement to the 2-pyrone was



SCHEME 32

the major pathway, and photocyclization was relatively minor. Additional alkoxy groups on the arene increased the efficiency of the cyclization step, and good yields of tricyclic trapping products were seen.

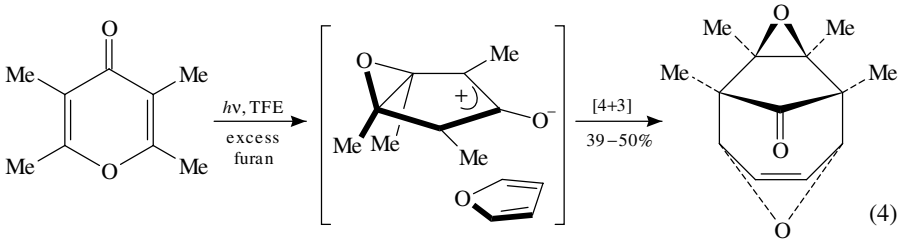


(3)

(142)

X = Y = H:	32%	51%
XY = OCH_2O:	75%	–

As noted above, formation of a furan [4 + 3]-cycloadduct during irradiation of a 4-pyrone was advanced as evidence for the zwitterionic intermediate. This process can be moderately efficient (equation 4)[68], and can be envisioned as an approach to substituted cyclooctanoids. Besides the formation of three new carbon–carbon bonds, an additional attractive feature is the complete diastereoselectivity, arising from a compact [4 + 3]-cycloaddition transition state with approach from the face opposite the epoxide. However, the generality of the intermolecular reaction is limited, as competing [2 + 2]-photodimerization, solvent trapping and rearrangement often predominate[58].

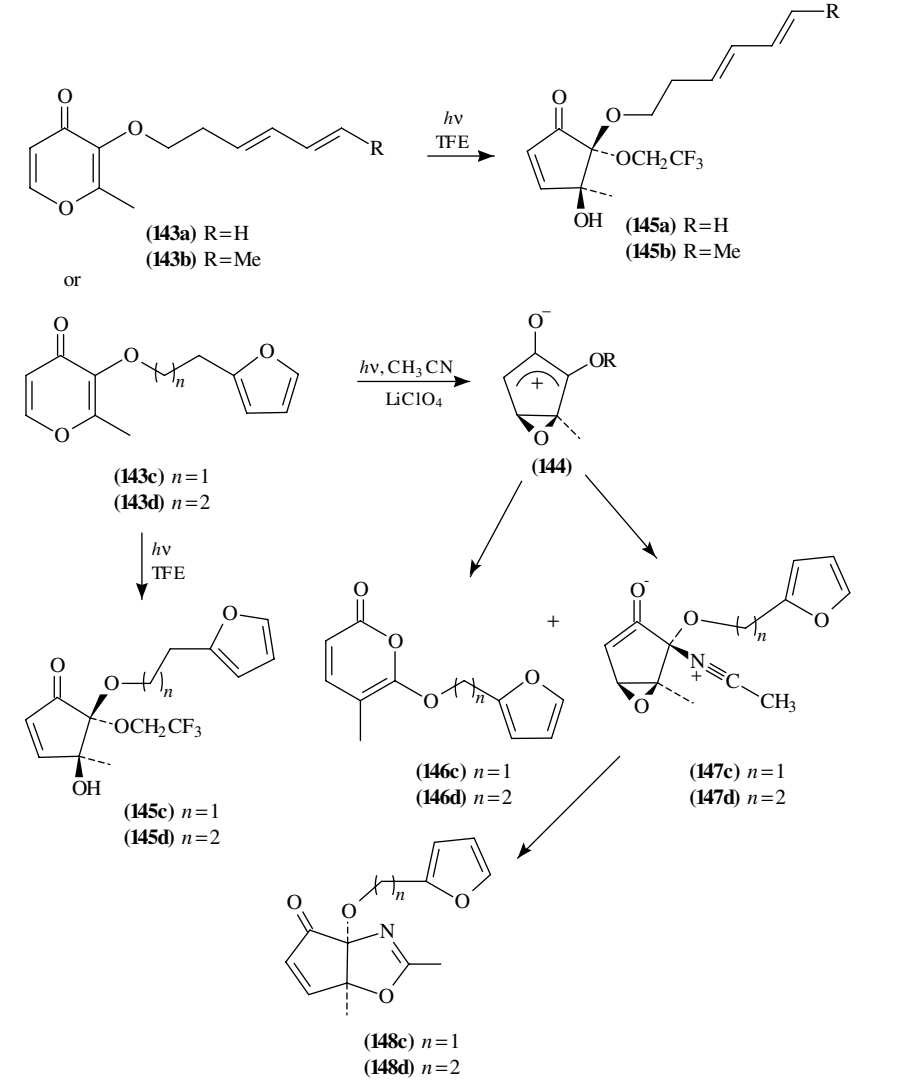


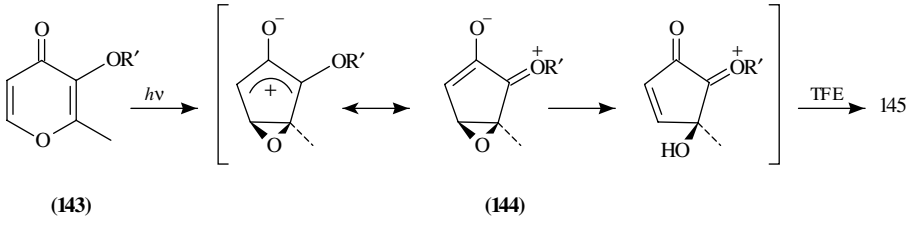
(4)

Irradiation of substrates **143** in trifluoroethanol led to their efficient consumption and formation in each case of a single new product, which surprisingly proved to be simple solvent adducts **145** rather than the expected intramolecular [4 + 3]-cycloadducts (Scheme 33)[68]. The unusually efficient capture by the relatively unreactive trifluoroethanol can be explained in terms of strongly polarized zwitterionic intermediates **144**, which undergo ionic processes in preference to the desired cycloadditions. Polar, aprotic solvent systems such as acetonitrile containing $LiClO_4$ were also examined, and in the case of **143c–d**, a mixture of 2-pyrones **146** and bicyclic oxazolines **148** was obtained[69]. The novel oxazoline products presumably arise from solvent capture of the zwitterion in a Ritter-type process, leading to nitrilium intermediates **147**. Subsequent epoxide opening would allow for attack of the alkoxide on the nitrilium to close the oxazoline ring.

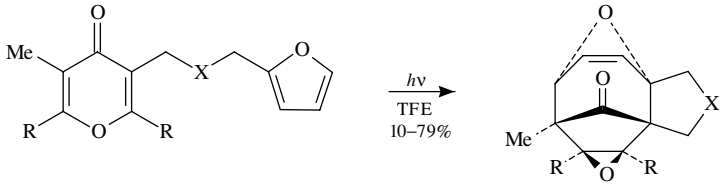
In contrast, substrates **149** all furnished [4 + 3]-cycloadducts **150** and **151** in yields ranging from 10–79% (Scheme 34)[68]. In all cases, exclusive approach of the furan from the zwitterion face opposite the epoxide ring was seen. In most cases, the *exo* diastereomer **151** was the major product or was formed to the exclusion of the *endo* diastereomer **150**. The contrasting diastereoselectivity seen in inter- and intramolecular cycloadditions may result from unfavorable nonbonding interactions in the *endo* transition state between the tether atoms and the alkyl groups at C-2 and C-5.

In some cases additional photoproducts were formed, including cage structure **152** (presumably arising from sequential intramolecular [2 + 2]-photocycloadditions in analogy to the previously discussed 4-pyrone dimers[54]). This is exemplified in Scheme 34 by the reaction of **149e**, leading to varying amounts of 2-pyrone rearrangement products **153e** and **154e**, and another side product[68]. The structure assigned was lactone bridged cyclooctadiene **155**, most likely formed via intramolecular [4 + 4]-photocycloaddition between the furan and 2-pyrone units of secondary photoproduct **153e**. This was confirmed by careful irradiation of **153e** and **154e** to give **155** and **156**, respectively, as the major photoproducts. A more detailed discussion of photochemical [4 + 4]-cycloaddition reactions of 2-pyrones and related diene systems is found elsewhere in this chapter.


hν
TFE
OCH2CF3
OH
(143a) R=H
(143b) R=Me
(145a) R=H
(145b) R=Me
or
hν, CH3CN
LiClO4
OR
(143c) n=1
(143d) n=2
(144)
hν
TFE
(145c) n=1
(145d) n=2
(146c) n=1
(146d) n=2
(147c) n=1
(147d) n=2
(148c) n=1
(148d) n=2

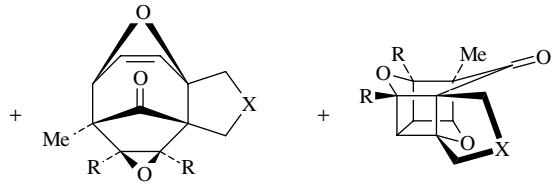

OR′
hν
HO
TFE
145
(143)
(144)

SCHEME 33



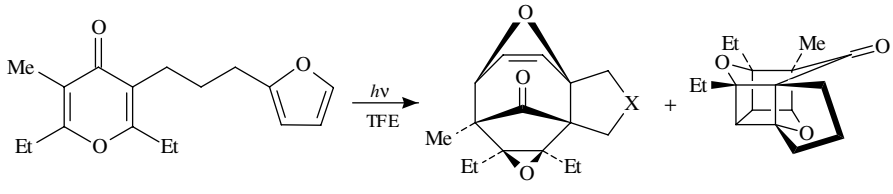
(149a) R=Me, X=O
(149b) R=Me, X=CH_2
(149c) R=H, X=O
(149d) R=Et, X=O

(150a) R=Me, X=O
(150b) R=Me, X=CH_2
–
(150d) R=Et, X=O

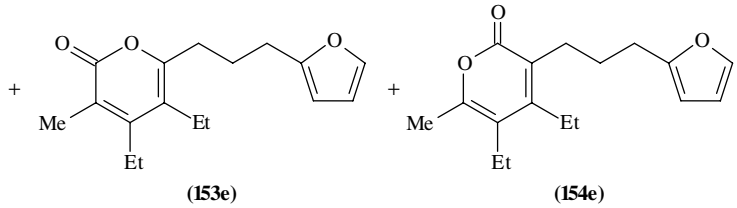


(151a) R=Me, X=O
(151b) R=Me, X=CH_2
(151c) R=H, X=O
(151d) R=Et, X=O

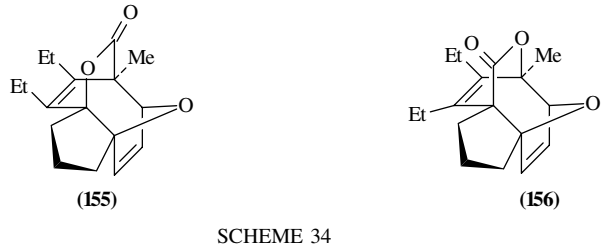
(152a) R=Me, X=O
(152b) R=Me, X=CH_2
(152c) R=H, X=O
(152d) R=Et, X=O



(149e) **(151e)** **(152e)**



(153e) **(154e)**



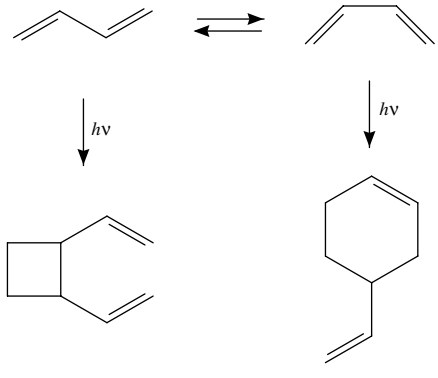
(155) **(156)**

SCHEME 34

III. PHOTOCYCLOADDITIONS INVOLVING DIENES AND POLYENES

A. [2 + 2]-Photodimerization of 1,3-Dienes

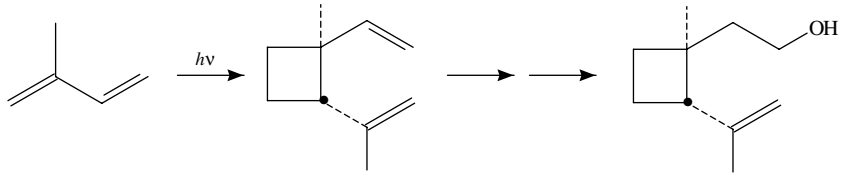
Sensitized irradiation of butadiene produces two significant photoproducts, the cyclobutane **157** as the major product and the minor cyclohexene isomer, **158** (Scheme 35)[70]. Based on extensive photophysical studies, **157** is thought to arise from excitation of the lower-energy s-*trans* ground state conformer, while **158** presumably arises primarily from the higher-energy s-*cis* ground state form. While this reaction has been well characterized, the photodimerization of other acyclic dienes often gives hopelessly complex mixtures of products, thereby limiting the synthetic utility of this process.



(157) **(158)**

SCHEME 35

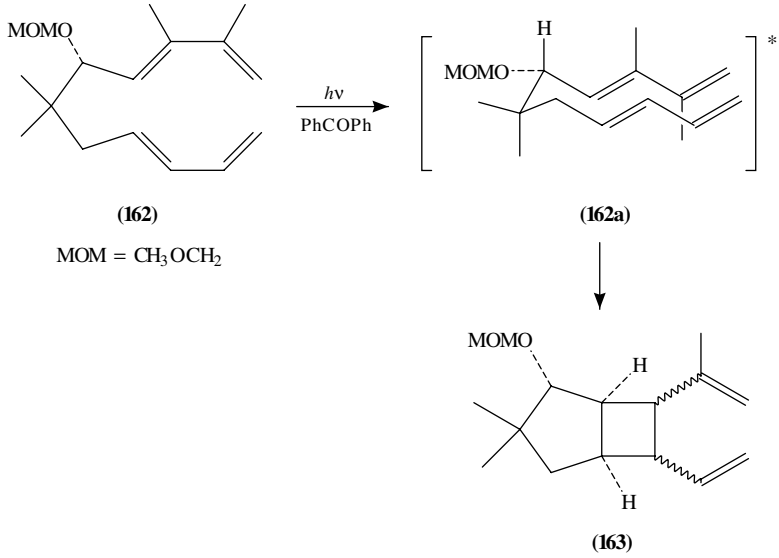
Though the triplet sensitized photolysis of isoprene **(159)** does, as noted above, produce a complex mixture of products, one of these adducts has been used in the context of complex molecule synthesis (equation 5)[71]. Cyclobutane **160**, which was formed in *ca* 20% yield by the benzophenone sensitized photolysis of **159**, could be easily transformed into fragrantolol, **161**, an isomer of grandisol isolated from the roots of the *Artemisia fragrans*, by simple hydroboration/oxidation of the less hindered double bond.



(5)

(159) **(160)** **(161)**

While the divinylcyclobutanes produced by the photodimerization of dienes would seem to possess considerable potential as synthons, the problems encountered by the often remarkably complex mixtures of regio- and stereoisomers produced in these reactions rendered these transformations unusable until recently. Wender and Correia have found an ingeneous solution to these problems by tethering the two reacting 1,3-diene moieties together, e.g. **162**, thereby eliminating most of the regio- and stereochemical issues which proved problematic in intermolecular diene photocycloadditions (Scheme 36)[72]. The initial [2 + 2] cycloadditon of bis(diene) **162** must afford adducts **163** in which the



(162)

MOM = CH_3OCH_2

(162a)

(163)

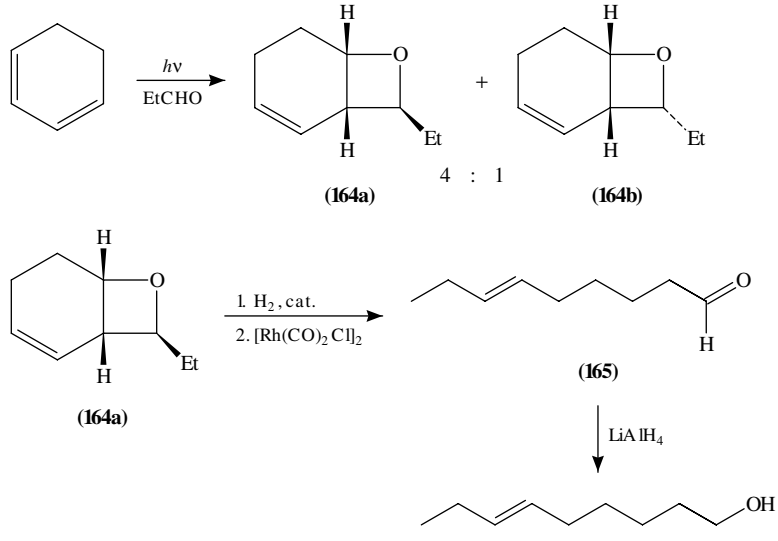
SCHEME 36

five- and four-membered rings in the adducts are *cis*-fused, as formation of the corresponding *trans*-fused products would be too energetically demanding. The regiochemistry of the photocycloaddition is also controlled by the tether. It is interesting to note that the protected alkoxy substituent on the tethering atoms in **162** profoundly affected the stereoinduction in the initial [2 + 2]-photocycloaddition; the high degree of stereocontrol exhibited during the formation of the three contiguous stereogenic centers in this adduct was rationalized in terms of this substituent adopting a pseudo-equatorial position in a reacting conformer such as **162a**. This approach was used as an entry into formal [4 + 4]-cycloadducts via subsequent ring-expansion of the divinylcyclobutanes (discussed below in Section III.C).

B. Paterno–Büchi Reactions Employing Conjugated Dienes

The [2+2]-photocycloaddition of carbonyl groups with olefins (Paterno–Büchi reaction) is one of the oldest known photochemical reactions and has become increasingly important for the synthesis of complex molecules. Existing reviews have summarized the mechanistic considerations and defined the scope and limitations of this photocycloaddition[73]. Although this reaction likely proceeds via initial excitation of the carbonyl compound and not the excited state of the diene, the many examples of this reaction in natural product synthesis justify inclusion in this chapter.

Synthetic application of Paterno–Büchi reaction of simple dienes with carbonyl compounds is rare[73]. While seemingly an extension of the photocycloaddition of olefins and carbonyl compounds, the reaction between dienes and carbonyls is often complicated by the fact that triplet excited states of carbonyl compounds are quenched by dienes, although the formation of oxetanes can be observed during these reactions[74]. Recall also that the photosensitized dimerization of diene triplet excited states is also a well known reaction (*vide infra*); these two observations would seem to naturally limit the synthetic potential of this process[75]. Kubota and coworkers found that irradiation of propanal in the presence of 1,3-cyclohexadiene produced oxetanes **164a** and **164b** in a 4:1 ratio (Scheme 37)[76].

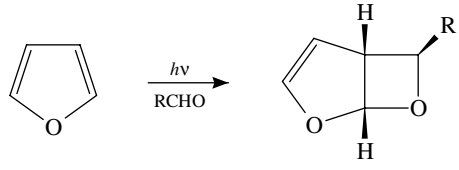


SCHEME 37

These adducts were thought to occur via attack of the first excited singlet state of propanal on the diene. Evidence from subsequent studies point to the fact that it is likely the excited singlet state of the aldehyde that is responsible for the Paterno–Büchi reaction with 1,3-dienes. This comes from a number of sources and includes evidence from a number of studies[73,77]. The synthesis of (*E*)-6-nonen-1-ol, a component of the sex pheromone of the Mediterranean fruit fly, applied this process as the first step[78]. Hydrogenation and metal catalyzed [2 + 2] cycloreversion gave **165**, which was then easily converted to the target by reduction (Scheme 37).

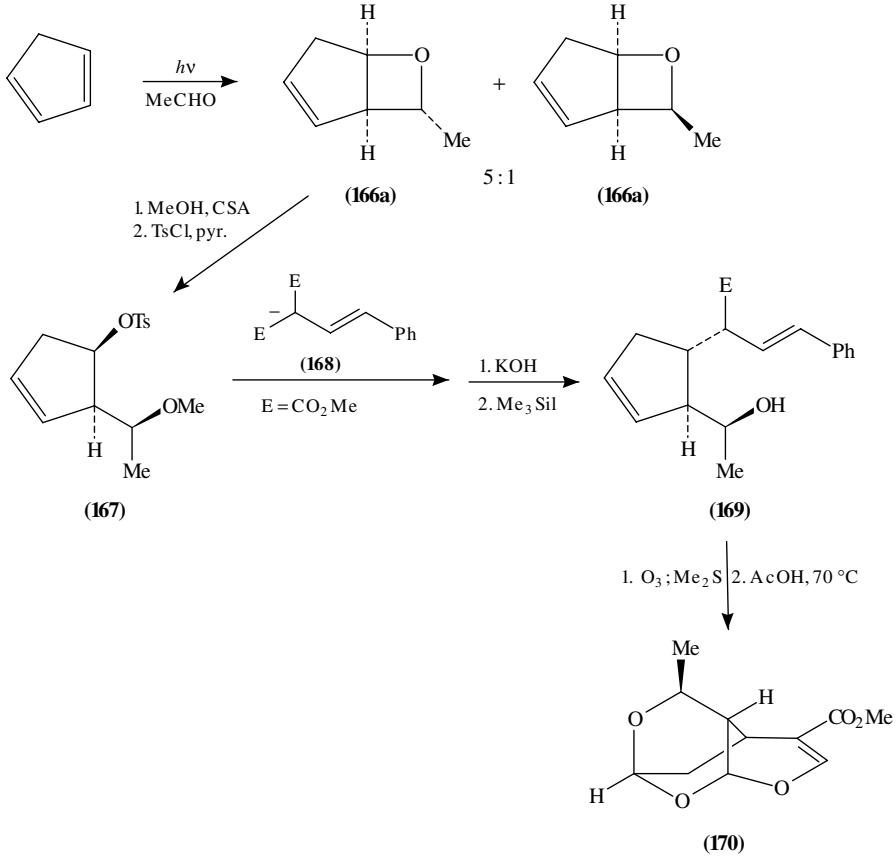
Hoye and Richardson have published an ingeneous synthesis of the tricyclic iridoid sarracenin **(170)** which relied on the Paterno–Büchi cycloaddition between acetaldehyde and cyclopentadiene as the intial step (Scheme 38)[79]. This reaction provided a 5:1 mixture of adducts **166a** and **166b**. The major adduct was opened with camphor-10-sulfonic acid (CSA) in methanol and the alcohol was tosylated to give **167**. Displacement with malonate **168** and decarboalkoxylation/demethylation steps gave **169**. Ozonolysis, reductive work-up and acid-catalyzed acetalization then furnished **170**.

The Paterno–Büchi photocycloaddition between carbonyl compounds and furans was first described in 1965 (equation 6)[80]. This report noted that only the head-to-head product **171** was formed, and that high *exo* face selectivity was exhibited. Subsequent to this and other early reports, this reaction has been systematically explored by several groups, owing largely to the various ways in which the 2,7-dioxabicyclo[3.2.0]hept-3-ene ring system can be exploited[73c,81].



(6)

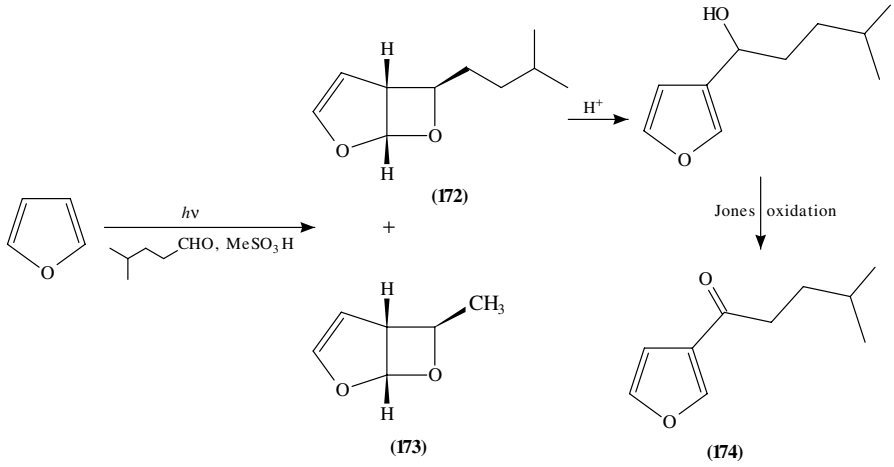
(171)



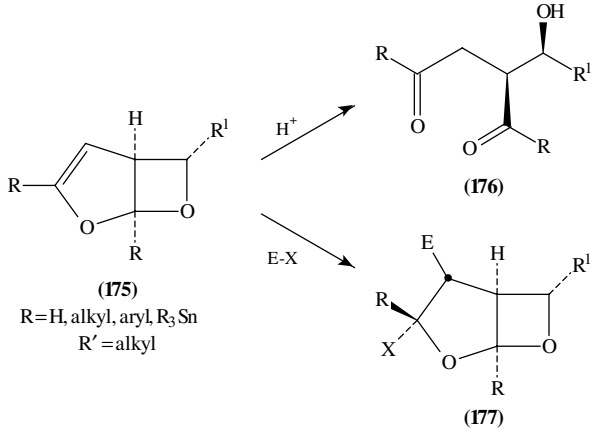
SCHEME 38

These cycloadducts, at their most elementary level, are excellent intermediates for the synthesis of 3-substituted furan derivatives. For example, Kawanisi and coworkers reported a synthesis of perillaketone **174** in which the critical step was a Paterno–Büchi photocycloaddition between furan and 4-methylpentanal in the presence of methanesulfonic acid (Scheme 39)[82]. This reaction furnished two initial photoadducts, **172** and **173**. The unexpected product **173** presumably arises from a Norrish Type II cleavage of 4-methylpentanal to give acetaldehyde, and subsequent cycloaddition with furan. The desired cycloadduct **172** was then converted uneventfully to **174** via acid-catalyzed aromatization and oxidation.

Schreiber and his coworkers have published extensively over the past decade on the use of this photocycloaddition for the synthesis of complex molecules[73c,81]. Schreiber was the first to recognize that the bicyclic adducts formed in these reactions could be unmasked under acidic conditions to afford *threo* aldol products of 1,4-dicarbonyl compounds (**175** to **176**) (Scheme 40). The *cis*-bicyclic system also offers excellent stereocontrol in the addition of various electrophilic reagents (E−X) to the enol ether of these photoadducts on its convex face (**175** to **177**). This strategy has been exploited in the synthesis of a variety of architecturally novel natural products.



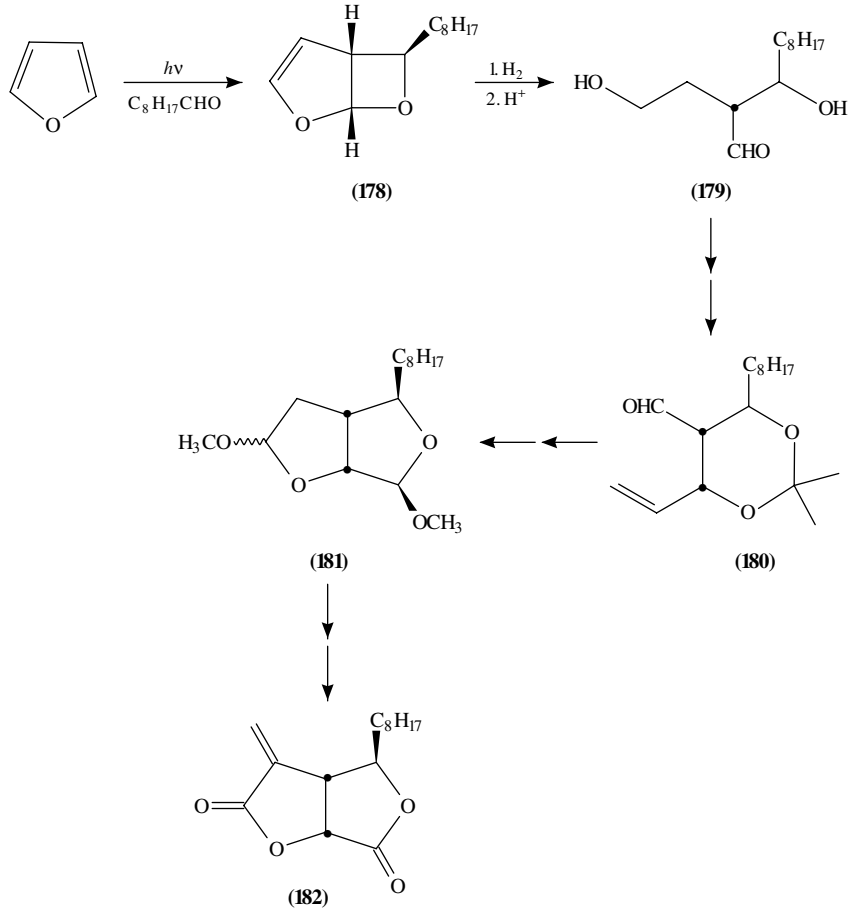
SCHEME 39



SCHEME 40

An application of this strategy to the synthesis of the antifungal metabolite (±)-avenaciolide **182** is shown in Scheme 41[83]. The photoadduct in this case, **178**, was hydrogenated and hydrolyzed to give **179**. Reaction of **179** with vinylmagnesium bromide and subsequent manipulation afforded aldehyde **180**, which could be transformed via ozonolysis, epimerization of the dialdehyde and acidification of the dialdehyde acetonide to protected bis(lactol) **181**. Oxidation and methylenation then afforded the desired target **182**.

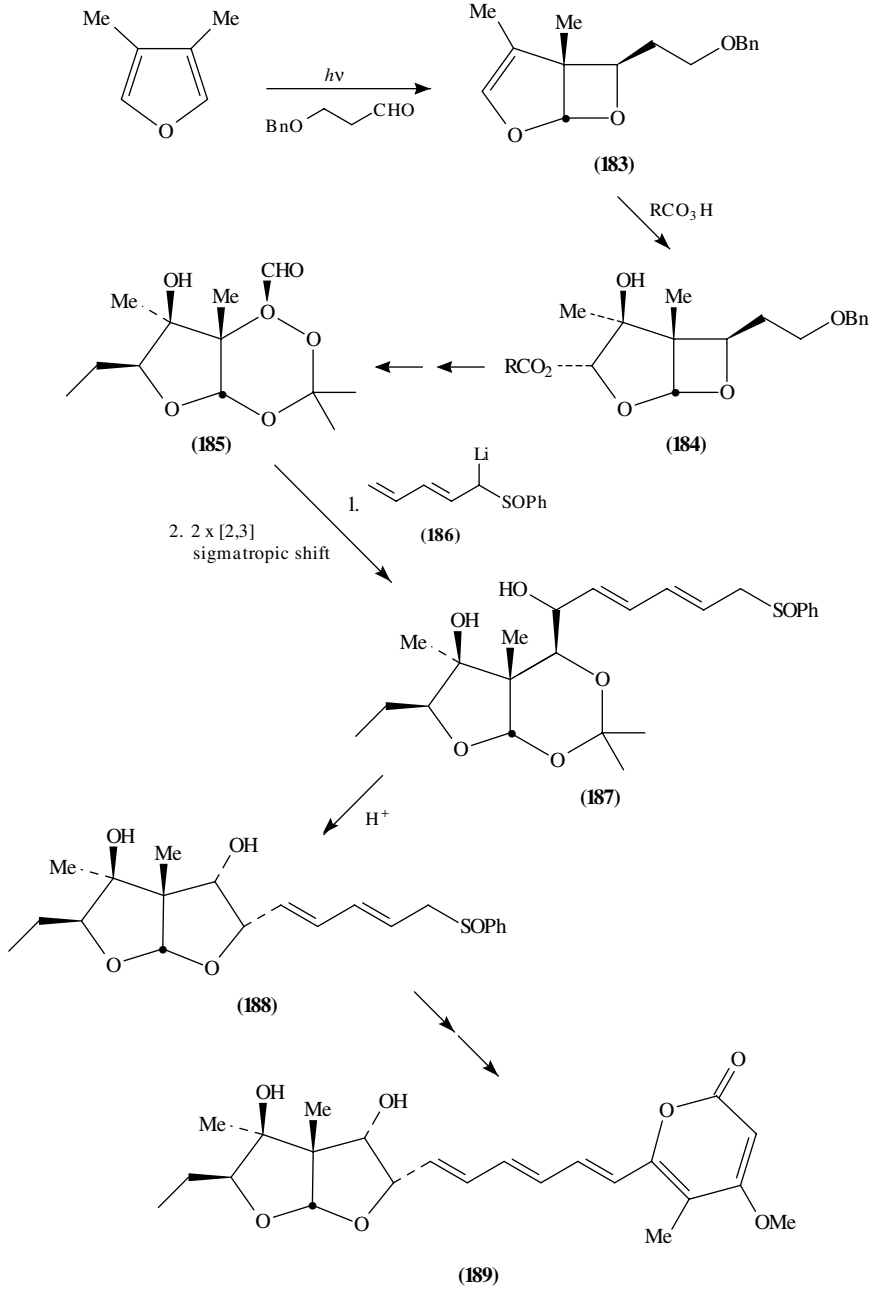
Efficient synthesis of the mycotoxin asteltoxin **189** was accomplished beginning with the cycloaddition between 3,4-dimethylfuran and 3-benzyloxypropanal, which furnished photoaldol **183** in 63% yield (Scheme 42)[84]. Epoxidation from the convex face of this adduct, with subsequent epoxide opening, afforded **184**, which was then elaborated through a series of steps to **185**. The side chain was introduced via lithiosulfoxide **186** to furnish, after double sigmatropic rearrangement, **187**. Hydrolysis of this afforded **188**, which was oxidized and elaborated to **189** in two steps.



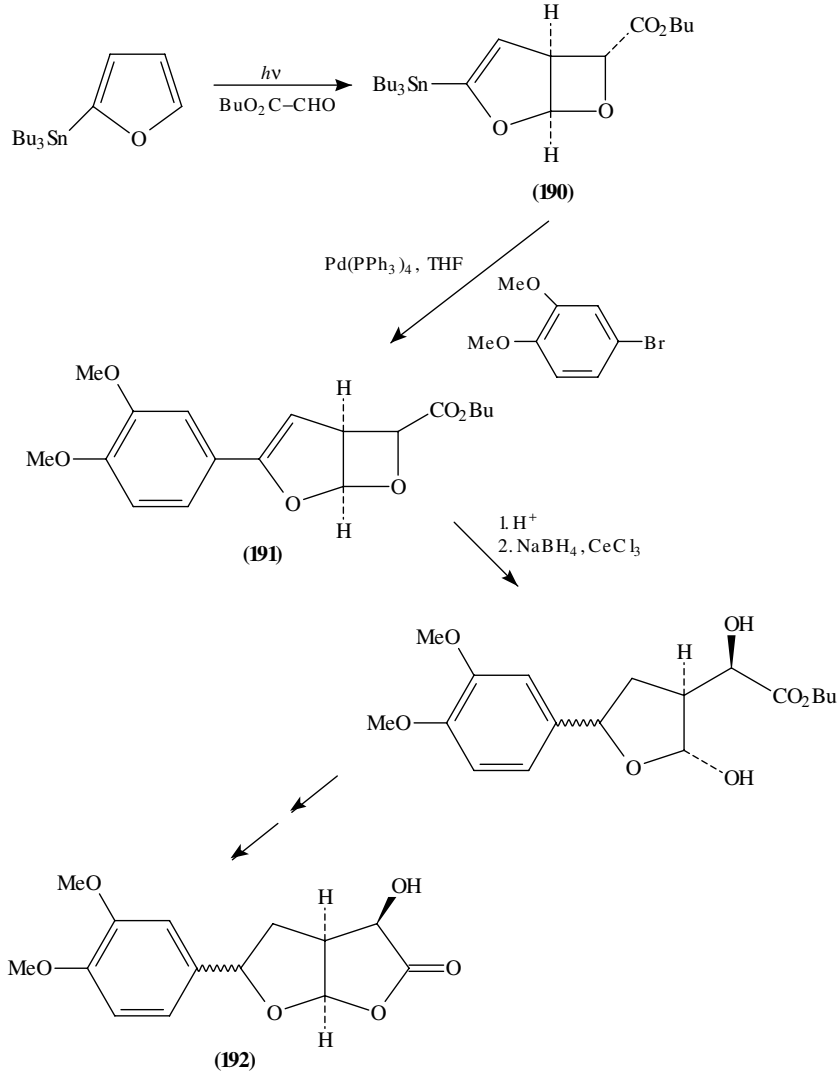
SCHEME 41

Schreiber and coworkers also have described an interesting variation on the furan-carbonyl photcycloaddition using silyl and stannyl furan derivatives[85]. These compounds have been developed to circumvent the lack of regioselectivity generally encountered when unsymmetrical furans are used in this photocycloaddition. This idea is nicely illustrated in the synthesis of **192**, which was designed to be a hybrid of ginkolide and kadsureneone, natural products which are both highly active PAF (platelet activating factor) antagonists (Scheme 43)[86]. Irradiation of 2-tributylstannylfuran and *n*-butyl glyoxylate gave adduct **190** as the sole photoproduct in 35% yield. Stille coupling of **190** with veratryl bromide afforded **191**, which could be elaborated to the target structure **192** in a series of steps. Note that in this strategy the main group element functions to both direct the photocycloaddition and allow introduction of a substituent via a transition metal catalyzed coupling reaction.

Hoveyda has also studied the intramolecular variant of the furan-carbonyl photocycloaddition[87]. Several examples of this reaction, each of which proceeds in modest yield, are shown in Scheme 44. However, given the ease of synthesis of the starting materials and the complexity of the adducts produced in these photocycloadditions, these

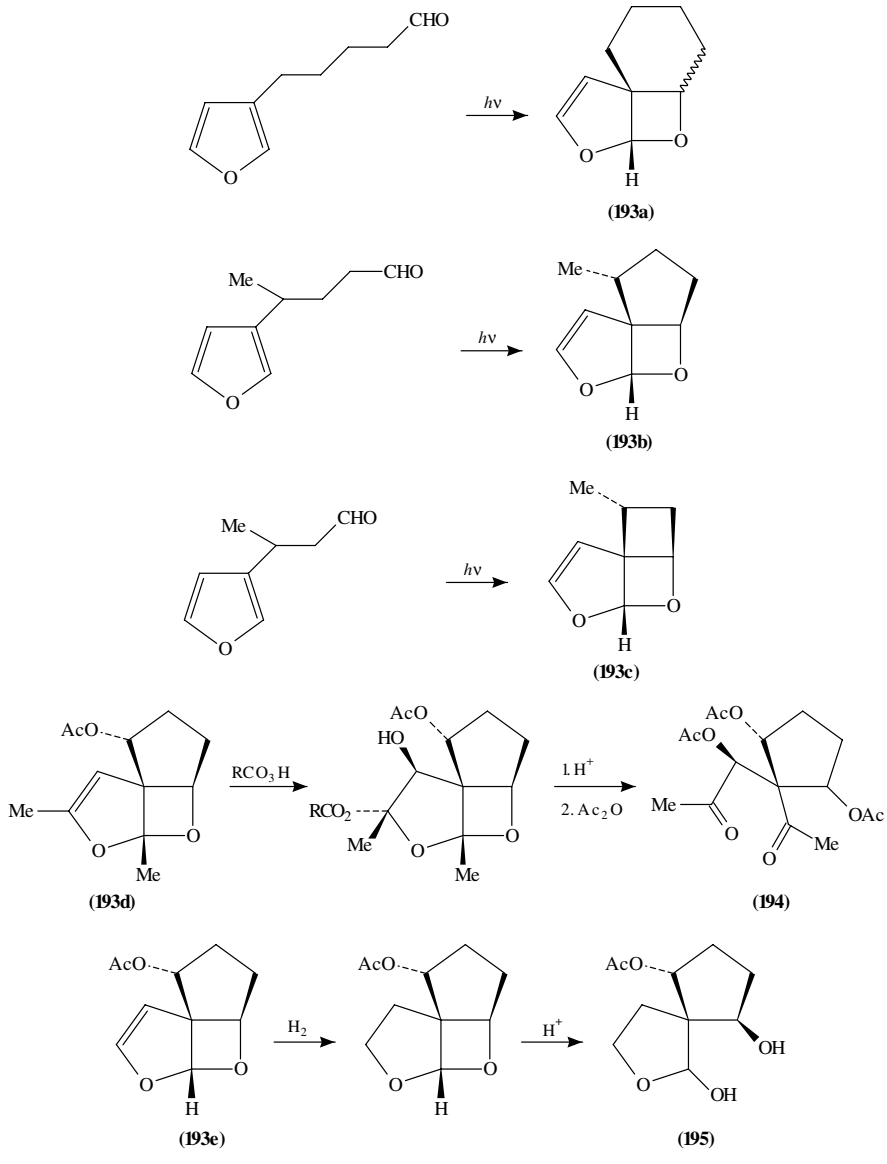

Me
Me
O
hν
BnO
CHO
Me
Me
OBn
O
O
(183)
RCO3H
OH
Me
Me
CHO
O
O
O
O
(185)
OH
Me
Me
O
RCO2
O
OBn
(184)
1.
Li
SOPh
(186)
2. 2 x [2,3]
sigmatropic shift
HO
SOPh
OH
Me
Me
O
O
O
(187)
H+
OH
Me
OH
SOPh
O
O
(188)
OH
Me
OH
O
O
O
O
Me
OMe
(189)

SCHEME 42



SCHEME 43

reactions certainly would seem to hold great promise in complex molecule synthesis. It was noted that the oxetane photoadducts produced in these reactions are much more difficult to manipulate and functionalize than their counterparts produced in the intermolecular photocycloaddition. For example, acidic hydrolysis of **193b** resulted in retro-[2 + 2]-photocycloaddition rather than the ring opening typically observed in the intermolecular photoadducts. Methods have been developed to circumvent these problems. Epoxidation of **193d** and hydrolysis afforded the dione **194**. Also, hydrogenation of the enol ether double bond in **193e** and subsequent hydrolysis gave the spirocycle **195**, again demonstrating the potential of this strategy for the rapid assembly of complex molecular architectures. It is also impressive to note that even highly strained systems (e.g. **193c**) can be produced

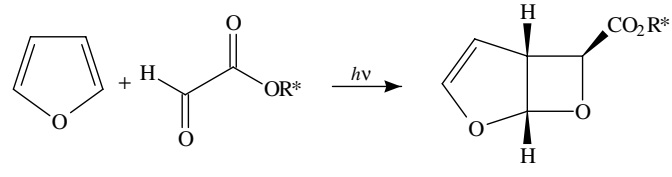


SCHEME 44

with good efficiency. A systematic study of the stereoinduction of substituents on the tether has also been conducted and the reader is referred elsewhere for a more detailed description[73c].

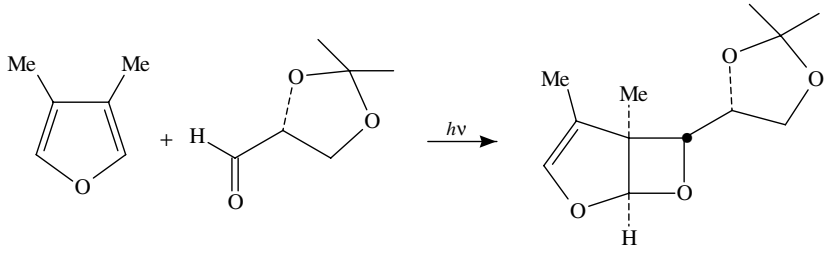
Zamojski and coworkers have explored the use of the furan-carbonyl photocycloaddition in asymmetric synthesis, with somewhat limited success[88]. Irradiation of chiral glyoxylate derivative **196** [R* = (*R*)(−)-menthyl and (*R*)(−)-8-phenylmenthyl] afforded

adducts **197** with low selectivity (7.3% and 15% ee, respectively, after saponification of the ester; Scheme 45). This may be due to a lack of *endo* or *exo* selectivity during the photocycloaddition, or to a bad ratio of s-*cis* and s-*trans* conformers. Schreiber and Satake also noted low selectivity in the reaction of the protected glyceraldehyde derivative **198** with dimethylfuran as a 1.2:1 mixture of the diastereomeric acetonides **199a** and **199b** was produced[84b]; each of these was only *ca* 50% ee, indicating that this aldehyde may be labile toward racemization under the reaction conditions. Other attempts to react furans with conformationally restricted chiral, nonracemic ketones have met with somewhat better results, but this is still an area that is in development[84b].

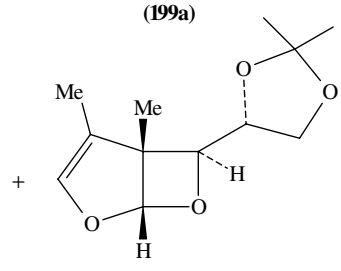


(196) **(197)**

R* = (–)-menthyl de = 7.3%
R* = (–)-8-phenylmenthyl de = 15%



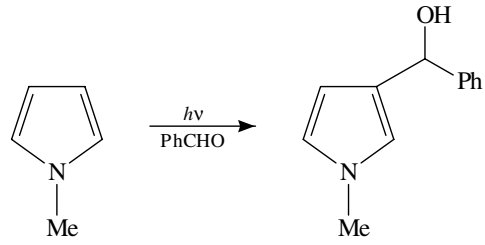
(198) **(199a)**



(199b)

SCHEME 45

Other aromatic heterocycles undergo Paterno–Büchi reaction with carbonyl compounds, although these reactions have seldom been applied to organic synthesis. For example, thiophene reacts cleanly with benzaldehyde to afford a single *exo* product in 63% yield[87]. Pyrroles also react with aldehydes and ketones; however, as a result of the lability of the presumed initial cycloadducts, the only products isolated, even with the rigorous exclusion of acid, are the 3-hydroxyalkylpyrroles **200** (equation 7)[89].

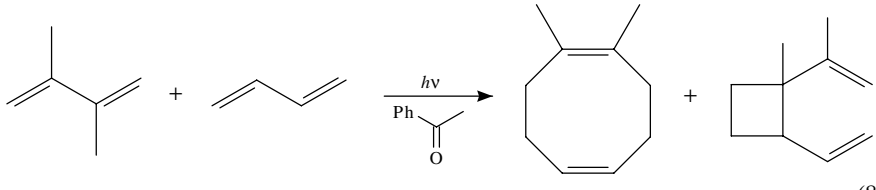


(7)

(200)

C. [4 + 4]-Photocycloadditions

Photodimerization of simple 1,3-dienes in a $4\pi + 4\pi$ cycloaddition process is typically an inefficient process[90]. This is not surprising, given the highly ordered transition state for [4+4]-cycloadditions, and the predominance of the unreactive s-*trans* conformation[70]. As a result, as noted above [2+2]-cycloadducts are often the major product, accompanied by varying amounts of vinylcyclohexenes and cyclooctadienes. Crossed photocycloadditions employing 1,3-dienes with substituents at the 2- or 3-positions can furnish greater amounts of cyclooctadiene products (equation 8)[91]. This presumably results from a perturbation of the diene conformational equilibration to provide a higher proportion of the s-*cis* conformer.

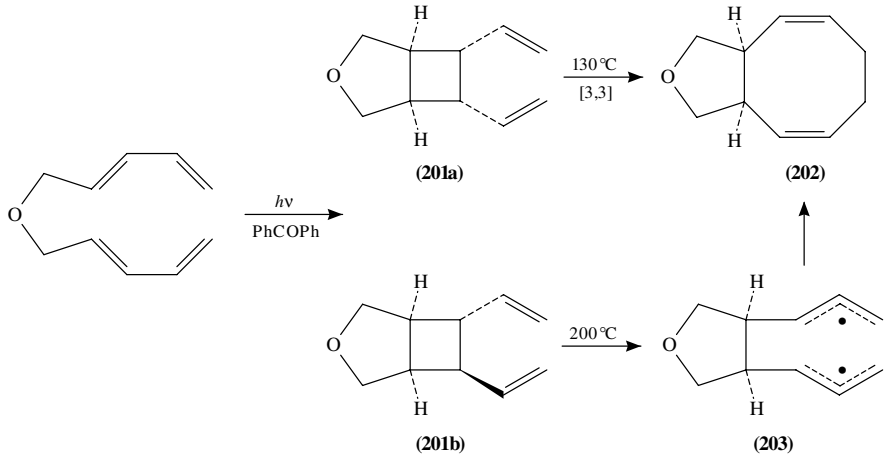


15% 58%

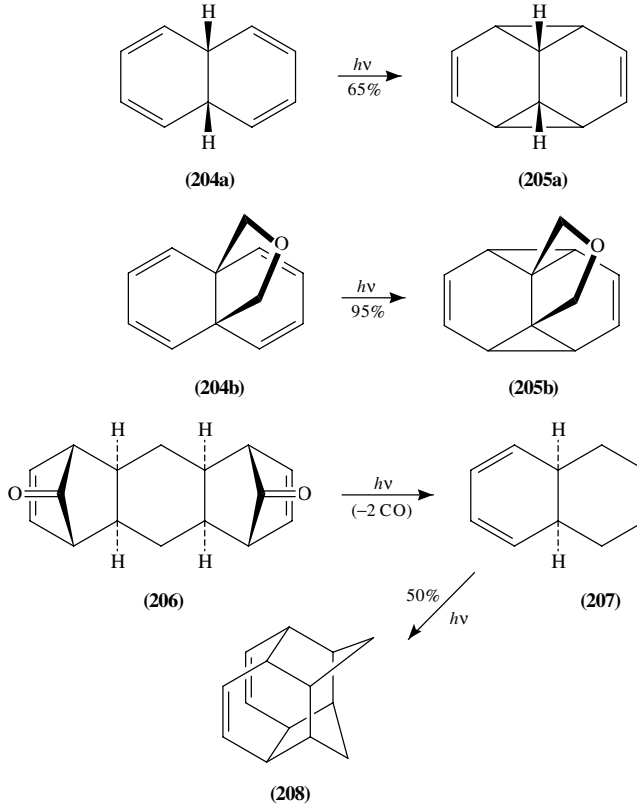
(8)

As noted previously in Section III.A, the [2 + 2]-cycloadducts formed from 1,3-diene dimerization are divinylcyclobutanes, and thus can potentially serve as precursors to cyclooctadienes via [3,3]-sigmatropic shift. This approach has been exploited by Wender and Correia (Scheme 46)[72]. Typically, the two diene units were joined by a three-atom tether, improving the efficiency of the photocycloaddition and leading to the generation of a bicyclo[3.2.0]heptane skeleton upon irradiation. Only the *cis* diastereomer **201a** can undergo the subsequent pericyclic process. However, at higher temperatures, the *trans* isomer **201b** also underwent conversion to the desired cyclooctadiene **202**, presumably via biradical intermediate. Mattay and coworkers have reported a similar tetraene to divinylcyclobutene process, using Cu(I) salts to preorganize the substrates in a reactive conformation[92].

There are a few exceptions to the generalizations made above regarding the periselectivity of 1,3-diene dimerization. These involve systems in which various structural constraints act to impede the typically favored [2 + 2]-cycloaddition process or enhance the [4 + 4]-cycloaddition. For example, *cis*-9,10-dihydronaphthalene **204a** furnished tetracyclic product **205a** in good yield (Scheme 47)[93]. Similarly, propellane **204b** underwent conversion to **205b** in nearly quantitative yield[94]. More recently, Srikrishna and Sunderbabu showed that hexahydroanthracene **207**, generated *in situ* from **206** via



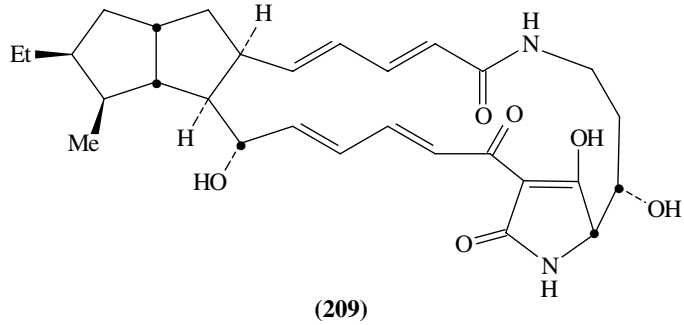
SCHEME 46



SCHEME 47

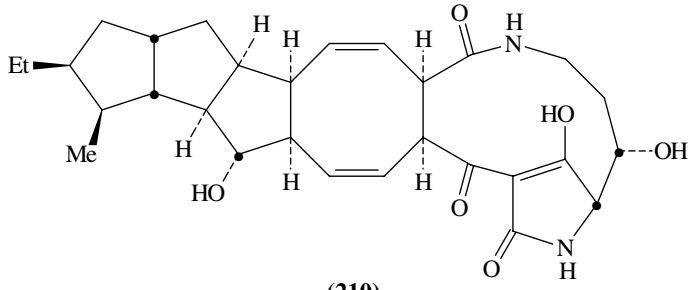
photochemical decarbonylation, suffered [4 + 4]-cycloaddition to give pentacyclic adduct **208** (Scheme 47)[95].

Another unique example was observed for the recently isolated marine natural product, alteramide A **(209)**, isolated from a symbiotic bacteria (*Alteromonas* sp.) found on the sponge *Halichondria okadai*[96]. It was found that the tetraene core of this compound underwent intramolecular [4 + 4]-photocycloaddition upon exposure to sunlight (equation 9). Deliberate irradiation led to a quantitative conversion to cyclooctadiene **210**.



(209)

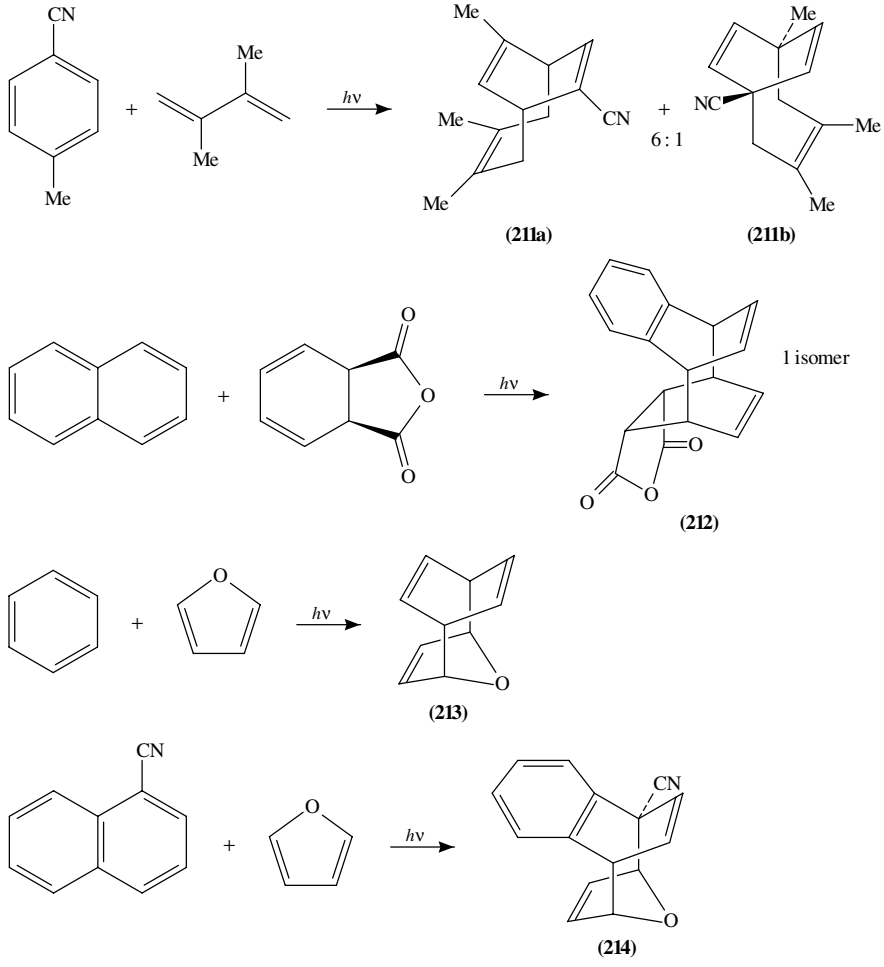
(9)



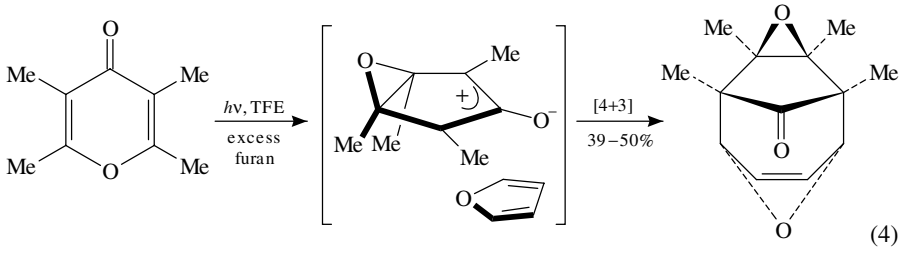
(210)

The literature of mechanistic aromatic photochemistry has produced a number of examples of [4 + 4]-photocycloadditions. The photodimerization of anthracene and its derivatives is one of the earliest known photochemical reactions of any type[97]. More recently, naphthalenes[98], 2-pyridones[99] and 2-aminopyridinium salts[100] have all been shown to undergo analogous head-to-tail [4 + 4]-photodimerization. Moreover, crossed [4+4]-photocycloaddition products can be obtained in some cases[101]. Acyclic 1,3-dienes, cyclohexadienes and furan can form [4 + 4]-cycloadducts **211–214** with a variety of aromatic partners (Scheme 48).

A common feature of these reactions is the incorporation of one or both of the reacting dienes within a ring, thereby ensuring that they exist in a reactive conformation. This strategy has been further explored by Sieburth and Chen, employing 2-pyridones as the diene units. These studies showed that mixed head-to-tail 2-pyridone dimers can be efficiently formed when the two heterocycles are joined by a three- or four-carbon chain, giving highly functionalized cyclooctadienes such as **215** bridged by two lactam units (equation 10)[102].



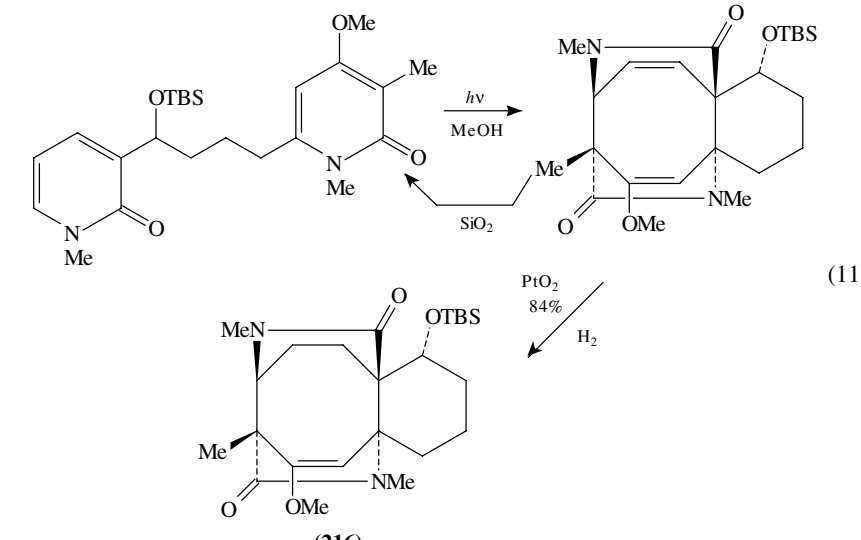
SCHEME 48



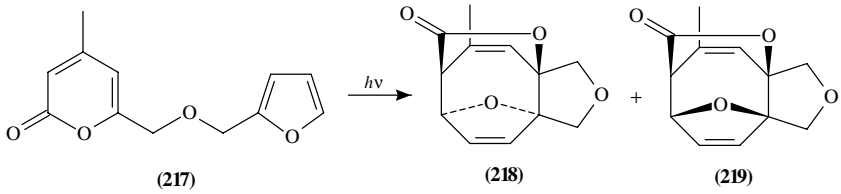
(4)

Further mechanistic work has revealed interesting solvent effects on diastereoselectivity[103]. A method for enriching isomer ratios in favor of the '*trans*' or *exo*

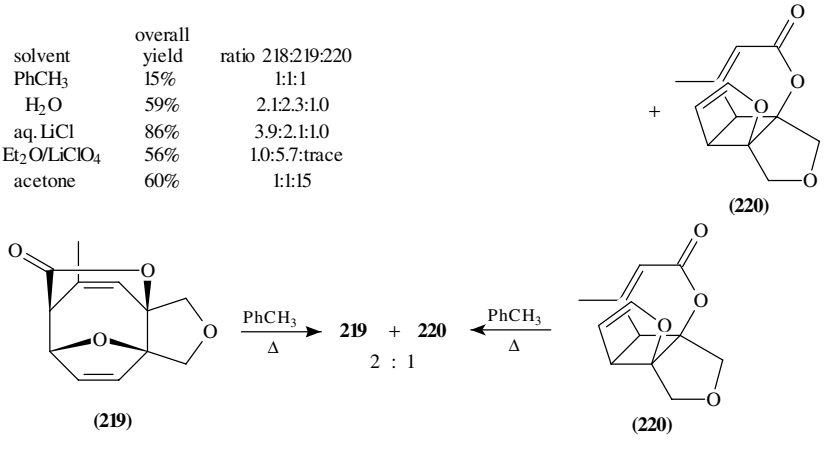
diastereomer via a photo/thermal equilibration have also been reported. As a demonstration of its applicability to natural product targets containing the cyclooctane ring, the pyridone photodimerization process was employed as the key step in the construction of a taxane B-C ring synthon **216** (equation 11)[104].



(11)



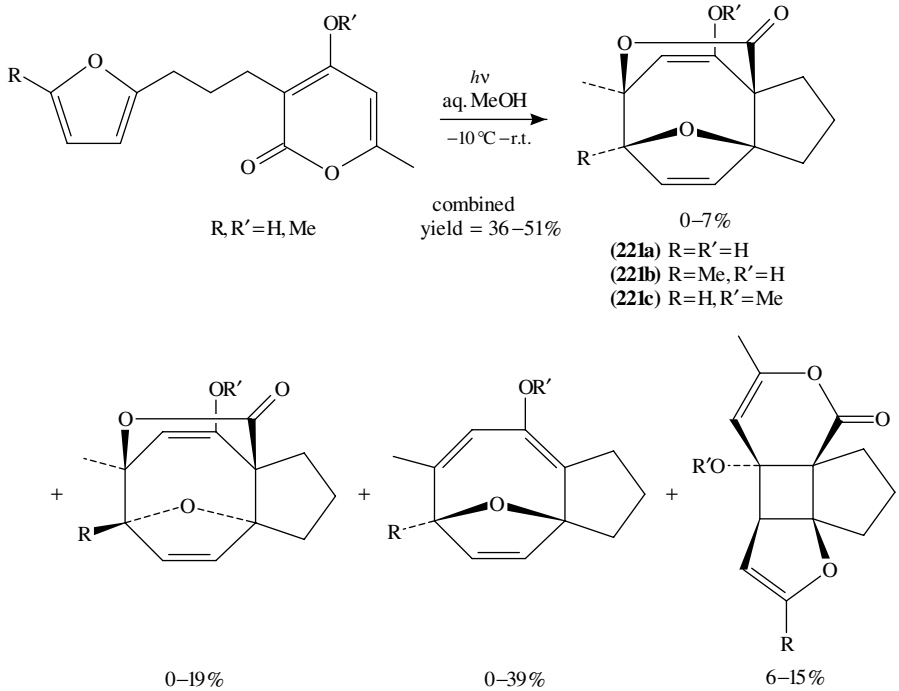
solvent	overall yield	ratio 218:219:220
$PhCH_3$	15%	1:1:1
H_2O	59%	2.1:2.3:1.0
aq. LiCl	86%	3.9:2.1:1.0
$Et_2O/LiClO_4$	56%	1.0:5.7:trace
acetone	60%	1:1:15



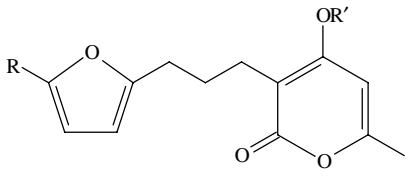
SCHEME 49

West and coworkers have reported a similar approach to functionalized cyclooctanoids via the analogous [4 + 4]-photocycloaddition chemistry of 2-pyrones[105]. Rather than a pyrone–pyrone dimerization process[106], this chemistry entails a crossed [4 + 4]-cycloaddition between a 2-pyrone chromophore and a spectator diene, typically a furan. For example, unsymmetrical ether **217** gave varying amounts of [4 + 4]- and [2 + 2]-cycloadducts **218**, **219** and **220**, depending upon conditions (Scheme 49). The best conversion to [4 + 4]-adducts was obtained by irradiation in the highly organized medium aqueous LiCl. The stereochemistry of *exo* and *endo* diastereomers **218** and **219** was rigorously assigned by heating either **219** or **220** in toluene to give identical ratios of both compounds, presumably through equilibration via [3,3]-shifts. It was also found that extended irradiation led to a disappearance of **220**, and this was shown to involve photocycloreversion to starting material and subsequent conversion to the photochemically inert [4+4]-adducts. This isomerization process bears close resemblance to the photo/thermal equilibration noted by Sieburth and Lin[103b]. Related substrates gave similar results.

Substrates in which the furan was tethered at C-3 have also been examined[107]. These cases typically possessed ring-oxygenation at C-4, and the nature of this substituent proved to be important (Scheme 50). Examples with a free hydroxyl or a methyl ether at this position led to low yields of cycloadducts **221–224** and substantial amounts of polar by-products, possibly via competing solvent trapping pathways which ultimately lead to

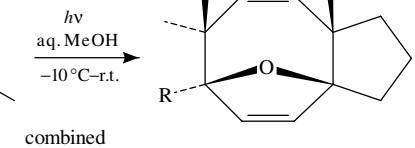


SCHEME 50



R=H, Me; R′ = Ac, Piv, Ts, Tf

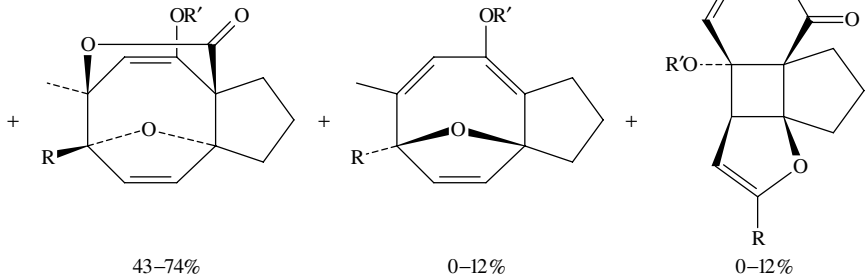
Piv = $Me_3CC(=O)$



combined yield = 67–91%

9–24%

(221d) R=H, R′ = Ac
(221e) R=H, R′ = Piv
(221f) R=Me, R′ = Piv
(221g) R=H, R′ = Ts
(221h) R=H, R′ = Tf



43–74%

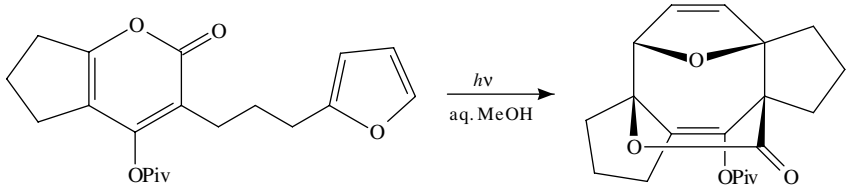
(222d) R=H, R′ = Ac
(222e) R=H, R′ = Piv
(222f) R=Me, R′ = Piv
(222g) R=H, R′ = Ts
(222h) R=H, R′ = Tf

0–12%

(223d) R=H, R′ = Ac
(223e) R=H, R′ = Piv
(223f) R=Me, R′ = Piv
(223g) R=H, R′ = Ts
(223h) R=H, R′ = Tf

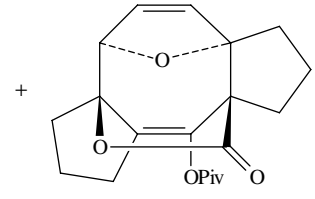
0–12%

(224d) R=H, R′ = Ac
(224e) R=H, R′ = Piv
(224f) R=Me, R′ = Piv
(224g) R=H, R′ = Ts
(224h) R=H, R′ = Tf



(225)

(226a) 20%



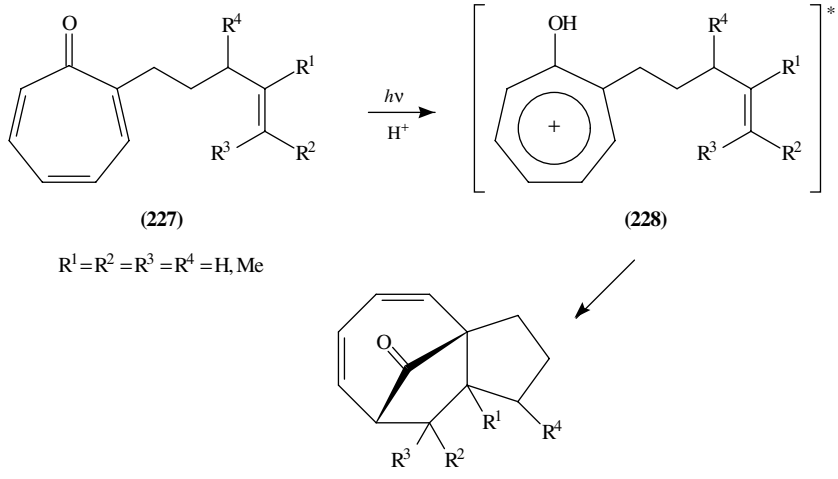
(226b) 58%

SCHEME 50. (*continued*)

acyclic carboxylic acid derivatives[13,14,108]. In contrast, carboxylate- or sulfonate-capped examples underwent efficient conversion to [4+4]-cycloadducts **221** and **222**. Significant amounts of trienes **223** were also observed in certain cases. This product seems to arise from *in situ* decarboxylation of **221** and/or **222**, and the extent of its formation is sensitive to both ring substitution and solvent polarity. The potential applicability of 2-pyrone [4+4]-photocycloaddition chemistry to complex targets was demonstrated in the conversion of **225** to adducts **226a** and **226b** in good yield and in a 1:3 ratio (Scheme 50). These products contain the 5-8-5 tricyclic core found in natural products of the fusicoccane and ophiobolane classes.

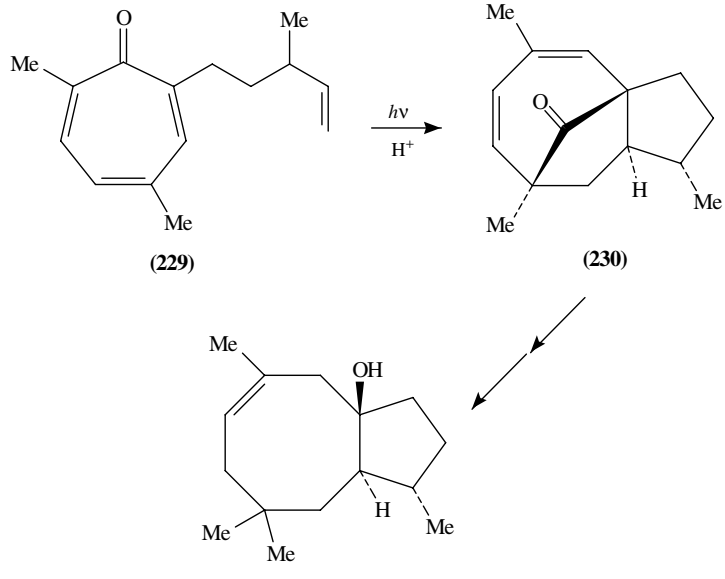
D. Other Higher-order Photocycloadditions

Tropone and its derivatives undergo an extensive and complex set of photochemical reactions[109], and it is only recently that the photochemistry of tropones has been efficiently utilized in natural products synthesis. Feldman and coworkers found that the complex photochemistry of tropones could be avoided by irradiating alkene tethered tropones (e.g. **227**) under acidic conditions and proceeding from the excited state of the corresponding hydroxytropylium ion **228** (Scheme 51)[110]. This critical observation has made the intramolecular [6 + 2]-photocycloaddition of alkene tethered tropones a useful synthetic tool. Though moderate yields of cycloadducts were observed in these reactions, these concerns are attenuated by the ease of preparation of the required substrates and the high degree of complexity change associated with this cycloaddition. Detailed considerations of both the mechanism and stereochemical consequences associated with this cycloaddition are given in the original papers. It is proposed that this photocycloaddition proceeds via an exciplex between the photoexcited tropylium ion and the tethered olefin. The stereochemistry and substitution inherent in this transient presumably determines the product distribution.



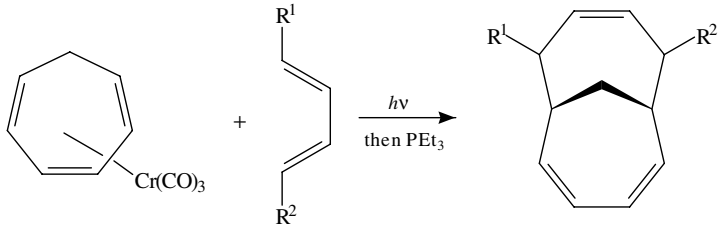
SCHEME 51

The power of this tropylium ion cycloaddition strategy for the synthesis of complex molecules can be seen in synthesis of dactylol **231** by Feldman and coworkers (Scheme 52)[111]. Irradiation of **229** (prepared from 4-methyltropone in two steps) afforded

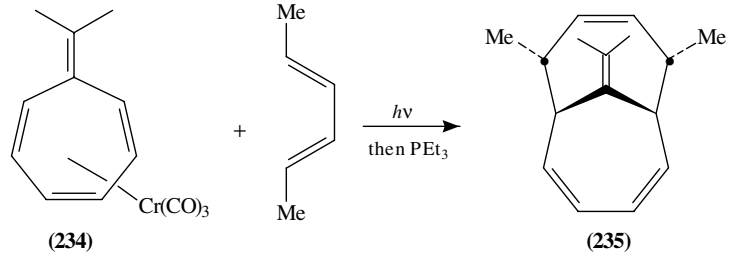


(229) **(230)** **(231)**

SCHEME 52



(232) (R^1 = Me, OAc, OTMS, CO_2Me) (R^2 = H, Me, OAc, CO_2Me) **(233)**



(234) **(235)**

SCHEME 53

230 in 41% yield. This intermediate could be elaborated to dactylol in another four steps via a regioselective cleavage of the one-carbon ketone bridge. This approach is clearly applicable to the bicyclo[6.3.0]undecane skeleton found in many cyclooctanoid natural products. However, the multiple bicyclic systems present in tricyclic adducts such as **230** should permit the use of this chemistry for a wide variety of targets.

In a similar vein, several groups have demonstrated that irradiation of metal complexes (generally chromium complexes) of cyclic polyenes in the presence of alkenes or dienes affords higher-order cycloadducts (either [6+2] or [6+4] cycloadditions, respectively) in good yields[112−120]. While not a 'traditional photochemical' process involving the polyene chromophore, the synthetic appeal and generality of these reactions argues for their inclusion in this chapter. The mechanism of these reactions, albeit complex, can be envisioned to entail initial photochemical loss of CO from the metal center; complexation of the alkene or diene in the vacant coordination site on the metal then initiates C−C bond formation and eventual cycloadduct formation.

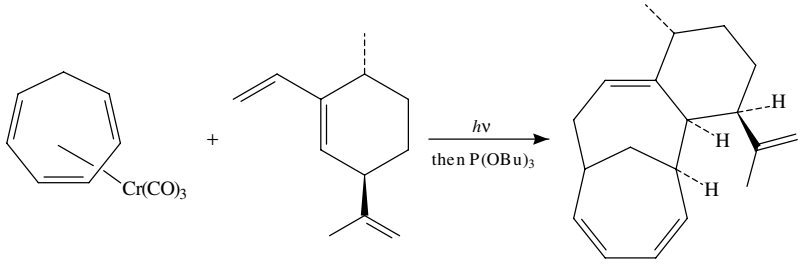
The potential of this technology in complex molecule synthesis is quite high. For example, in early exploratory studies, Kreiter's group found that irradiation of chromium complex **232** in the presence of dienes afforded the cycloadducts **233** in excellent yields following decomplexation of the metal (Scheme 53)[113a,b]. While not specifically delineated in this work, these cycloadditions provide the *endo* adducts exclusively, providing further evidence of the metal acting as a template in the reactions. The same group also found that irradiation of the chromium complex of heptafulvene **234** in the presence of a variety of dienes afforded high yields of the *endo* adducts **235**[113c]. Again, photochemically initiated loss of CO appears crucial to the initiation of this cycloaddition.

Rigby has quite elegantly expanded the scope and generality of these cycloadditions for the construction of complex systems, showing that both [6 + 4]- and [6 + 2]-photocycloadditions using these types of metal complexes provide rapid, efficient entry into a variety of structurally interesting skeleta[114]. For example, irradiation of **232** in the presence of diene **236** [derived from (*R*,*R*)-dihydrocarvone] afforded [6+4]-photoadduct **237** (Scheme 54). Tricyclic adduct **237** can be viewed as a model for the unusual sesterterpene cerorubenol I **(238)**[115]. The [6+2]-photocycloaddition of electron-deficient alkenes with these chromium complexes also proceeds well. This is illustrated by the reaction of **232** with ethyl acrylate, which furnished cycloadduct **239** in good yields following removal of the metal[116].

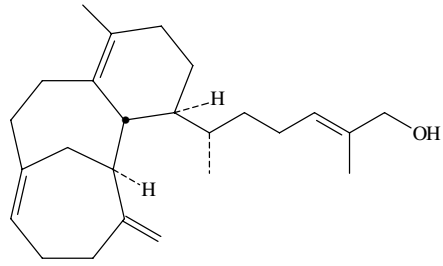
Intramolecular variants of this [6+4]-photocycloaddition efficiently produce very complex polycyclic materials (Scheme 55)[117]. Irradiation of **240** in hexanes followed by decomplexation of the metal with trimethyl phosphite **(241)** afforded the cycloadduct **242** in 85% yield. The corresponding tropone derivative gives the analogous [6 + 4]-cycloadduct in slightly lower yields. The ease of substrate construction coupled with the highly complex nature of these adducts portends great things for this strategy in complex molecule synthesis. The related intramolecular [6 + 2]-cycloaddition (**243** to **244**) was also reported in this paper. It is interesting to note that, in contrast to the intermolecular [6+2]-cycloadditions, the unactivated olefin reacted smoothly to furnish the cycloadduct in an intramolecular sense.

Rigby and coworkers have elegantly demonstrated the utility of these [6 + 4]-photocycloadditions in complex molecule construction in a recent paper which detailed the use of [6 + 4]-cycloadduct **245** as a common intermediate for ingenane **(246)** and phorbol **(247)** fragments (Scheme 56)[118]. It was also found that cycloadduct **248** could be efficiently converted to **249**, which has the generalized taxol ring skeleton, through a Lewis acid catalyzed rearrangement process.

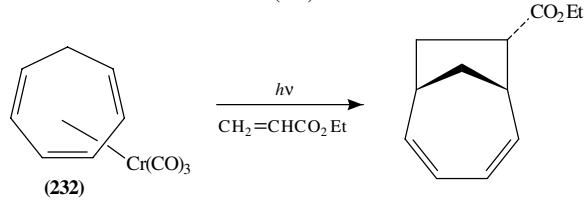
The use of metal complexed heterocyclic polyenes in these cycloadditions has also proven useful, as both the 1,1-dioxythiepine and azepine derivatives **250** and **253** took part in [6+4]- and [6+2]-photocycloadditions, respectively, to afford good yields of the



(232) **(236)** **(237)**

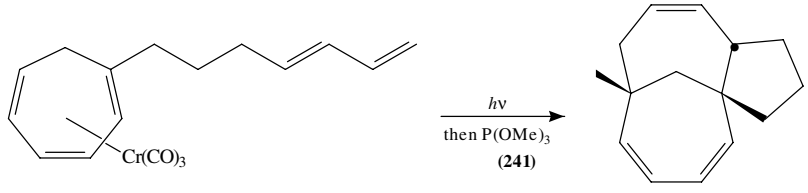


(238)



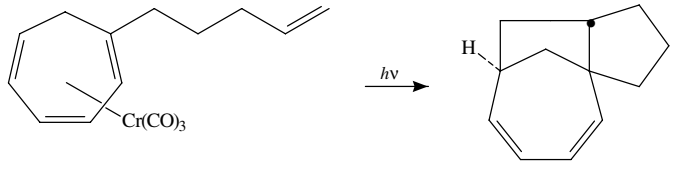
(232) **(239)**

SCHEME 54



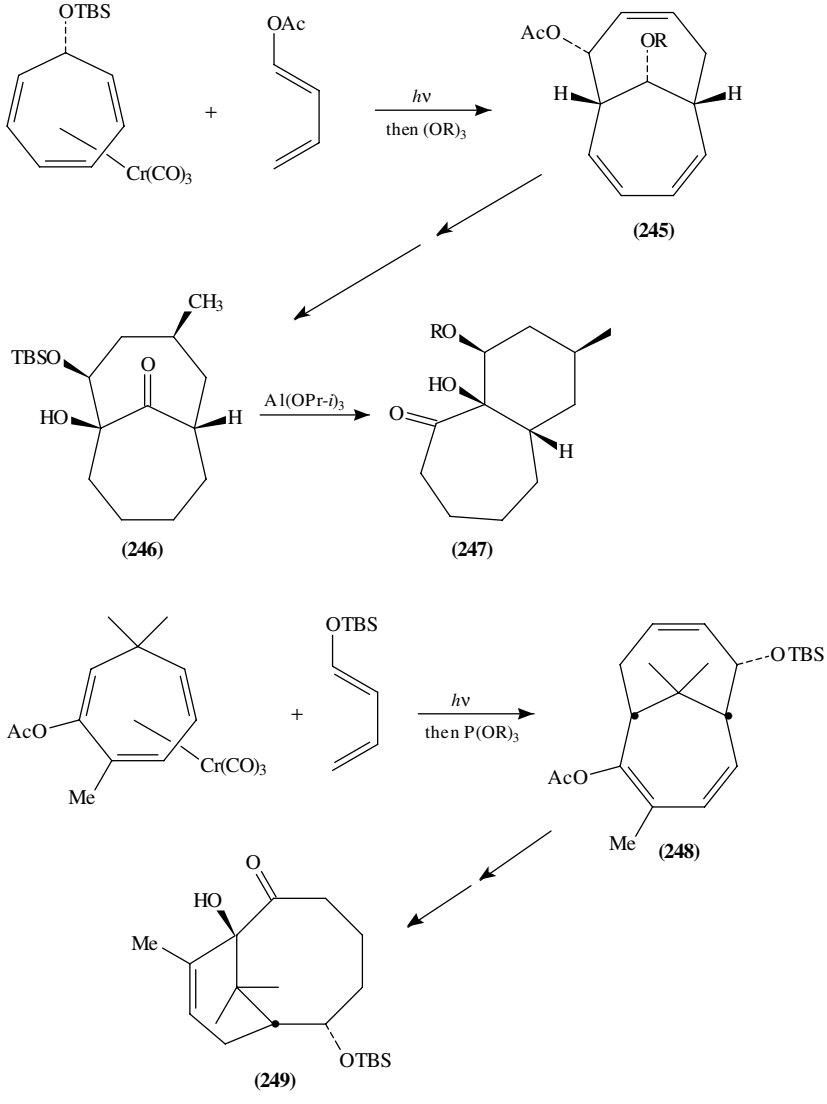
(241)

(240) **(242)**



(243) **(244)**

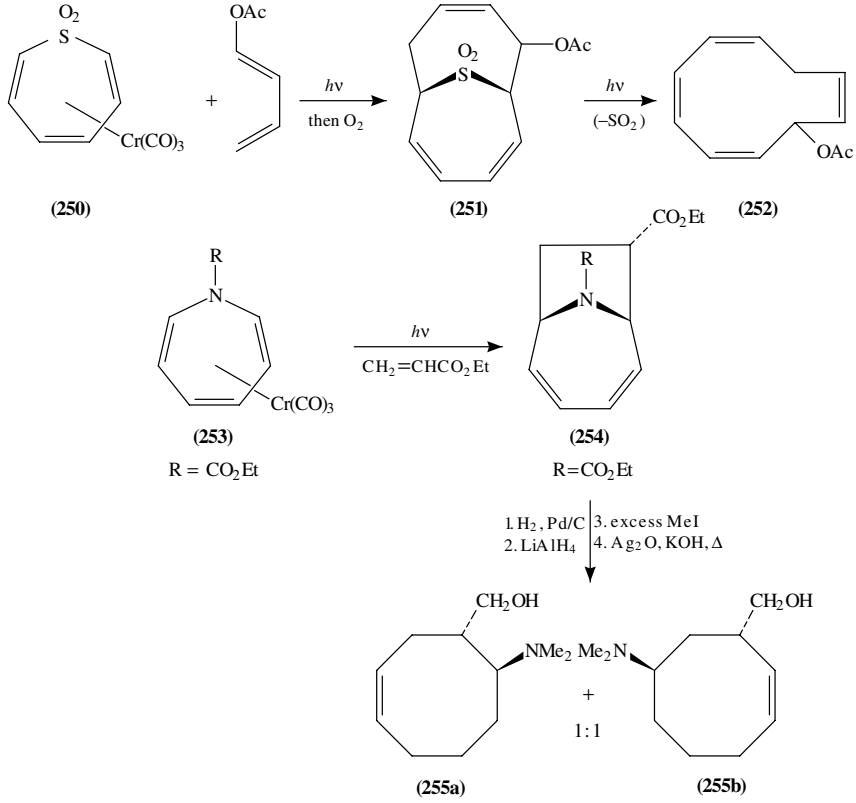
SCHEME 55



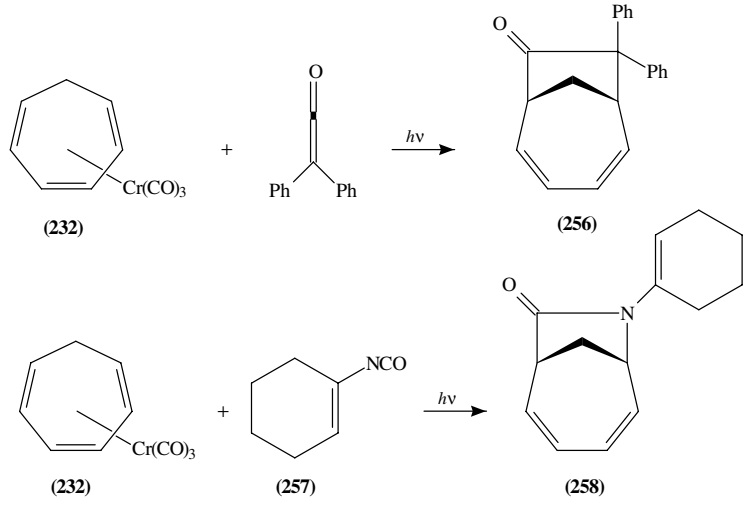
SCHEME 56

cycloadducts **251** and **254** (Scheme 57)[119]. These could be elaborated easily to cyclodecatetraene **252** or isomeric cyclooctenes **255a** and **255b**.

Ketenes and isocyanates also undergo facile [6 + 2]-photocycloaddition with metal complexed cyclic polyenes. Irradiation of **232** in the presence of diphenylketene gave **256** in good yield (Scheme 58)[120]. This should be contrasted with the normal behavior of ketenes toward alkenes, which typically involves [2 + 2]-cycloaddition. Isocyanates such as **257** work as well. The adducts are produced in high yields and have considerable potential in synthesis.



SCHEME 57



SCHEME 58

IV. CONCLUDING REMARKS

It is apparent from the quantity of material included in this chapter that there is an extensive body of work concerning the utilization of diene and polyene photochemistry in a synthetic setting. The unique behavior of the excited chromophores permits the application of powerful new methods for the construction of complex molecules. Unusual photochemical rearrangements and photocycloaddition pathways often lead to substantial increases in molecular complexity, allowing such processes to serve as key strategic steps in target oriented syntheses.

In light of the voluminous amounts of work already accomplished, one may well wonder what remains to be accomplished. In fact, there is much to do in the area of synthetic photochemistry in general, and with synthetic diene and polyene photochemistry in particular. First, many of the powerful transformations described above have not yet been used in total synthetic routes which adequately exploit the new connectivity that is produced. Furthermore, while asymmetric versions exist for many commonly employed reactions, this remains to be explored for most of the photochemical transformations covered in this chapter. In an era which increasingly emphasizes the importance of optically pure target molecules[121], this is clearly an area of emerging importance for synthetic photochemistry. Finally, with a greater understanding of the complex set of factors which control the photochemical reactivity of these systems will come new opportunities to take advantage of predictable photochemical behavior in new media, such as intact biological systems (for controlled formation or release of small, bioactive molecules) or the solid state (for the controlled modification of the structure or properties of 'designer solids'). Given this list of goals, it seems likely that the future will witness the increasing use of these fascinating processes in many new settings.

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CHAPTER **8**

Radiation chemistry of dienes and polyenes

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I. INTRODUCTION

Radiation chemistry is the study of the chemical effects produced in a system by the absorption of ionizing radiation. This definition includes the chemical effects due to radiation from radioactive sources, high-energy charged particles and short-wavelength (less than about 400 Å) electromagnetic radiation from accelerators[1]. The principal characteristic of high-energy radiation is that it causes ionization in all materials. This makes a distinction between radiation chemistry and photochemistry[2,3]. Photochemistry deals with longer-wavelength electromagnetic radiation which have lower energy (less than about 30 eV). This relatively low energy leads in many cases only to the excitation of

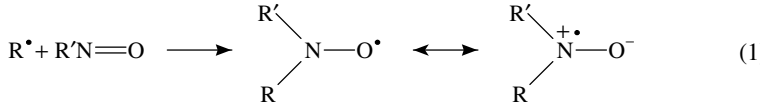
the molecules and does not produce ions. Usually, the energy of the particles and photons applied in radiation chemistry is much higher. The whole energy is not absorbed by a single molecule, as in photochemistry, but rather distributed over several molecules, along the track of the ionizing particle or photon. The high-energy photons and particles are not selective and may ionize, excite or dissociate any molecule lying in their path, while in photochemistry only some compounds may interact with the radiation, in accordance with the energy of the photons.

The high-energy photons or particles lose energy in successive events and produce ions and primary electrons, which in turn form several secondary electrons with lower energies[4]. The chemical effects of ionizing radiation occur almost exclusively through the secondary electrons, most of which have less than 100 eV. These electrons will cause ionization and excitation of the surrounding molecules and will lose energy until they reach thermal energies. In many solvents these thermal electrons polarize the solvent molecules and are bound in a stable quantum state to them; these electrons are called *solvated* electrons. On the average, half of the absorbed energy is spent on ionization while the other half leads to excited molecules.

The study of radiation chemistry might be divided, from the experimental point of view, into two parts. The first is the study of unstable intermediates which have short lifetimes and thus cannot be studied by the usual methods of chemistry. The second part is the study of the final products of the radiolysis which are measured by common chemical techniques.

One way to make the short-lived intermediates amenable to study is to increase their lifetime, usually by irradiation in the solid state and/or at very low temperatures. Then, the intermediates can be detected at the end of the irradiation by ESR or optical absorption spectroscopy. The ESR study of radicals in the solid state is done on single crystals, polycrystalline samples or frozen aqueous solution. In case of polycrystalline samples or frozen aqueous solution the identification of the radicals from the ESR spectra is difficult in many cases and, for better identification, the ESR experiment should be conducted on irradiated single crystals. Later, the method of spin trapping, developed for the liquid phase[5], was extended to polycrystalline solids. In this technique the polycrystalline solids are γ-irradiated and subsequently dissolved in a solution containing the spin trap.

An important method of making the lifetime longer in the liquid phase is by adding compounds which, upon addition of radicals, produce long-lived radicals; this method is called *spin trapping*[5]. In this method a diamagnetic spin-trap is used to convert radicals, which are short-lived, into long-lived radicals. For example, using nitroso compounds (as, e.g., *t*-nirosobutane, *t*-NB) the short-lived radicals form long-lived nitroxide radicals (the spin-adduct) according to equation 1[5]. Several spin traps were used[6].



(1)

More common in the liquid phase is pulse radiolysis[7,8]. In this technique, electron accelerators which can deliver intense pulses of electrons lasting a very short time (ns up to μs) are used. Each single pulse can produce concentrations of intermediates which are high enough to be studied by various methods, such as light absorption spectroscopy or electrical conductivity.

The yields of radiolysis products are always expressed by the G value, which is defined as the number of particles (molecules, radicals, ions) produced or consumed per 100 eV of energy absorbed in the system, or the number of tenths of micromoles produced by 1 joule, i.e. the absorption of 1 joule leads to formation of 1×10^{-7} mole if $G = 1$ or to 0.6 μmole if $G = 6$.

The units for the absorbed energy (dose) are the rad, defined by 1 rad = 100 erg g^{-1} = 6.243×10^{13} eV g^{-1}, and the gray (Gy) defined by 1 Gy = 100 rad.

When radiolysing a solution, the radiation interacts mainly with solvent molecules, since the solution consists mainly of the latter and the radiation interacts with the molecules unselectively. Consequently, the radiation chemistry of a solution is the combination of the production of initial intermediates from the solvent, which will be the same as in pure solvents, and the reaction of those intermediates with the solute.

II. RADIOLYSIS OF AQUEOUS SOLUTIONS OF DIENES

Ionizing radiations (α, β and γ) react unselectively with all molecules and hence in the case of solutions they react mainly with the solvent. The changes induced in the solute due to radiolysis are consequences of the reactions of the solute with the intermediates formed by the radiolysis of the solvent. Radiolysis of water leads to formation of stable molecules H_2 and H_2O_2, which mostly do not take part in further reactions, and to very reactive radicals: the hydrated electron e_{aq}^-, hydrogen atom $H^\bullet$ and the hydroxyl radical $OH^\bullet$ (equation 2). The first two radicals are reductants while the third one is an oxidant. However there are some reactions in which H atom reacts similarly to OH radical rather than to e_{aq}^-, as e.g. abstraction of an hydrogen atom from alcohols, addition to a benzene ring or to an olefinic double bond, etc.

$$\begin{aligned} H_2O &\longrightarrow H_2O^+ + e^- + H_2O^* \\ H_2O^+(+nH_2O) &\longrightarrow {}^\bullet OH + H^+ \\ e^-(+nH_2O) &\longrightarrow e_{aq}^- \\ H_2O^* &\longrightarrow H^\bullet + {}^\bullet OH \end{aligned} \tag{2}$$

In neutral water the radiation chemical yields G are 2.7×10^{-7} mol J^{-1} for the hydrated electron, 2.8×10^{-7} mol J^{-1} for the $^\bullet OH$ radical and 6×10^{-8} mol J^{-1} for the H atom. These values vary slightly with the solute concentration, due to increased reaction with the solute in the radiation spurs. In order to study the reaction of one radical without interference of the others, scavengers have to be added to the system. The best scavengers are those which will convert the unwanted radical to the studied one. This can be done with e_{aq}^-, which can be converted to $^\bullet OH$ or to $H^\bullet$ by the addition of N_2O or H^+, respectively (equations 3 and 4).

$$e_{aq}^- + N_2O \longrightarrow N_2 + OH^- + {}^\bullet OH \quad (k = 9 \times 10^9\ M^{-1}\,s^{-1}) \tag{3}$$

$$e_{aq}^- + H^+ \longrightarrow H^\bullet \quad (k = 2.3 \times 10^9\ M^{-1}\,s^{-1}) \tag{4}$$

The reaction of H atoms can be studied in acidic solution if the OH radicals are scavenged by *t*-butyl alcohol, in a very fast reaction, while hydrogen atoms react only very slowly with this alcohol (equations 5 and 6). The radical produced in equation 5 is relatively unreactive and does not interfere with the study of the reaction of H atoms with the solute.

$$^\bullet OH + (CH_3)_3COH \longrightarrow H_2O + {}^\bullet CH_2C(CH_3)_2OH \quad (k = 5 \times 10^8\ M^{-1}\,s^{-1}) \tag{5}$$

$$H^\bullet + (CH_3)_3COH \longrightarrow H_2 + {}^\bullet CH_2C(CH_3)_2OH \quad (k = 1.7 \times 10^5\ M^{-1}\,s^{-1}) \tag{6}$$

Another method to remove OH radicals and preserving H atoms is by addition of CD_3OH[9,10]. However, due to the high cost of CD_3OH this method was not used after the effect of *t*-butyl alcohol was found.

Hydrated electrons are obtained as predominant radicals by removing the OH radicals with *t*-butyl alcohol. The removal of both H and OH radicals is accomplished by isopropanol (equations 7 and 8).

$$H^{\bullet} + (CH_3)_2CHOH \longrightarrow H_2 + (CH_3)_2C^{\bullet}OH \quad (k = 7.4 \times 10^7\ M^{-1}\,s^{-1}) \tag{7}$$

$$^{\bullet}OH + (CH_3)_2CHOH \longrightarrow H_2O + (CH_3)_2C^{\bullet}OH\ (86\%) + (CH_3)_2CHO\ (1\%) + {}^{\bullet}CH_2CH(OH)CH_3\ (13\%) \quad (k = 1.9 \times 10^9\ M^{-1}\,s^{-1}) \tag{8}$$

A. The Reaction of e_{aq}^- with Dienes

A large difference in the reactivity toward hydrated electrons was found between unconjugated and conjugated dienes. Unconjugated dienes, like 1,4-cyclohexadiene[10], react very slowly with hydrated electrons ($<10^6\ M^{-1}\,s^{-1}$) similarly to a mono double-bond compound, like cyclohexene. On the other hand, compounds with conjugated double bonds react very fast with hydrated electrons. Hart and coworkers[11] found that e_{aq}^- reacts with butadiene with a rate constant of $8 \times 10^9\ M^{-1}\,s^{-1}$, and Michael and Hart[10] found that 1,3-cyclohexadiene reacts with a rate constant of $1 \times 10^9\ M^{-1}\,s^{-1}$. They did not try to explain the quite large difference between butadiene and 1,3-cyclohexadiene.

B. The Reaction of $H^{\bullet}$ Atoms with Dienes

Michael and Hart[10] found that H atoms react quite rapidly with alkenes ($3\times10^9\ M^{-1}\,s^{-1}$ with cyclohexene) and there is not much change for dienes. 1,4-Cyclohexadiene reacts with hydrogen ($4.7\times10^9\ M^{-1}\,s^{-1}$) slightly (*ca* 60%) faster than cyclohexene. The increase of less than two-fold indicates that the hydrogen atom reacts not only by addition to the double bonds, but also by abstraction of the allylic hydrogens (the concentration of double bonds is twofold in 1,4-cyclohexadiene while the number of allylic hydrogens is the same). The reaction of H atoms with 1,3-hexadiene ($k = 9.8 \times 10^9\ M^{-1}\,s^{-1}$) is twice as fast as that with 1,4-hexadiene, indicating that H atoms are mainly added to the conjugated double-bond system. It should be mentioned that later studies on the reaction of H atoms with simple alkenes found higher rate constants, e.g. 7.0×10^9 for 1-butene, 1.0×10^{10} for 2-methylpropene and $5.2 \times 10^9\ M^{-1}\,s^{-1}$ for cyclohexene[12].

C. The Reaction of $^{\bullet}OH$ Radicals

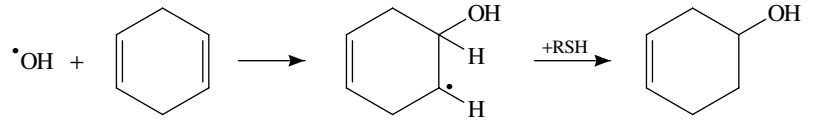
OH radicals react very fast (almost in a diffusion-controlled rate) with simple alkenes ($k = 7.0 \times 10^9$ for 1-butene or cyclopentene and $8.8 \times 10^9\ M^{-1}\,s^{-1}$ for cyclohexene) and there is almost no change for 1,3- or 1,4-cyclohexadiene. Cycloheptatriene reacts very fast with all the three radicals formed in the radiolysis of water: $k = 6 \times 10^9$ with e_{aq}^-, 8×10^9 with H atoms and $1 \times 10^{10}\ M^{-1}\,s^{-1}$ with hydroxyl radicals[13].

D. Absorption Spectra of Intermediates

Michael and Hart[10] found that the reaction of OH radicals (formed by pulse radiolysis of aqueous solutions saturated with N_2O) with 1,3- and 1,4-cyclohexadienes leads to formation of an intermediate absorbing at 310 nm. In the case of 1,4-cyclohexadiene, another band at $\lambda \leqslant 240$ nm was also found. In this system there are both $^{\bullet}H$ atoms and $^{\bullet}OH$ radicals, however the yield of the OH radicals is 10 times higher than that of the $H^{\bullet}$ atoms. Michael and Hart[10] assumed that the band at 310 nm is due to $C_6H_7^{\bullet}$

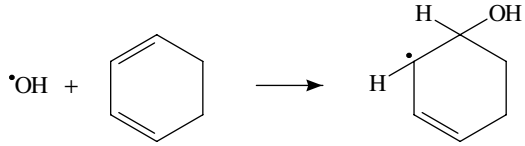
radical formed by •OH radical abstracting an hydrogen atom from either 1,4- or 1,3-cyclohexadiene. The proof for this assignment is that the same spectrum was obtained by the reaction of H atoms with benzene, where addition of the H atom to the benzene ring forms the C_6H_7• radical. Using the molar absorption of the C_6H_7• radical formed in the latter reaction (3300 $M^{-1}\,cm^{-1}$) and the absorption measured with the cyclohexadienes, it can be calculated that •OH abstracts hydrogen from the cyclohexadienes only partially, while the other fraction of radicals probably adds to the double bonds. They calculated that 45% of the •OH radicals abstract hydrogen from 1,4-C_6H_8, while 30% abstract hydrogen from the 1,3-isomer. The lower percentage in the case of the 1,3-isomer agrees with a higher tendency of addition to conjugated double bonds. Since H• atoms react unusually fast with these compounds, they assumed that the H• atoms add exclusively and do not abstract hydrogen atoms.

Von Sonntag and coworkers[14] repeated Michael and Hart's study of the reaction of •OH radical with 1,3- and 1,4-cyclohexadienes and extended it. They found that in the case of 1,4-cyclohexadiene, 50% of the •OH radicals abstract an hydrogen atom, while only about 25% of the •OH radicals abstract an hydrogen atom from 1,3-cyclohexadiene. The remaining •OH radicals probably add to the double bond. The addition to the double bond was confirmed by final products analysis in the case of the 1,4-isomer. When N_2O-saturated aqueous solution of 1,4-cyclohexadiene (10^{-2} M) together with lower (10^{-4} M) concentration of the thiol (1,4-dithiothreitol) was γ-radiolysed, it was found that 4-hydroxycyclohexene was produced with a yield of 0.29 $\mu mol\,J^{-1}$, i.e. a yield of 50% of the OH radicals (equation 9).



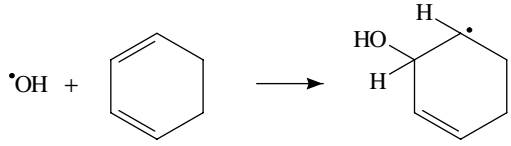
(9)

The 1,3-cyclohexadiene could not be prepared with higher purity than 98% and hence the analysis based on the final products is less meaningful. The yield of 3- and 4-hydroxycyclohexenes show that only 31% (0.18 $\mu mol\,J^{-1}$/0.58 $\mu mol\,J^{-1}$) of the OH radicals add to the double bonds. There is no information about the missing 44% (100% − 25% − 31%). Von Sonntag and coworkers suggested that the yield of hydroxycyclohexenes is not indicative of the OH addition to the double bonds due to non-quantitative reaction of the allylic radical **1** (equation 10) with RSH. Since, in the case of 1,4-cyclohexadiene, they found complete material balance, they concluded that the alkylic radical formed in reaction reacts quantitatively with the thiolic compound. Thus, radical **2** formed in reaction (11) will react quantitatively with RSH. The inefficiency of the reduction of the allylic radical by the thiol is probably due to the weak allylic C−H bond which leads to a six orders of magnitude lower rate constant for the RSH+ allylic radical reaction compared with the RSH+ alkyl radical reaction[15]. If all the material imbalance is due to incomplete reduction of the allylic radical, its formation is the main path of reaction of •OH with 1,3-cyclohexadiene.



(10)

(1)



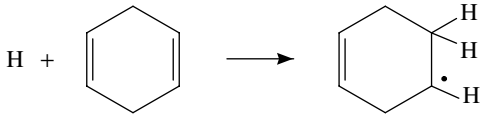
(11)

(2)

The pK_a of the •OH radical is 11.9. The basic form is $O^{-\bullet}$, which predominates at pH $\geqslant$ 12. Von Sonntag and coworkers[14] found that the absorption at 310 nm of pulse radiolysis of pH = 13 N_2O saturated solution of 1,4- or 1,3-cyclohexadiene indicates that $O^{-\bullet}$ anion radical only abstracts hydrogen atoms but does not add to the double bond.

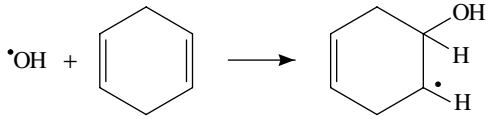
H• atom can both abstract hydrogen atoms and add to the double bonds. However it was found that the predominant reaction is the addition to the double bond. From the absorption of the cyclohexadienyl radical (formed by H abstraction) in acidic solution containing *t*-butanol (to scavenge the •OH radicals) it was concluded[14] that only 22% and 7% of the H atoms abstract hydrogen from 1,4- and 1,3-cyclohexadiene, respectively.

Pulse radiolysis of N_2O-saturated aqueous solution of 1,4-cyclohexadiene leads to formation of three radicals, two by addition of either •OH or H atoms to give the cyclohexenyl radicals **3** and **4** (equation 12 and 13) and one by abstraction of H atoms (equation 14). The last one, the cyclohexadienyl radical, can exist in two mesomeric forms (**5a** and **5b**). Fessenden and Schuler[16] found that the spin density of the cyclohexadienyl radical was highest at the central atom, i.e. form **5a** is the predominant one.



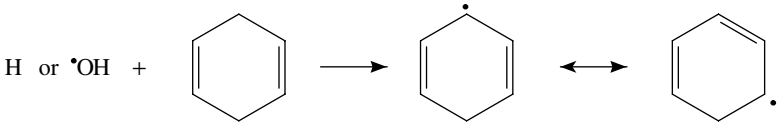
(12)

(3)



(13)

(4)

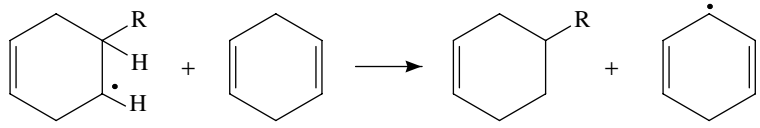


(14)

(5a) **(5b)**

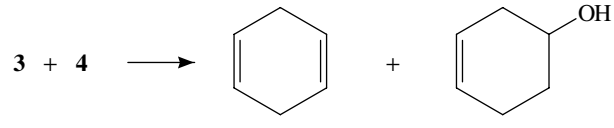
The cyclohexadienyl radicals decay by second-order kinetics, as proven by the absorption decay, with almost diffusion-controlled rate ($2k = 2.8 \times 10^9$ $M^{-1}\,s^{-1}$). The cyclohexyl radicals **3** and **4** decay both in pseudo-first-order bimolecular reaction with the 1,4-cyclohexadiene to give the cyclohexadienyl radical **5** and cyclohexene (or its hydroxy derivative) (equation 15) and in a second order bimolecular reaction of two radicals. The cyclohexene (or its hydroxy derivative) can be formed also in a reaction of radical **3** or

4 with another radical by disproportionation (equation 16).



(15)

(3) R = H or **(4)** R = OH **(5)**



(16)

The fact that 4-hydroxycyclohexene can be formed both by a reaction in which two radicals disappear[16] and in a reaction which does not consume radicals complicates the calculation of the yield of radicals in the γ-radiolysis (continuous radiolysis) of N_2O-saturated aqueous solution of 1,4-cyclohexadiene. Von Sonntag and coworkers[14] wrote that the yield of radical **4** is 0.31 μmol J^{-1}. From their data it must be concluded that 4-hydroxycyclohexene (yield of 0.25 μmol J^{-1}) is formed solely by reaction 15, neglecting its formation by disproportionation (reaction 16). However, they found a yield of 0.085 μmol J^{-1} benzene which can be formed only by disproportionation. Since in pulse radiolysis it was found that the yield of radical **4** is 0.29 μmol J^{-1}, and since its yield in dimers is 0.06 μmol J^{-1} (2×0.02 for dimer **4–4** and 0.02 for 'dimer' **4–5**), it can be concluded that a maximum 0.23 μmol J^{-1} of 4-hydroxycyclohexene was formed by reaction 15 and 0.02 μmol J^{-1} of it came from disproportionation.

The 0.23 μmol J^{-1} of reaction 15 increases the yield of radical **5** from 0.29 in pulse radiolysis to 0.52 μmol J^{-1} in γ-radiolysis. Summing up all the yields of radical **5** gives $2 \times (0.085 + 0.056 + 0.067 + 0.021) + 0.02 = 0.48$. In this calculation we assume that benzene is formed solely from **5** + **5** disproportionation and none from reaction 16. In order to obtain closer agreement between the pulse and continuous radiolysis yields, less than 0.23 μmol J^{-1} should be formed in reaction 15.

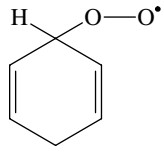
Three types of dimers could be formed by dimerization of the mesomeric radical **5**, i.e. **5a–5a**, **5b–5b** and **5a–5b**. From the yields of the various dimers the equilibrium concentration (the fractional spin density of the two mesomeric forms) can be calculated. (A typographical error in Reference 15 gave two dimers as **5b–5b**). The ratio of the equilibrium concentration can be calculated by

$$\mathbf{5a}/\mathbf{5b} = \sqrt{(\mathbf{5a} - \mathbf{5a})/(\mathbf{5b} - \mathbf{5b})} = 1.63 \text{ or } \mathbf{5a}/\mathbf{5b} = 2(\mathbf{5a} - \mathbf{5a})/(\mathbf{5a} - \mathbf{5b}) = 1.67$$

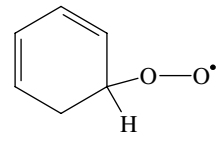
If the product ratios indicate the contribution of hybrid forms **5a** and **5b**, 62% of radicals **5** exist in the **5a** form.

Von Sonntag and coworkers[17] extended this study to the radiolysis of an aqueous solution of 1,4-cyclohexadiene saturated with N_2O:O_2 (4:1) mixture. Due to the higher solubility of N_2O in water all the hydrated electrons react with N_2O to give $^{\bullet}OH$ radicals, as in N_2O-saturated solution. However, the concentration of oxygen is sufficient

to convert the radicals formed from cyclohexadiene to peroxyl radical, before reacting between themselves. O_2 can react also with H atom to produce $HO_2^{\bullet}$. The rate constant for $H^{\bullet} + O_2 \rightarrow HO_2^{\bullet}$ is four times higher than that for $H^{\bullet}$+ cyclohexadiene (2×10^{10} vs 4.7×10^9 $M^{-1}\,s^{-1}$). If the concentration of 1,4-cyclohexadiene is considerably higher than that of O_2(2.4×10^{-4} M), the hydrogen atoms will react preferentially with the cyclohexadiene. The absorption of radical **5** at 310 nm decays faster and, in first-order kinetics, in the presence of oxygen. Using N_2O/O_2 mixtures with at least 80% N_2O showed that the pseudo-first-order rate constant of the decay of the 310-nm maximum is linearly dependent on the oxygen concentration. The slope of this dependence yields the rate constant for $\mathbf{5} + O_2 \rightarrow$ peroxyl radical as $k = 1.2 \times 10^9$ $M^{-1}\,s^{-1}$. Two isomers of cyclohexadienylperoxyl radicals **6a** and **6b** can be formed, by reaction at the two termini of the cyclohexadienyl radical (**5a** ↔ **5b**).



(6a)



(6b)

Most peroxyl radicals are oxidants[18], however the peroxyl radicals formed from the reaction of O_2 with the radicals induced by $H^{\bullet}$/$^{\bullet}OH$ reacting with 1,4-cyclohexadiene are reductants, as was proven by reduction in pulse radiolysis of tetranitromethane (TNM) to yield the strongly absorbing nitroform anion $C(NO_2)_3^{-}$[17]. The build-up of the nitroform anion has two distinctive steps. The major step is a very fast build up with $G = 1.7 \times 10^{-7}$ mol J^{-1}. The second step has a lower yield (0.4×10^{-7} mol J^{-1}) and is about 50 times slower. Only the origin of the first step was studied. Its rate was found to be linearly dependent on the concentration of TNM for low concentration and to reach a plateau at higher concentration. The rate at the plateau was found to be equal to the rate of formation of the peroxyl radical. For high concentration (0.5 mM) of TNM the rate of formation of the nitroform anion depends on O_2 concentration up to 40% O_2, where it reaches a plateau. This plateau can be either due to the rate constant of unimolecular decay of the cyclohexadienyl radical (equation 17), or due to the rate of the deprotonation of $HO_2^{\bullet}$ (equation 18).

$$C_6H_7O_2 \longrightarrow C_6H_6 + HO_2^{\bullet} \tag{17}$$

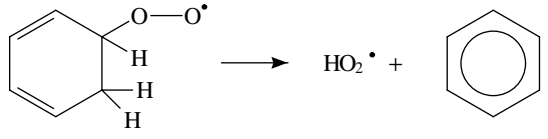
$$HO_2^{\bullet} \longrightarrow H^+ + O_2^{-\bullet} \tag{18}$$

It is known that $HO_2^{\bullet}$ reacts with TNM too slowly to be responsible for the fast build-up, and the build-up must be due to

$$C(NO_2)_4 + O_2^{-} \longrightarrow C(NO_2)_3^{-\bullet} + NO_2 + O_2$$

Using basic pH leads to higher plateau rate constants, indicating that the rate-determining step is reaction 18. Reaction 17 must be at least as fast as the rate of O_2 addition in the highest O_2 concentration used, $k_{17} \geqslant 8 \times 10^5$ s^{-1}, which is the limit of the instrument measurement. The G of benzene in pulse radiolysis was found to be equal to that of the nitroform anion (1.6×10^{-7} mol J^{-1}) as can be expected from reactions 17–19. Since the yield of the cyclohexadienylperoxyl radical is 2.9×10^{-7} mol J^{-1} it means that only a fraction (*ca* 60%) of the cyclohexadienylperoxyl radicals eliminates $HO_2^{\bullet}$. The $HO_2^{\bullet}$ elimination occurs by H-transfer of the allylic hydrogen to the oxygen

atom carrying the odd electron. It can be expected that the rate for this reaction will depend on the distance between these two atoms. Von Sonntag and coworkers[19] estimated that the H–O distance for the 1,3-cyclohexadiene isomer is 1.4–2.2 Å whereas for the 1,4-cyclohexadiene isomer it is 3.5–4.2 Å. Thus, they concluded that only the 1,3-isomer eliminates $HO_2^{\bullet}$ (at least fast enough) to give benzene (equation 19).



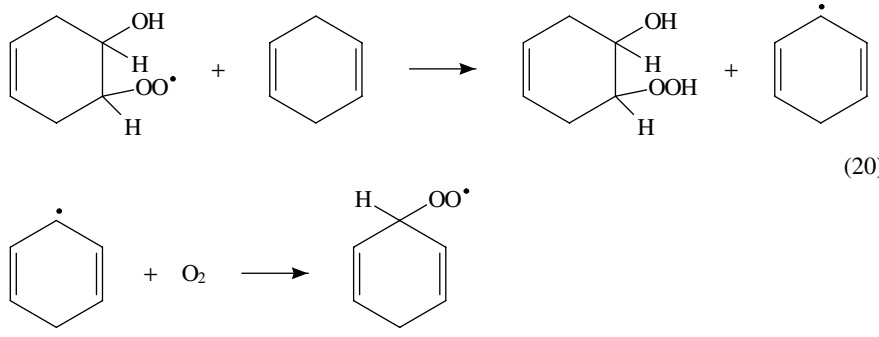
(19)

(6b)

This conclusion is supported by results of detailed study on the decay of hydroxyhexadienylperoxyl radicals, formed by addition of $^{\bullet}OH$ to benzene, followed by addition of dioxygen molecule. It was found that in the high dose rate of pulse radiolysis, hydroquinone is the major product whereas catechol was not observed, indicating that only the 1,3-isomer loses $HO_2^{\bullet}$ and hence does not lead to dihydroxybenzene. The observation that the yield of O_2^- is 60% of the yield of the cyclohexadienyl radicals indicates that when dioxygen molecules react with the cyclohexadienyl radical, the radical is 60% trapped in the mesomeric form of **5b**, whereas the results from the final products of dimerization in γ-radiolysis show that 60% react in the form **5a**.

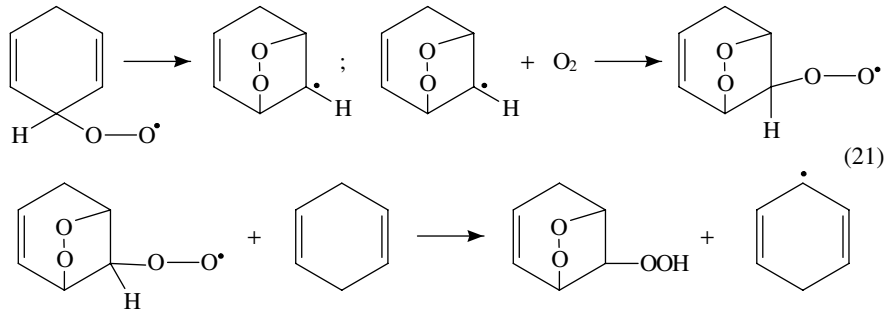
E. Final Products in the Continuous γ-Radiolysis of 1,4-Cyclohexadiene

In the γ-radiolysis of N_2O/O_2 saturated aqueous solution of 1,4-cyclohexadiene (CHD) (10 mM), the major final products are benzene with a radiolytic yield of 2.8×10^{-7} mol J^{-1} (higher than the yield for electron beam pulse radiolysis, where it is 1.6×10^{-7}) and 6-hydroxycyclohex-3-enyl hydroperoxide with the same radiolytic yield (1.5×10^{-7} and 1.3×10^{-7} mol J^{-1}) for the *trans* and *cis* isomers. The other major products are hydrogen peroxide (yield = 2.3×10^{-7} mol J^{-1}), formaldehyde (0.7×10^{-7}), acetaldehyde (0.44×10^{-7}) and cyclohexene endoperoxidic hydroperoxide (0.4×10^{-7}), lactic acid (0.32×10^{-7}) and cyclohex-3-enyl hydroperoxide (0.3×10^{-7} mol J^{-1}). The total oxygen uptake is 7.5×10^{-7} mol J^{-1}. The high oxygen uptake, which is higher than the yield of the radical, is due to some of the radicals reacting consecutively with two molecules of oxygen in the route to produce the hyperoxides, by abstracting hydrogen atom from the cyclohexadiene (CHD), producing another radical which reacts with oxygen (equation 20).



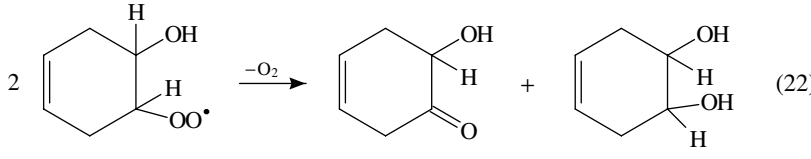
(20)

The peroxyl radical formed in this reaction, as well as by $^{\bullet}OH$ and $H^{\bullet}$ hydrogen abstraction from CHD, can react with another oxygen molecule after intramolecular addition of the peroxyl radical to the double bond to give an endoperoxidic radical (equation 21).



(21)

In the case of low CHD concentration, The abstraction of hydrogen from CHD can be replaced, by reaction with O_2^- and H^+ to give O_2, due to the relatively high concentration of O_2^-. In order to remove O_2^- von Sonntag and coworkers[17] added superoxide dismutase. It was found that for low concentration of CHD and in the presence of superoxide dismutase, the yield of benzene is the same as in pulse radiolysis. In these conditions the oxygen uptake is only 0.56 $\mu mol\,J^{-1}$, equal to the yields of the initially formed OH radicals. The yield of the hydroperoxides is very low (0.6×10^{-7} compared to 3.5×10^{-7} $mol\,J^{-1}$ in the high CHD concentration). In solutions containing superoxide dismutase the yield of the hydroperoxide is an increasing function of the CHD concentration in the range studied (0.5–10 mM). The yield of benzene in pulse radiolysis, or in γ-radiolysis of low CHD concentration with superoxide dismutase, represents the primary yield of 1,3-cyclohexadiene peroxyl radical, which eliminates $HO_2^{\bullet}$ to give benzene. The peroxyl radicals formed from the OH-adduct of CHD disproportionate bimolecularly to 6-hydroxycyclohex-3-en-1-one and 4,5-dihydroxycyclohexene (equation 22).



(22)

cis + *trans*

The yields of 6-hydroxycyclohex-3-en-1-one and 4,5-dihydroxycyclohexene are about equal (0.13 and 0.11 $\mu mol\,s^{-1}$, respectively), in accordance with this mechanism. Their yields account for more that 80% of their precursor — the peroxyl radical of the OH adduct ($G = 0.29$ $\mu mol\,J^{-1}$). Both the *cis* and *trans* isomers of 4,5-dihydroxycyclohexene are formed with the latter being predominant (*ca* 64%).

III. RADIOLYSIS IN NON-AQUEOUS SOLVENTS

We saw previously that hydrated electrons react very rapidly with the conjugated 1,3-butadiene ($k = 8 \times 10^9$ $M^{-1}\,s^{-1}$). In less polar solvents the attachment of an electron to 1,3-butadiene (with adiabatic electron affinity of -0.62 eV[20]) will be slower. The

rate of attachment for non-polar solvents can be increased by increasing the pressure or decreasing the temperature[21,22]. Shida and Hamill[23] γ-irradiated methyltetrahydrofuran glass containing 1,3-butadiene or several homologs at 77 K. They found that the electrons are attached to the 1,3-butadiene, as can be seen by suppression of the solvent-trapped electron band and formation of new bands at 388 and 570 nm. These bands are formed also in other conjugated dienes: isoprene, *cis*-1,3-pentadiene, 2,4-hexadiene, 2,3-dimethyl-1,3-butadiene, 1,3-cyclohexadiene and 1,3-cyclooctadiene. The addition of non-conjugated dienes such as 1,4-cyclohexadiene and 1,5-hexadiene did not decrease significantly the solvent-trapped electron absorption (at 1000–1500 nm), indicating that the electrons are not attached to non-conjugated dienes. The formation of the conjugated diene anion is suppressed by the addition of efficient electron scavengers.

Shida and Hamill[23] found that the positive and negative molecular ions of 1,3-butadiene and its homologs have similar absorption spectra. Band maxima of the anions are not sensitive to substituent alkyl groups, whereas those of the cations are red-shifted as the number of substituent methyl groups increases. In alcoholic matrices the butadiene anions abstract the alcoholic proton to form an allylic radical (equation 23), as was proven by ESR spectroscopy.

$$(CH_2{=}CH{-}CH{=}CH_2)^{-\bullet} + ROH \longrightarrow CH_2{=}CHC^{\bullet}HCH_3 + RO^- \qquad (23)$$

The ESR spectrum obtained for irradiated methanol solution of 1,3-butadiene or *cis*-1,3-pentadiene is similar to that of irradiated methanol solution of allyl chloride, in which case it is known that the electron leads to reductive dehalogenation (equation 24).

$$CH_2{=}CHCH_2Cl + e^- \longrightarrow CH_2{=}CHC^{\bullet}H_2 + Cl^- \qquad (24)$$

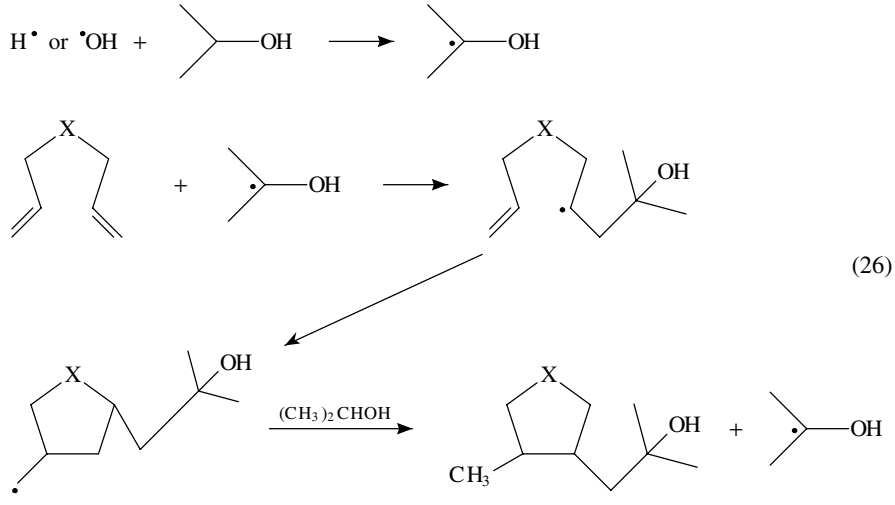
Holroyd and coworkers[24] studied the attachment of excess electrons to 1,3-butadiene in *n*-hexane solution, and the detachment of an electron from the butadiene anion. It was found that the equilibrium constant K for equation 25 increases rapidly with pressure and decreases with increasing temperature, as was found earlier for other molecules with negative electron affinities in non-polar solvents[21]. At $-7\,^{\circ}C$ attachment is observed at 1 bar. At high pressure it was found that the rate of the attachment is diffusion-controlled. Freeman and coworkers[25] measured the free-ion yields in several liquid hydrocarbons, three of which were cyclic dienes, as a function of temperature. At room temperature they measured free-ion yields of 7.5 nmol J^{-1} and 23 nmol J^{-1} for 1,3- and 1,4-cyclohexadiene, respectively. They attributed the lower yield in the case of the conjugated diene to anion formation. It should be pointed out that the yield is even lower in the case of the bicyclic non-conjugated diene, bicyclo[2.2.1]heptadiene where the yield is 5.3 nmol J^{-1}. This is ascribed to a through-space conjugation.

$$e^- + \text{1,3-butadiene} \underset{k_d}{\overset{k_a}{\rightleftharpoons}} (\text{1,3-butadiene})^- \quad K = k_a/k_d \qquad (25)$$

Gamma radiolysis at 77 K of glassy alkanes leads to materials that emit weakly in the visible range on warming, thermoluminescence (TL). Brocklehurst and Robinson[26] studied the radiolysis of glassy 3-methylpentane (MP) and its solutions of olefins. MP alone emits on warming at 430 nm with a broad band, with a G value of 10^{-3}. MP solution of conjugated dienes (1,3-pentadiene and 2,4-hexadiene) give a very strong ($G = 0.05$–0.5) TL broad peak at 490 nm, similar to that found for aromatic solutes (naphthalene and toluene)[27]. This yield shows that both the efficiency of formation and the luminescence quantum yield of the emitter are high. Solution of mono olefins or of non-conjugated dienes give much lower yield with G values of 0.001 to 0.05.

These findings were explained by formation of a luminescent precursor-X, which is formed with very low yield in pure MP, but with higher yield in conjugated dienes solutions. The intermediate, X, was tentatively ascribed to twisted excited states although the possibility of emission by free radicals was not excluded. The assignment of the emitter in solution of butadiene derivatives was studied in detail recently[28]. The authors used glasses (at 77 K) of 2:1 mixtures of methylcyclohexane and isopentane, which were 2 and 10 mM in 10 various butadiene derivatives. After irradiation at 77 K (with doses of 375 or 750 Gy), the thermoluminescence spectra (TL) were measured. The solvent itself gave an emission band in TL at 450 nm. The maximum intensity is about 10 times weaker than that of the dienes, although it is broader, so that the integrated intensity is not much lower. The diene solution TL is at 480–520 nm. Both the width of the spectra (full width half maximum *ca* 85 nm) and the glow peaks were narrower than that of the solvent itself. It was found that the TL spectra were changed only very little with the substitution of the dienes, leading to the conclusion that the luminescence is due to excited states of the parent compound and to radicals formed by abstraction or addition of a hydrogen atom, similar to earlier conclusions for aromatic solutes[26,29].

Shevlin and coworkers[30] studied the radiolysis-induced addition of the α-hydroxy isopropyl radical to substituted 1,6-heptadienes and analogs containing a heteroatom. The radical was generated by γ-irradiation of propanol solutions of various 1,6-heptadienes. It was found that the adduct to the double bond decomposed to give a compound containing a five-membered ring (equation 26).



(26)

X = O, CH_2, CHCOOH, $C(COOH)_2$, NH, NCH_3 $N(CH_2CH{=}CH_2)$, $N(CH_3)_2{}^+Cl^-$

Bobrowski and Das published a series of papers on the transients in the pulse radiolysis of retinyl polyenes[31–37], due to their importance in a variety of biomolecular processes. They studied[32] the kinetics and mechanisms of protonation reaction. The protons were released by pulse radiolysis, on a nanosecond time scale, of 2-propanol air-saturated solutions containing, in addition to the retinyl polyenes, also 0.5 M acetone and 0.2 M CCl_4. Within less than 300 ns, the electron beam pulse results in formation of HCl. The protonated products of retinyl polyenes were found to absorb optically with λ_{max} at the range of 475–585 nm and were measured by this absorption. They found that the protonation rate constants of polyene's Schiff bases depend on the polyene chain

length and geometry. The rate constants are close to the value for diffusion control. As the polyene chain length is increased, a slight increasing trend was observed for the protonation rate constants. They found that the protonation rate constant for all-*trans* retinal is smaller by more than two orders of magnitude than that for its Schiff base, in accordance with the lower basicity of a carbonyl oxygen relative to that of imino nitrogen.

Bobrowski and Das[33] studied the transient absorption phenomena observed in pulse radiolysis of several retinyl polyenes at submillimolar concentrations in acetone, *n*-hexane and 1,2-dichloroethane under conditions favourable for radical cation formation. The polyene radical cations are unreactive toward oxygen and are characterized by intense absorption with maxima at 575–635 nm. The peak of the absorption band was found to be almost independent of the functional group (aldehyde, alcohol, Schiff base ester, carboxylic acid). In acetone, the cations decay predominantly by first-order kinetics with half life times of 4–11 μs. The bimolecular rate constant for quenching of the radical cations by water, triethylamine and bromide ion in acetone are in the ranges $(0.8–2) \times 10^5$, $(0.3–2) \times 10^8$ and $(3 - 5) \times 10^{10}$ $M^{-1} s^{-1}$, respectively.

Bobrowski and Das[35] found that pulse radiolysis of O_2-saturated acetone solution of high concentration (1–10 mM) of all-*trans* retinal, retinoic acid and methyl retinoate give rise to a fast transient absorption process, which is suggested to be due to formation of a dimer cation radical, by association of the original cation radical with the parent polyene. The dependence of the absorption rate of formation on the polyene concentration yields an equilibrium constant (K) of dimerization of 220–440 M^{-1}. For 1,2-dichloroethane solutions of all-*trans* retinal and retinoic acid, K values are larger almost by an order of magnitude. Using non-protic solvents they observed[37] transient species (life time 0.5–7 μs, $\lambda_{max} = 575–590$ nm) from all-*trans* retinal and retinyl methyl ether which were identified as the radical anions. In case of retinyl esters (acetate and palmitate), the radical anions lose instantaneously carboxylate anions to give retinylmethyl radical.

Many studies used radiation chemistry to produce the radical and radical cations and anions of various dienes in order to measure their properties. Extensive work was devoted to the radical cation of norbornadiene in order to solve the question whether it is identical with the cation radical of quadricyclane[38–44]. Desrosiers and Trifunac[45] produced radical cations of 1,4-cyclohexadiene by pulse radiolysis in several solvents and measured by time-resolved fluorescence-detected magnetic resonance the ESR spectra of the cation radical. The cation radical of 1,4-cyclohexadiene was produced by charge transfer from saturated hydrocarbon cations formed by radiolysis of the solvent. In a similar system[46], the radical cations of 1,3- and 1,4-cyclohexadiene were studied in a zeolite matrix and their isomerization reactions were studied. Dienyl radicals similar to many other kinds of radicals were formed by radiolysis inside an admantane matrix[47]. Korth and coworkers[48] used this method to create cyclooctatrienyl radicals by radiolysis of bicyclo[5.1.0]octa-2,5-diene in admantane-D_{16} matrix, or of bromocyclooctatriene in the same matrix. Williams and coworkers irradiated 1,5-hexadiene in $CFCl_3$ matrix to obtain the radical cation which was found to undergo cyclization to the cyclohexene radical cation[49,50] through the intermediate cyclohexane-1,4-diyl radical cation.

Land and coworkers[51] produced by pulse radiolysis of benzene solution, flushed with argon, of carotenoid polyenes, the radical anion and the radical cation of the polyenes. The formation of the radical anion (with absorption at λ_{max} 975 nm) was found to be prevented by saturating the solution with N_2O — an efficient electron scavenger. Kubozono and colleagues[52] irradiated low-temperature (70–130 K) solid solutions of 1,3,5-cycloheptatriene and 1,3-cycloheptadiene in perhalocarbons, in order to produce their radical cations (by losing one electron from the molecule) and measured their structure and dynamics by ESR. For the radical cation of 1,3,5-cycloheptatriene in CCl_3CF_3 they found that ring inversion occurs across the molecular plane. Above 90 K they found

thermal deprotonation of this radical in CCl_2FCFCl_2. Takamuku and coworkers[53] produced the radical cations of 1,ω-bis(diarylethenyl)alkanes $Ar_2C{=}CH(CH_2)_nCH{=}CAr_2$ (Ar = *p*-methoxyphenyl; $n = 2$–4), both by pulse radiolysis and by continuous γ-radiolysis, in 1,2-dichloroethane solution (pulse radiolysis) and in a butyl chloride matrix at 77 K (γ-radiolysis). They found that for $n = 3$, 4 the initially formed radical cations undergo intramolecular cyclization to form 1,4-distonic radical cations (i.e. radical cations in which the cationic and radical sites are separated) as can be proven by their reaction with oxygen.

Takemura and Shida[54] prepared the allene radical ion by γ-radiolysis of halocarbon solid solution of allene at low temperatures and showed that the radical cation has a lower D_2 structure than the precursor with a skew angle of 30–40°. Kubonzo and coworkers[55,56] produced by γ-radiolysis in a low-temperature halocarbon matrix several derivatives of the allene radical cation, i.e. the radical cations of 1,2-butadiene, 3-methyl-1,2-butadiene, 1,2-pentadiene and 2,4-dimethyl-2,3-pentadiene. They studied the structure by ESR spectroscopy, compared it with semiempirical MO calculations and discussed the structure and thermal conversion into neutral radical species. They later extended this study to the radical cations of butatriene and tetramethylbutatriene. By comparing the experimental hyperfine splittings of the ESR spectra with those calculated by semiempirical MO they found skew angles of 25° and 50°, respectively. In all these studies the degassed halocarbon (CCl_3CF_3, CCl_3F, CCl_2FCClF_2, CCl_2FCCl_2F) solid solutions of the diene/triene is irradiated by γ-rays from a ^{60}Co irradiator at 77 K. Fujisawa and coworkers[57] produced, by low-temperature γ-radiolysis, the radical cations of *cis*- and *trans*-1,3-pentadiene and showed that they isomerized to the radical cation of cyclopentene, similar to the findings of Williams and colleagues[49,50] for the 1,5-hexadiene in some matrices. Kubozono and coworkers[58] found that the radical cation of 2,5-dimethyl-1,5-hexadiene in CCl_3CF_3 also isomerized. However, Prasad and coworkers[59] did not find cyclization of the radical cation of 2,5-dimethyl-2,4-hexatriene and 2,7-dimethyl-2,4,6-octatriene in frozen matrices of either CCl_4 or CCl_3F. In low-concentration solution (1%) they obtained the monomeric radical cations, while using 5–10% solution of the polyene together with $AlCl_3$ leads to the formation of the dimeric radical cation.

Prasad and coworkers[60] studied the ESR spectra of cation radicals of dienes, trienes, tetraenes and pentaenes formed in $CFCl_3$ matrix by X-ray irradiation. The structures of the resulting cation radicals were deduced by comparing the experimental coupling constant to those derived from INDO calculation. The unpaired spin density decreases with increasing chain length.

Pulse radiolysis is used also for preparation of excited states of dienes and polyenes. This is done by irradiation of the diene/polyene in toluene solution. The radiolysis of toluene yield high concentration of molecules in the triplet excited state of the solute. Wilbrandt and coworkers[61] pulse-radiolysed 1 mM solution of all-*trans*-1,3,5-heptatriene in toluene solution and observed the absorption spectra of the triplet state of the heptatriene with a maximum at 315 nm. The same group[62] produced and measured the absorption spectra of several isomeric retinals in their lowest excited triplet state by pulse irradiation of their dilute solution in Ar-saturated benzene containing 10^{-2} M naphthalene. Nakabayashi and coworkers[63] prepared the lowest triplet states of 1,3-cyclohexadiene, 1,3-cycloheptatriene and several bicyclic dienes by pulse radiolysis of benzene solution of the cyclic dienes, and measured the triplet life time. Gorman and coworkers[64] produced the triplet state of cycloheptatriene by pulse radiolysis of its solution in toluene. They found that it has considerably longer life (6 ± 1 μs) than the acylic trienes (*ca* 300 ns).

Woodruff and coworkers[65] produced triplet states for several carotenoid pigments by pulse radiolysing benzene solution of the carotenoids with higher concentration of naphthalene. The initially produced excited states of benzenes (both singlet and triplet) are

rapidly converted by energy transfer and intersystem crossing to the triplet state of naphthalene which transfers its energy to the carotenoid. Gust and colleagues[66] prepared in a similar way the triplet states of both polyenes and carotenoporphyrins by using either a benzene solution alone or with a biphenyl as a triplet donor.

IV. REACTIONS WITH DIENES STUDIED BY RADIOLYSIS

Many studies used radiation chemistry and mainly pulse radiolysis, in which a high-intensity pulse of electrons hit the sample, producing high concentration of radicals, to study the reaction of various radicals with several dienes. Nielsen and coworkers[67] used this method to study the rate constants of NO_3 with a series of 7 dienes (1,3-butadiene, isoprene, 2,3-dimethyl-1,3-butadiene, *cis*- and *trans*-1,3-pentadiene, all-*trans*-2,4-hexadiene and 1,3-cyclohexadiene) in the gaseous phase at 295 K and total pressure of 1 atmosphere. The concentrations of NO_3 radicals were measured spectrophotometrically and their temporal behaviour was recorded digitally. Addition of dienes to a gas mixture whose radiolysis leads to formation of NO_3 radicals (0.3% HNO_3 + 99.7% SF_6) accelerates the rate of the decay of NO_3 radicals, and this acceleration is used to derive the rate constant of NO_3 with dienes. Nielsen[68] studied the reaction of SH radicals with 1,3-butadiene in a similar method by pulse radiolysis of H_2S/Ar mixture. Umemoto and coworkers[69] studied in this way the rate constant of a ground-state atomic nitrogen with 1,3-butadiene. Perner and Franken[70] measured the rate constant for the reaction of SH with 1,3-butadiene, 1,4-cyclohexadiene and allene. Nahor and Neta[71] produced, by radiolysis of perfluorobutyl iodide in aerated methanol solutions, the perfluorobutyl radical which reacts subsequently with O_2 to form the perfluoroperoxyl radical. They found that the radical added to the double bond rather than even abstract the doubly allylic hydrogens. Reasonable correlation was found between the rate constants and the σ^* Taft substituent constants.

V. RADIOLYSIS OF BULK DIENES AND OLIGOENES

The yield of free ions in the radiolysis of dienes is very similar to those found for monoalkenes ($G = 4.0–4.2$)[72]. Freeman and coworkers[73] measured the yield of the free ions (G_{fi}) and the secondary electron penetration (b_{Gp}) in radiolysis of unsaturated hydrocarbons. Some of the data are given in Table 1. It can be seen that the yield of the free ions is considerably smaller for the dienes studied. Also, the secondary electron penetration is smaller for the dienes, all of them having a similar value (3.9–4.4 nm).

Ionizing radiation leads also to formation of excited molecules in the triplet state. Okazaki and coworkers[74] calculated the yield of the triplets and found that the yields for conjugated dienes are significantly higher than those of monoalkenes. The yield for 1,3-butadiene is 2.66, whereas the values for 1-butene, 2-butene and 2-methylpropene are 1.51, 1.55 and 1.54, respectively.

The yields of the final products in the radiolysis of liquid aliphatic diene hydrocarbons were studied by van der Heyde and Wagner[75] for 1,5-hexadiene and by Shellberg and coworkers[76] for 2,6-dimethyl-2,6-octadiene. The results are summarized in Table 2. For 1,5-hexadiene, higher yields were obtained for C_6, C_9 and C_{12} products. Also, C_3 products have slightly higher yield. The high yield of C_9 and C_3 products are due to a weaker C−C bond in the allylic position, especially since the rupture of the σ bond between carbon atoms 3 and 4 leads to formation of two allylic radicals. Shellberg and coworkers[76] deduced from their results a free radical mechanism for the formation of hydrogen and light hydrocarbons in the radiolysis of 2,6-dimethyl-2,6-octadiene. The high yield of C_5 products is probably due to larger rupture of the σ bond between carbons 4 and 5 due to simultaneous formation of two allylic radicals.

TABLE 1. Yield of free ions (G_{fi}) and the secondary electron penetration (b_{Gp}) for radiolysis of unsaturated hydrocarbons

Hydrocarbons	T (K)	G_{fi}	b_{Gp} (nm)
Monoalkenes			
1-Butene	293	0.093	5.4
trans-2-Butene	293	0.080	5.3
cis-2-Butene	293	0.23	7.4
Isobutene	293	0.25	7.4
2-Methyl-2-butene	292	0.26	8.0
2,3-Dimethyl-2-butene	293	0.44	10.1
1-Hexene	293	0.10	5.2
trans-2-Hexene	293	0.092	5.1
trans-3-Hexene	293	0.10	5.3
cis-3-Hexene	293	0.13	5.6
Cyclohexene	293	0.20	6.2
Dienes			
Propadiene	282	0.050	4.3
1,3-Butadiene	269	0.038	3.9
1,4-Pentadiene	293	0.067	4.4
1,5-Hexadiene	292	0.066	4.2
1,6-Heptadiene	292	0.066	4.2
1,7-Octadiene	292	0.065	4.1
Alkynes			
Propyne	260	0.17	4.8
2-Butyne	293	0.32	9.7
1-Hexyne	253	0.10	4.4
2-Hexyne	293	0.19	6.8
3-Hexyne	293	0.21	7.1

TABLE 2. Yields of final products from radiolysis of liquid aliphatic dienes (G, molecule/100 eV)

Hydrocarbons / Products	1,5-Hexadiene	2,6-Dimethylocta-2,6-diene
Hydrogen	0.45	0.80
Methane		0.052
C_2 products	0.06	0.07
C_3 products	0.09	0.023
C_4 products	0.06	0.050
C_5 products	0.02	0.068
C_6 products	0.41	
C_7 products	0.02	
C_8 products	0.02	
C_9 products	0.42	
C_{10} products	0.02	
C_{12} products	0.77	

The radiation chemistry of cyclic oligoenes was studied, and the radiolytic yields of the final products are summarized in Table 3, which shows that 1,4-cyclohexadiene differs from all others in its high yield of hydrogen, both in the gas phase and in the liquid phase. Cserep and Foldiak[84] attributed it to the presence of two doubly allylic CH_2 groups. In addition, the geometric orientation of the allylic hydrogens is favourable for hydrogen

TABLE 3. Radiolytic yields of the final products of the radiolysis of cyclic oligoenes

I. Liquid phase

Substrate / Product	1,3-cyclo hexadiene[77]	1,4-cyclo hexadiene[78]	cyclo heptatriene[80]	1,3-cyclo octadiene[77]	cycloocta tetraene[81]	1,5,9-cyclo dodecatriene[77]
Hydrogen	0.22	1.18, 0.94[a]	0.06	0.24[a]	0.02	0.44
Methane	0.0015		0.0014	0.01		
$C_2 + C_4$ products	0.0079	0.08	0.016	0.021	0.018	0.57
1,3,5-Hexatriene		2.3				
Benzene		2.9				
Toluene			0.5			

[a]Reference 79.

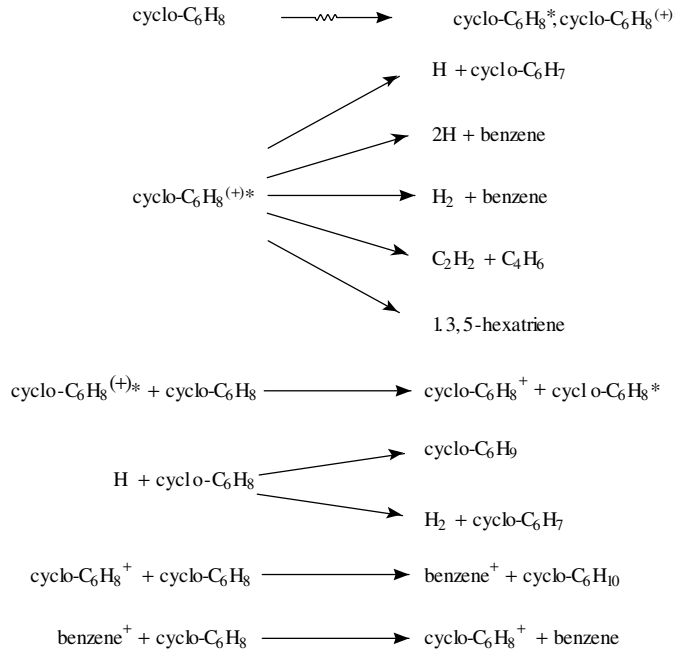
II. Gas phase

Substrate / Product	1,4-Cyclohexadiene[82]	Cycloheptatriene[83]
Hydrogen	1.95	0.50
Methane	trace	0.16
$C_2 + C_4$ products	1.25	1.52
Cyclopentadiene		0.29
Cyclohexene	14.0	
1,3-Cyclohexadiene	1.0	
1,3,5-Hexatriene	1.0	
Benzene	28.5	0.65

elimination. Two of the allylic hydrogens are perpendicular to the plane of the −CH=CH− group and are on the same side of the ring. However, Sakurai and coworkers[82] suggested a predominantly radical pathway for hydrogen formation in the gas-phase radiolysis of 1,4-cyclohexadiene, on the basis of the effect of NO on the yield of hydrogen. The geometric orientation is not important for the radical mechanism. While the yield of H_2 from radiolysis of cyclohexene is independent of dose up to 2000 J g^{-1}, the radiolytic yield of hydrogen from 1,4-cyclohexadiene decreases with increasing dose already from 300–400 J g^{-1}. This was ascribed to the effect of the other products, 1,3-cyclohexadiene, benzene and 1,3,5-hexatriene. Sakurai and coworkers[82] suggested Scheme 1 for the gas-phase radiolysis of 1,3-cyclohexadiene. In this scheme $C_3H_8^{(+)^*}$ denotes an excited molecule or ion.

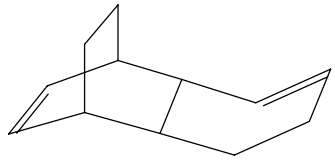
Okada and coworkers[78] studied the γ-radiolysis of 1,3- and 1,4-cyclohexadienes. From ESR studies and product determination they concluded that the main primary process for radiolysis of both isomers is the dissociation of allylic C−H bonds. The formed hydrogen atoms may add to double bonds or abstract other hydrogen atoms (mainly allylic ones). The ESR spectrum of the radiolysis product at 77 K showed the presence of the cyclohexadienyl radical in the case of 1,4-cyclohexadiene, whereas the main intermediate from 1,3-cyclohexadiene is the 2-cyclohexenyl radical[78,85], formed by addition of hydrogen atom to the parent molecule. This difference is in agreement with the higher reactivity to addition of radicals of the conjugated alkadienes.

Irradiation of mixtures of cyclohexene with 1,3-cyclohexadiene leads to high yield of dimers ($G = 6.3$)[86]. Schutte and Freeman[87] found that radiolysis of 1,3-cyclohexadiene dissolved in various solvents gives dimers mainly via cationic Diels-Alder addition,

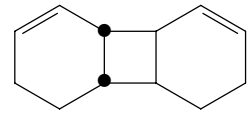


SCHEME 1

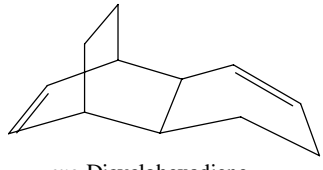
however another process is also involved, probably through a triplet excited state. Both processes are sensitized by benzene. Hammond and coworkers[88] postulated the formation of the four different dimers shown below from radiolysis of 1,3-cyclohexadiene, all of which are formed via the triplet state.



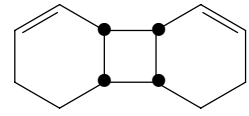
endo-Dicyclohexadiene



trans, cis, trans-Tricyclo [6.4.0.0] dodeca-3, 11-diene



exo-Dicyclohexadiene



cis, cis, cis-Tricyclo [6.4.0.0] dodeca-3, 11-diene

On the other hand, the 1,3,5-hexatriene was postulated to be formed from the singlet excited state. On the basis of electron-scavenging experiments it was concluded that the

triplet state is probably largely due to neutralization, whereas the higher-energy singlet state is formed by primary excitation.

Cyclopentadiene behaves differently than the cyclohexadienes in that its radiolysis leads to high molecular weight polymer via a cationic mechanism[89], whereas such compounds are not formed in high yield from cyclohexadienes irradiated in the liquid phase.

The radiolysis of cycloheptatriene was studied in both the liquid and the gaseous phase. Increase of the pressure in the gas-phase radiolysis enhances the yields of acetylene and dimers and decreases those of benzene, toluene and cyclopentadiene. ESR studies[80] show similar signals to those obtained from benzene. The production of toluene in the radiolysis of cycloheptatriene was assumed to be via isomerization of excited heptatriene molecules, which were supposed also to lead to cyclopentadiene and acetylene, since their yields were almost unaffected by radical or ion scavengers. The energy of the precursor to cyclopentadiene and acetylene is probably higher than the energy of the precursor of toluene, since the yields of the two former compounds is pressure-independent. Since the yield of acetylene is higher than that of cyclopentadiene, it must be formed also by other processes, probably breaking the C_7 molecule into two C_2 and one C_3 molecules, or otherwise the cyclopentadiene is destroyed by a further reaction.

Shida and coworkers[81] found that cyclooctatetraene is even more radiation-resistant than benzene.

VI. RADIATION-INDUCED OLIGOMERIZATION AND POLYMERIZATION OF DIENES

Brown and white[90] studied the polymerization of several olefins and dienes in thiourea canal complexes, as molecular templates, for carrying out radiation-induced selective and stereospecific polymerization. High melting, crystalline, *trans*-1,4-addition polymers were obtained from 2,3-dimethylbutadiene, 2,3-dichlorobutadiene, 1,3-cyclohexadiene and cyclohexadiene monoxide. The yield and quality of the poly-*trans*-1,4-dimethylbutadiene obtained from a given dose of irradiation was virtually independent of temperature in the range $-78\,^{\circ}C$ to $+30\,^{\circ}C$ and of dose rate in the range 2.9 to $2.3 \times 10^5\ r\,s^{-1}$. This behaviour is indicative of the absence of bimolecular interactions between growing chains, as would be expected for the polymerization of physically isolated sequences of monomers in canals. The lengths of the polymer obtained from carefully prepared dimethylbutadiene complexes were found to be 100–200 monomer units. Impurities, such as alkanes or cresols, reduce the molecular weight of the polymer.

White[91] used a 1,3-butadiene–urea canal complex to produce all-*trans*-1,4-polybutadiene. The complex is formed only at temperatures in the range $-55\,^{\circ}C$ to $25\,^{\circ}C$ and needs a small amount of methanol to be formed.

Alcock and coworkers[92] studied the polymerization of butadiene (as well as of monoolefins, acetylene and aromatic olefins) trapped within the tunnel clathrate system of tris(*O*-phenylenedioxy)cyclotriphosphazene, induced by ^{60}Co-γ-radiation. The host was used in order to find if the concatenation and orientation of the monomer molecules under the steric forces generated within the host crystal lattice will lead to stereospecific polymerization. The clathrate was prepared by addition of liquid butadiene to the pure host at low temperature. The irradiation was conducted at low temperatures. Irradiation of pure butadiene (unclathrated bulk monomer) leads to formation of a mixture of three addition products: 1,2-adduct, *cis*- and *trans*-1,4-adducts. In contrast, the radiation-induced polymerization within the tunnel system of the host yielded almost pure *trans*-1,4-polybutadiene. A small percentage of 1,2-addition product was observed, but no evidence for the formation of *cis*-1,4-adduct was found, confirming the earlier observation by Finter and Wegner[93]. The average molecular weight was about 5000,

corresponding to 100 monomer units. This work was extended[94] to several dienes: 2,3-dimethylbutadiene, isoprene, *trans*-piperylene, *trans*-2-methyl-1,3-pentadiene, 4-methyl-1,3-pentadiene, chloroprene and 1,2-cyclohexadiene. Some mixtures of two dienes were also studied. It was found that for all these monomers, radiation-induced polymerization of the clathrate leads to *trans*-1,4-addition polymers. Radiation-induced polymerization of the monomers alone (without the host material) lead also to other reactions. Bulk polymerization (not constrained in clathrate) of 2,3-dimethylbutadiene yields a polymer that contained a mixture of both 1,4-*cis* and 1,4-*trans* sequences, in equal proportion. The molecular weight is about 3700 (45 monomer units). Similar results were obtained for ^{60}Co-radiation-induced polymerization at $-78\,^{\circ}$C and $25\,^{\circ}$C. The molecular weight of the polymer formed in the clathrate was 1000 (12 monomer units), all-1,4-*trans* addition for both $-78\,^{\circ}$C and $25\,^{\circ}$C irradiation. γ-Ray-induced polymerization of isoprene monomer in the bulk state yielded a high polymer that contained both 1,4-*cis* and 1,4-*trans* addition sequences, with higher proportion of the *trans* addition product. The molecular weight was 140,000 (2000 monomer units). Similar results were obtained at $25\,^{\circ}$C and $-78\,^{\circ}$C. Radiation-induced polymerization of clathrated isoprene yielded only 1,4-*trans*-polyisoprene with molecular weight of 24,000 (350 monomer units), at both $-78\,^{\circ}$C and $25\,^{\circ}$C irradiation. No noticeable post-polymerization effects could be detected (also for 2,3-dimethylbutadiene). For *trans*-piperylene, similar results to those of isoprene were found, except for the molecular weight. Bulk monomer radiative polymerization lead to molecular weight of 5700 (85 monomer units), whereas the polymerization of the clathrate yielded polymer with molecular weight of 13,000 (190 monomer units). In this case the clathrate leads to higher molecular weight, whereas for the previous monomers the opposite trend was observed.

Bulk polymerization of *trans*-2-methyl-1,3-pentadiene lead only to 1,4-*trans* addition polymer, however it allows randomization of the *trans* structure, leading to an atactic polymer. The polymerization of the clathrate of *trans*-2-methyl-1,3-pentadiene yielded an isotactic 1,4-*trans* addition polymer. The polymer formed from the bulk had a molecular weight of 20,000 (240 monomer units), and that formed from the clathrate had a molecular weight of 1000 (12 monomer units). Similar results were obtained for other dienes, and the results are summarized in Table 4. It can be concluded that polymerization of dienes in the clathrate lead exclusively to a 1,4-*trans* addition polymer, except in the case of 1,3-cyclohexadiene. For this monomer, although the polymer is formed entirely by 1,4-addition, the polymer formed is essentially atactic. In bulk polymerization, the polymerization proceeds in most cases through 1,4-addition (both *trans* and *cis*), but in the case of butadiene and 1,3-cyclohexadiene 1,2-additions were also observed. Actually, in the case of the bulk γ-induced polymerization of 1,3-cyclohexadiene the 1,2-addition process was favoured over the 1,4-addition process by a ratio of 4:3.

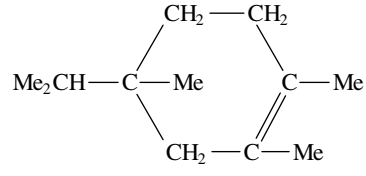
Ichikawa and coworkers[95,96] studied the polymerization and oligomerization of 2,3-dimethylbutadiene together with 2,3-dimethylbutane in thiourea clathrates. They found that the addition of 2,3-dimethylbutane to 2,3-dimethylbutadiene clathrates markedly lower the radiolytic yield of disappearance of monomers, G(-monomers), together with reducing the length of the formed polymer, as can be observed by the decrease of the melting point of the polymer, similar to the results of Brown and White[90]. An ESR study[97] showed that both monomer and polymer radicals of 2,3-dimethylbutadiene (DBE) are trapped in irradiated clathrate containing a mixture of 30% DBE and 70% 2,3-dimethylbutane (DBA). The ESR result suggests the formation of oligomer radicals of DBE. Ichikawa and coworkers[96] studied the formation of dimers of DBE by irradiation of thiourea clathrates containing mixtures of DBE and DBA. Three different dimers were formed — the linear dimer 2,3,6,7-tetramethyl-2,6-octadiene **(7)** and the two cyclic dimers 1,2,4-trimethyl-4-isopropylcyclohexene **(8)** and 1,2,4-trimethyl-4-isopropenylcyclohexene **(9)**. (Note however, that **9** is not a dimer, since it contains two fewer hydrogens).

TABLE 4. Characteristics of the polymers obtained by ^{60}Co-radiation-induced polymerization of dienes

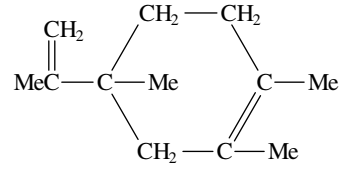
Monomer	Physical state	Stereochemistry	Molecular weight (kD)
Butadiene	bulk	1,4-*cis*, 1,4-*trans* and 1,2-	—
Butadiene	clathrated	1,4-*trans*	5.0
2,3-Dimethylbutadiene	bulk	1,4-*cis* and 1,4-*trans*	3.7
2,3-Dimethylbutadiene	clathrated	1,4-*trans*	1.0
Isoprene	bulk	1,4-*cis* and 1,4-*trans*	140
Isoprene	clathrated	1,4-*trans*	24
trans-Piperylene	bulk	1,4-*cis* and 1,4-*trans*	5.7
trans-Piperylene	clathrated	1,4-*trans*	83
trans-2-Methyl-1,3-pentadiene	bulk	atactic 1,4-*trans*	20
trans-2-Methyl-1,3-pentadiene	clathrated	isotactic 1,4-*trans*	1.0
4-Methyl-1,3-pentadiene	bulk	1,4-*trans*	38
4-Methyl-1,3-pentadiene	clathrated	1,4-*trans*	3.6
Chloroprene	bulk	1,4-*trans*	84
Chlotoprene	clathrated	1,4-*trans*	2.9
1,3-Cyclohexadiene	bulk	1,2- and 1,4-	4.5
1,3-Cyclohexadiene	clathrated	atactic 1,4-	6.7
Isoprene/2,3-dimethylbutadiene (1:1, V:V)	bulk	1,4-*cis* and 1,4-*trans*	50
Isoprene/2,3-dimethylbutadiene (1:1, V:V)	clathrated	1,4-*trans*	1.6
Isoprene/butadiene (1:1, M:M)[a]	bulk	1,2; 1,4-*cis* and 1,4-*trans*	3.0
Isoprene/butadiene (1:1, M:M)[a]	clathrated	1,4-*trans*	1.0
Isoprene/*trans*-piperylene (1:1, M:M)[a]	bulk	1,4-*cis* and 1,4-*trans*	3.9
Isoprene/*trans*-piperylene (1:1, M:M)[a]	clathrated	1,4-*trans*	4.0

[a]M:M = monomer:monomer

(7)



(8)



(9)

The yields of each of the dimers reached maxima at about the same DBA content of 80% (DBA:DBE = 4:1). The total dimer yield reached 6% of the DBE at a dose of 3 MGy. At the same time the yield of the polymer is 11% and the unreacted DBE is 3%. Thus 80% of DBE is converted to trimers and higher oligomers.

Chapiro[98,99] irradiated liquid butadiene at 15 °C with γ-rays at a very low dose rate. The polymerization rate was very slow, 1×10^{-8} s^{-1}, at a dose rate of 0.023 rad s^{-1}. The

product was a high-molecular-weight rubber. Anderson[100] used high-energy electrons to polymerize butadiene in the temperature range of $-195\,^{\circ}C$ to $0\,^{\circ}C$. Both the rates of the polymerization and the molecular weight of the polymer decreased with increasing temperature. The infrared spectrum of the polymer showed that the relative *cis*-1,4-, *trans*-1,4- and 1,2-double bonds were the same as with polybutadiene prepared with cationic initiators. The structure of the polymer did not change considerably with the polymerization temperature, indicating that the radiation-induced polymerization of butadiene occurs via a cationic mechanism, at least at the lower temperatures. However, in emulsion the cationic process was suppressed and the reaction proceeded mainly via a free radical mechanism.

Few experiments with poor reproducibility were done[101] on γ-ray-induced polymerization of butadiene adsorbed on carbon black.

Chapiro[102] polymerized liquid isoprene at 20 and $45\,^{\circ}C$ by γ-ray irradiation. The rate was found to be temperature independent and to increase with the square root of the dose rate (in the range 0.5–9.7 rad s^{-1}). Burlant and Green[103] polymerized isoprene at $-40\,^{\circ}C$ with a higher dose rate (35 rad s^{-1}) and obtained about 5.5 times higher rate of polymerization than Chapiro at 9.7 rad s^{-1}, which suggests that the reaction has a negative activation energy, similar to butadiene. The negative activation energy together with the structure of the resulting polymer indicate that the polymerization, at least in part, is due to ionic processes.

VII. RADIATION CHEMISTRY OF POLYBUTADIENE AND POLYISOPRENE

Butadiene and isoprene have two double bonds, and they polymerize to polymers with one double bond per monomeric unit. Hence, these polymers have a high degree of unsaturation. Natural rubber is a linear *cis*-polyisoprene from 1,4-addition. The corresponding *trans* structure is that of gutta-percha. Synthetic polybutadienes and polyisoprenes and their copolymers usually contain numerous short-chain side branches, resulting from 1,2-additions during the polymerization. Polymers and copolymers of butadiene and isoprene as well as copolymers of butadiene with styrene (GR-S or Buna-S) and copolymers of butadiene with acrylonitrile (GR-N, Buna-N or Perbunan) have been found to cross-link under irradiation.

Golub[104] studied the radiolysis of high *cis*-polybutadiene. He found that the olefinic group concentration decreased with high yield [G(-double bond) $= 7.9$] together with a similar yield of conversion of the *cis* to the *trans* form ($G = 7.2$). Kuzminski and coworkers[105] reported earlier on a much higher radiolytic yield of double-bond disappearance [G(-double bond) *ca* 2000]. More extensive study was done by Parkinson and Sears[106]. They found that both *cis*-1,4-polybutadiene and *trans*-1,4-polybutadiene lose part of their olefinic groups after irradiation. In the *cis* specimens they found formation of olefinic groups in the *trans* form (the *cis* form absorbs at 740 and 3012 cm^{-1}, whereas the *trans* olefinic form absorbs at 967 cm^{-1}). In the high *trans*-1,4 polymer they found that an additional change is the destruction of the crystallinity. Since the degree of crystallinity influences the absorbance, it is difficult to measure accurately the radiation yields of loss of olefinic groups in *trans*-1,4 specimens. Using the absorptivities of crystalline and amorphous polymers they could set the upper and lower yields of double-bond destruction. At moderate doses the decrease of *cis*-vinylene groups follows a linear rather than a semilogarithmic plot, i.e. a zero-order rather than first-order decay as a function of dose. The formation of *trans*-vinylene groups in the radiolysis of *cis*-1,4-polybutadiene is a complex process, reaching a maximum when the concentration of the *cis*-vinylene groups has been reduced to less than one-third of its original value. They found G(-*cis*-vinylene groups) $= 15 \pm 1$ and G(-*trans*-vinylene groups) $= 16.5 \pm 5.5$. The activation energies for the yields are 3.7 ± 0.3 kcal mol^{-1}. Although it seems that the loss

of olefinic groups are the same for the *cis* and *trans* specimens, actually since for *cis*-poly-1,4-butadiene G is 6.8 for the formation of the *trans* vinylene groups, the total destruction of the olefinic groups is almost twice that in the case of *trans*-1,4-polybutadiene. Higher yields of destruction of olefinic groups were found for polymers with vinylic side chains (1,2-polybutadiene). In this case G(-vinylic groups) is 40 and the rate of disappearance decreased with increasing dose according to a first-order kinetics.

It is most reasonable that the loss of the olefinic groups leads to cross-linking. However, measurement of cross-linking[107,108] of polybutadienes shows yields of only $G = 3.6$. Golub[104] suggested that part of the destroyed olefins form cyclic structures as has been observed in irradiated polyethylenes[109,110].

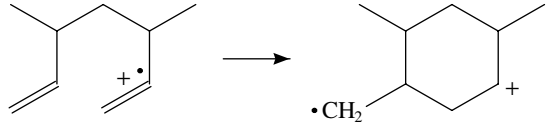
Other evidence for the wrong value of the very high yield of double-bond destruction can be found from the lower G(-double bond) found by Turner[111] and Turner and coworkers[112] in the case of irradiation of squalene and natural rubber.

Charlesby[113] studied the radiolysis of natural specimens (smoked sheets) under reactor irradiation. The swelling of the cross-linked gel was studied as a function of the radiation dose and the average molecular weight between cross-links M_c was determined from the Flory–Rehner equation[114]. The value of M_c was found to decrease linearly with radiation dose, indicating that the extent of cross-linking increased linearly with dose; G(cross-linking) was estimated to be approximately 2.0. Further studies by Charlesby and coworkers lead to G(cross-linking) of 1.5[115] for natural rubber and 1.05[116] for oriented rubber. The cross-linking yield of polybutadiene was found to be significantly higher than that of natural rubber; G(cross-linking) can be estimated to be approximately 3.5[115]. Much lower cross-linking yields were found for polybutadiene–styrene copolymer, where the cross-linking yields decrease with increasing styrene content in the polymer[117]. Kuzminski and coworkers[105] obtained approximately half of the cross-linking yield than the values reported by Charlesby's group. They found that the cross-linking yield increases monotonously with the temperature.

Turner and coworkers[111,118,119] used specially purified rubber samples and irradiated them in the absence of air. They found the yield of the physical cross-linking to decrease with the dose; the initial yield is $G = 3.5$. However, the yield of chemical cross-linking was found to be 1.3.

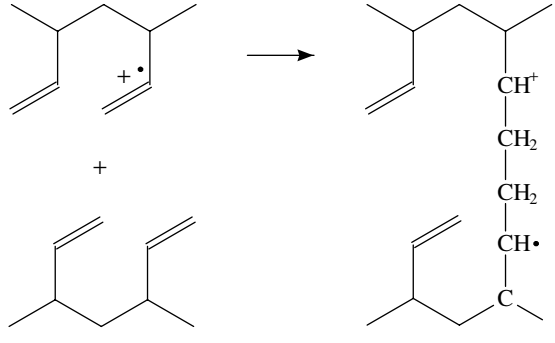
The effect of oxygen was studied extensively. An important post-irradiation oxidation of rubber was reported by Sears and Parkinson[120]. When oxygen is present, radiation-induced changes are often quite different (usually more severe) than under inert atmosphere (or in vaccum). The radiation-induced free radicals added to molecular oxygen dissolved within the material to produce peroxyl radicals[121]. A common phenomenon in radiation-induced oxidative degradation is the occurrence of heterogeneous oxidation[122,123]. This takes place when the rate at which oxygen is consumed within the polymer is higher than the rate at which it can be supplied from the surrounding atmosphere by diffusing into the material. Clough and Gillen[124] studied the γ-ray degradation of poly(butadiene-co-styrene) and poly(butadiene-co-acrylonitrile), SBR and Buna-n rubbers, respectively, in the presence of air. They found that the degradation of these materials is very heterogeneous through the sample thickness. There was a broad, paraboloid-shaped modulus profile through the sample interior, together with a dramatic change in modulus in the surface regions. They concluded by mechanistic studies that the radiation-induced degradation of these materials resulted from two different processes: (1) The standard free-radical-mediated radiation chemistry, which gave rise to oxidation involving O_2 dissolved in the polymer and which led to heterogeneous oxidation due to oxygen diffusion effects; and (2) ozone chemistry in the surface regions of the samples, which resulted from attack by O_3 generated by the action of ionizing radiation on the air atmosphere surrounding the samples.

Heusinger and coworkers[125–128] studied the radiation chemistry of 1,2-polybutadiene and 1,2- or 3,4-polyisoprene, in which there is a vinyl group in the side-chains rather than in the backbone of the polymer. Von Raven and Heusinger[125] studied the radiolytic changes in 1,2-polybutadiene. They found that the *G* value for double-bond conversion depends on the molecular weight, decreasing with decreasing molecular weight. The *G* values for cross-linking also decreased with decreasing molecular weight. The *G* value for double-bond conversion (20 to 200) is much higher than the *G* value for ion-pair formation (about 3), indicating that the disappearance of the double bonds is a chain reaction. The decrease of *G* with molecular weight is probably due to a larger effectivity of the chain-terminating step in viscous low molecular weight samples in comparison to the rubbery high molecular weight samples. *G* values for cross-linking is considerably smaller than *G* values for double-bond elimination, 7–12 vs 20–200, indicating that the double bonds disappear by other reactions than cross-linking, probably by cyclization. They proposed a mechanism for the double-bond conversion which involves intiation by a transformation of the primary radical ion in the vinyl group into a carbenium ion and a radical. Reaction of the carbenium ion with a vinyl group in the same chain leads to cyclization (equation 27) whereas reaction with a vinyl group in a neighbouring chain results in cross-linking (equation 28).



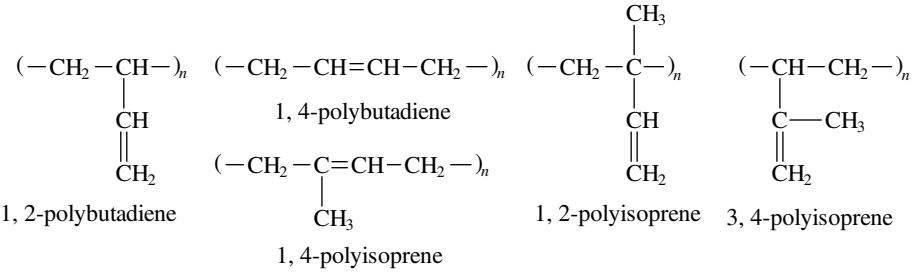
(27)

(10)



(28)

(11)



ESR studies at 77 K showed the presence of a five-line spectrum, corresponding to structure **11**. A spectrum corresponding to species **10** could not be found, probably due to its short life-time at 77 K. The carbenium ion and the radical in species **10** or **11** can start a chain reaction either via a cationic reaction or through a radical addition to a double bond. Von Raven and Heusinger suggested only cationic chain reaction. Comparison of the G values for elimination of the double bond with the G values for cross-linking shows that cyclization exceeds the formation of cross-links by a factor of about 10. It is interesting to note that these values of G(-double bond) and G(cross-linking) are much higher than those found for 1,4-polybutadiene, indicating that pendent vinyl groups in 1,2-polybutadiene are much more reactive than the vinylidene groups in the backbone of 1,4-polybutadiene. Von Raven and Heusinger studied the thermal degradation of irradiated and non-irradiated samples of 1,2-polybutadiene. In the non-irradiated samples, an important product is butadiene formed by depolymerization. However, for irradiated samples only very little butadiene was formed. Besides, the ratio of fragments with bicyclic rings (naphthalene, substituted naphthalene, dihydronaphthalene compounds) to fragments with monocyclic rings was found to be larger in irradiated than in non-irradiated samples. These results indicate that radiolysis of 1,2-polybutadiene leads to formation of condensed cyclohexane rings.

Katzer and Heusinger[127] studied the radiolysis of polyisoprenes with high content of 1,2- and 3,4-units. They found that G(-double bonds) is about 130 and G(cross-linking) is about 10. These values depend slightly on the molecular weight.

The G values are higher than the G values for initial species (*ca* 2.5), indicating a chain reaction. The much higher yield for the disappearance of a double bond indicates that cyclization occurs more frequently than cross-linking. Katzer and Heusinger concluded from the studies on the influence of dose rate, temperature and additives (air, anthracene and hydroquinone) that the chain proceeds via a cationic mechanism.

Kaufmann and Heusinger[128] studied the mechanism of radiolysis of 3,4-polyisoprene. They found G(cross-linking) = 2 and G(-double bonds) = 120. They found that G(-double bonds) depends on the dose rate exponentially with a coefficient of 0.9, and depends on the temperature with an activation energy of 11.7 kJ mol^{-1}. Addition of the radical scavenger, anthracene, markedly decreased the cross-linking while the conversion of double bonds did not change. Kaufmann and Heusinger suggested that the radiation-induced radical cation forms one cross-link by a radical reaction and, on the other hand, starts a cationic chain reaction leading to cyclization. Besides cross-linking, also chain scissions were found to occur to a small extent. The chain scissions are suggested to occur in the polymer containing a low content of the 1,4-units.

Zott and Heusinger[129] studied the radicals formed in γ-irradiation of 3,4-polyisoprene and 1,2-polybutadiene by ESR. In both polymers, alkyl and allyl radicals are formed. Alkyl radicals (shown as a septet spectra with 23 G hyperfine splitting for 3,4-polyisoprene and as a quintet of 27 G hyperfine splitting for 1,2-polybutadiene) are formed by a cross-linking reaction and are stable only at low temperatures. Allyl radicals (shown in the ESR spectra as a septet of 15–16 G hyperfine splitting) are formed by hydrogen abstraction from the main chain. They could be observed even at temperatures up to 0 °C. The irradiation of 1,2-polybutadiene or 3,4-polyisoprene adsorbed on silica gel leads to the same ESR spectra but with enhanced resolution. The enhanced resolution (lower line width) was explained as due to a reduction of the dipole–dipole interaction, which is achieved by the formation of a thin polymer layer. In the ESR spectrum of irradiated 3,4-polyisoprene they observed a singlet with a line width of 11G. The intensity of the singlet signal depends on the pre-treatment of the polymer and therefore on the physical structure of the polymer samples. The largest signal intensity was obtained for polymer samples prepared by dry-freezing and storing below the glass transition

temperature (*ca* 0 °C). The singlet intensity for samples stored above the glass transition temperature before the γ-irradiation was either very low or not observable. The singlet is optically bleachable with near-infrared light ($\lambda > 800$ nm), but the ESR spectrum is not affected by illumination with visible light. The photobleaching with infrared light indicates that the ESR singlet is due to trapped electrons in the polymer. This conclusion is further supported by saturation of the ESR singlet amplitude with increasing microwave power at the power level of 0.06 mW. The saturation at relatively low power level indicates the presence of a weak interacting paramagnetic species such as trapped electrons. The addition of electron scavengers such as pyrene, anthracene and biphenyl had no influence on the singlet intensity, probably due to the trapping of the electrons in the crystalline parts of the polymer, since additives go only into amorphous regions.

Hesse and Heusinger[130] studied the ESR signal due to $\Delta m = 2$ transition of radical pairs in a number of γ-irradiated polymers including 1,2-polybutadiene (both atactic and isotactic) and 3,4-polyisoprene. It was found that the distance between the radicals in the pair is 0.53 ± 0.04 μm; $1.0 \pm 0.5\%$ of the radicals in 1,2-polybutadiene and 3,4-isoprene are arranged in pairs.

Sisman and Bopp[131], Charlesby[113], Turner[111] and Petrov and Karpov[132] studied the yield of total gas evolution from natural rubber, polybutadiene and various GR-S type copolymers subjected to ionizing radiation (reactor, ^{60}Co or electron accelerator). Most of the gas is $H_2 + CH_4$ (100% in the case of polybutadiene), however for some rubbers a small amount of $CO_2 + C_3H_6$ was found also. Turner[111] found that under bombardment with accelerated electrons, the evolution of hydrogen from purified natural rubber was linear with dose, up to 180 megarads, and corresponded to $G(H_2) = 0.64$. This radiolytic yield is noticeably smaller than those found in low-molecular-weight olefins.

Yamamoto and coworkers studied the effect of hydrogen atmosphere upon the radiation-induced gas evolution (light hydrocarbon molecules) from polyisoprene[133] and polybutadiene[134]. Samples were irradiated in hydrogen atmosphere from 0 to 1 MPa by ^{60}Co γ-rays up to 160 kGy at room temperature. The yield of the saturated hydrocarbons increased and the yield of the unsaturated hydrocarbons decreased with increasing hydrogen pressure. The following mechanism was suggested for radiolysis of polybutadiene in the presence of hydrogen. The main radical species formed on irradiation of 1,4-polybutadiene was found to be of an allylic type[135], either by C−H or C−C bond ruptures. The lighter hydrocarbons, methane and ethane, are supposed to be the product of chain end scission[136]. The reaction of the allylic radical formed by C−C scission with hydrogen atom (or with hydrogen molecule) increases the number of terminal CH_3 groups of the chain (equation 29).

$$-CH_2CH{=}CHCH_2^{\bullet} + H \longrightarrow -CH_2CH{=}CHCH_3 \tag{29}$$

The reduction of evolution of ethylene in the presence of hydrogen was suggested to be due to the addition of the hydrogen to the ethylene formed by irradiation (equation 30).

$$CH_2{=}CH_2 + 2H \longrightarrow CH_3CH_3 \tag{30}$$

This reaction decreases the ethylene yield while increasing the G of ethane.

The irradiated polybutadiene in atmosphere of hydrogen is hardly soluble in any solvent, indicating that the dominant reaction is cross-linking.

Smirnova and coworkers studied the influence of various types of ionizing radiations on the physiomechanical characteristics of a statistical polymer of butadiene and acrylonitrile[137]. Although the polymer is a statistical polymer, the nature of its thermomechanical curve indicates a block nature of the polymeric basis of the rubber; there is a

statistically distributed admixture of polar (acrylonitrile) and non-polar (butadiene) blocks. In the case of irradiation (γ-rays of ^{60}Co, reactor neutrons or 100-MeV protons) in the presence of air, cross-linking was predominating in the polar blocks, whereas in the non-polar blocks, containing mainly chains with unsaturated bonds, destruction predominates. Whereas the results of irradiation in the presence of air are almost independent of the type of irradiation, the situation is substantially different for irradiation under vacuum. Under vacuum, the concentration of the internodal chains in the polar block is a maximum-type function of the dose for γ-radiation and protons, while it is a monotonous function for neutrons for the entire dose range (0.9 Mrad). In the non-polar block, γ-radiation and protons under vacuum do not change considerably the average concentration of internodal chains (ν), while neutrons at large doses increase sharply the intensity of cross-linking, just as in the polar blocks. Under air, protons, γ-rays and neutrons behave similarly, increasing ν slightly with the dose in the polar block, and decreasing it considerably in the non-polar blocks.

The total gas evolved from irradiation of the rubber is relatively small, due to the protective action of the π orbitals. The main gas liberated from the rubber is H_2. The amount of hydrogen evolved as a function of dose is a saturation-type curve. The amount is increasing in the order protons < gamma-rays < neutrons. The ratio hydrogen/hydrocarbon gases changes with the dose. The largest value of the ratio was found for reactor neutrons, probably due to a smaller number of double bonds formed in the polymer basis in the case of protons and γ-irradiation. In addition to hydrogen the following hydrocarbon gases were observed: C_2H_2, C_2H_4, C_3H_6 and C_4H_8. The authors suggested that the formation of unsaturated hydrocarbons is due to hydrogen transfer reactions in the main chain. The amount of hydrocarbons is largest for neutrons irradiation. The larger effect of the neutrons is suggested[138] to be due to neutron interaction creating defects in the polymer — cavities of molecular dimensions. Then, under a subsequent influence of radiation on the damaged structure, the chemical changes increased. In the irradiation of hydrogen-containing polymers by neutrons with an average energy of 2 MeV, the neutrons cause recoiling of protons, mainly of 1-MeV energy. Those protons mainly collide elastically with atoms of the chain backbone, leading through cascade processes with increased local density of energy liberation to the formation of structural defects. It was suggested that the displacement of atoms may occur by both scattering and track formation, which collectively displaces whole channels of atoms of the lattice. Bond ruptures promote the appearance of cross-links.

Basheer and Dole[139] studied the γ-irradiation of block and random copolymers of butadiene and styrene in comparison to the homopolymers polybutadiene and polystyrene. The following aspects were studied: formation of trapped electrons, contribution of ionic species to cross-linking and hydrogen gas evolution. They found that in block copolymers the yield of trapped electrons $G(e^-)$ increased linearly with increasing polystyrene content. In random copolymers they observed a deviation from linearity; $G(e^-)$ is smaller for random copolymers than for block copolymers (with the same styrene content). They found that 25–35% of the cross-linking is taking place by ionic reactions, whereas most of the cross-linking occurs by radical processes. The yield of hydrogen evolved on irradiation decreases with increasing styrene content. For block copolymers the decrease is linear, whereas for random copolymers a curved dependence was observed; $G(H_2)$ is higher for block copolymers than for random copolymers. The yields of cross-linking of the butadiene–styrene copolymer was studied for irradiation at 77 K and room temperature[140]. The measured yields were less than calculated from linear interpolation of the cross-linking yields of the homopolymers. This was attributed to energy transfer processes at the interface from polybutadiene segments to polystyrene, and to radiation resistance of polystyrene due to its aromatic nucleus.

VIII. RADIATION CHEMISTRY OF POLYALKYNES

Polyalkynes are polymers of conjugated double bonds. Yen and coworkers[141] studied the radiation stability of *trans*-polyacetylene. The radiation fields used were: (1) 1.6-MeV electrons with flux of 2×10^{11} electrons cm^{-2} s^{-1} for 5000 s totalling 10^7 rad, (2) ^{60}Co-γ-ray totalling 10^5 rad. It was found that the radiation decreases only slightly the electrical resistance, from 3×10^4 ohm cm to 2.6×10^4 for 10^5 rad γ-rays and to 2×10^4 for 10^7 rad electrons. The solar absorbance and the thermal emissivity was not changed at all by the radiation. *cis*-Polyacetylene is a highly conductive (after doping) organic polymer which can be used as an electrode-active material in chemical batteries. A serious hindrance for the practical use of polyacetylene is the rapid degradation of the polymer during storage, due to conversion of the *cis*-polyacetylene to the *trans* form. As isomerization occurs, the elastic polymer film becomes brittle and loses partially its electromechanical activity. Tkachenko and coworkers[142] suggested using ^{60}Co γ-irradiation or an electron beam in order to form a number of cross-links in order to stabilize the polymer film, due to the limited mobility of the polymer chains. They found that irradiation under argon at a dose of 75–100 Mrad, regardless of the form of radiation (γ-rays, accelerated electrons), has little effect on the cyclic voltammetry curve, indicating that the film does not lose its electrochemical activity by the irradiation. However, the non-irradiated film suffers in a 3-month storage a 2–3-fold decrease in the conductivity (as evidenced by the decrease of the area under the anode and cathode curve in cyclic voltammetry), whereas the cyclic voltammetry curves of the irradiated films changes negligibly in 3–6 months storage. They found that 75 Mrad was optimal for the stabilization of thin films (*ca* 100 μm), whereas for thicker films (*ca* 350 μm) the optimum is 100 Mrad. They found that while in non-irradiated film, storage at 0 °C for 170 days leads to change in the content of the *cis* isomer from 97% to 66%, the same storage of the irradiated film changes the concentration of the *cis* isomer from 90.5% to 88%.

Nagels and Krikor[143] studied the effect of γ-irradiation on the electrical properties of *trans*-polyacetylene. They reported a marked decrease of the conductivity and a slight increase of the thermopower after γ-irradiation of 10 kGy (1 Mrad). Their study showed that no essential structural changes occur during irradiation.

Hola and coworkers[144–147] studied the ESR spectrum of non-irradiated and irradiated *trans*-polyacetylene. The spectrum displayed as a simple symmetrical line, as a result of reorientation of an isolated spin. They found[144] that irradiation leads first to a decrease in the relative spin concentration up to 0.33 kGy. Further irradiation increases the relative spin concentration up to 0.55 kGy. Above this dose the relative spin concentration decreases slightly again but the observed value is close to the initial one. They found that the line width of the ESR spectra was not changed with irradiation, indicating that the spin mobility remains unchanged. The observed minimum of spin concentration after 0.33 kGy could be due to a combination of the initial spins with the irradiation-initiated spins. The further increase of spin concentration is probably the result of those spins formed by the irradiation, but can be due also to oxidation and to the effect of impurities. This was studied[145] by high dose irradiation, up to doses of 3 MGy (300 Mrad), where they found that the relative spin concentration is approximately constant, independent of dose, up to 3000 kGy. The constant spin concentration indicates a high stability of the primary paramagnetic centres, in spite of the very high γ-doses. The previous results of initial decrease of the spin concentration were not found in this study. The authors suggest that the different results are due to the different methods used in the two studies. In the first study, the material was irradiated in one tube and then transferred to the ESR tube. In the second experiment the polyacetylene was sealed under inert atmosphere in the ESR tube and irradiated in this tube. Thus, the initial decrease of spin concentration in the first paper was suggested to be due to the presence of oxygen and other impurities. It

was found[147] that the irradiation did not cause any changes, not only after the end of the irradiation but also after 17 months.

Masuda and coworkers[148–151] studied the radiation effects on high molecular weight polyacetylene with various substituents and hetero atoms. The molecular weights of polymers from disubstituted aliphatic acetylenes (2-octyne and 2-decyne) were remarkably reduced with irradiation in air, whereas no degradation occurred in radiolysis in vacuum[148]. The G values for chain scission in air were found to increase with dose and were 3.3–12.2 (for poly-2-octyne) in the dose range of 1–73 Mrad. The degraded polymers contain carbonyl and hydroxyl groups and are soluble in polar solvents such as methyl ethyl ketone and acetone. In contrast to the substituted aliphatic polyacetylene, polymers of 2-substituted phenyl acetylenes (1-phenyl-1-propyne and 1-chloro-2-phenylacetylene) degraded in air only slightly, even with radiation up to 40 Mrad. Whereas 40 Mrad changes M_n of poly-2-octyne from 8.4×10^4 to 2.5×10^3 and that of poly-2-decyne from 6.1×10^4 to 2.1×10^3, the change for poly(1-phenyl-1-propyne) was from 2.4×10^5 to 1.6×10^5 and for poly(1-butylacetylene) it is intermediate between the aliphatic and the aromatic substituted compounds as M_n is changed from 2.2×10^5 to 4.1×10^4. The degradation mechanism was suggested to involve H-atom addition to the triple bond, and reaction of the radical formed with oxygen to form peroxyl radical, followed by decomposition of the hydroperoxide to give a carbonyl compound and an alcohol, together with rupture of the backbone of the polymer. They suggested that the aromatic substituted polymers are stable since the resulting peroxyl radicals do not possess the ability of abstracting a hydrogen from the phenyl groups, due to higher bonding energy of aromatic hydrogens. However, while this explanation[148] may be plausible for poly(1-chloro-2-phenylacetylene), it is not possible for poly(1-phenyl-1-propyne), where the peroxyl radical can abstract the hydrogen of the methyl group as is done in poly(t-butylacetylene). The reason for the radiation stability of the aromatic substituted polymer is probably the reaction of H atoms with the aromatic ring rather than with the alkenic bond. Although the reaction of hydrogen atoms with olefinic double bonds ($k = 4 \times 10^9$ M^{-1} s^{-1} for cyclohexene and 3×10^9 M^{-1} s^{-1} for ethylene) is slightly faster than their reaction with benzene ($k = 9 \times 10^8$ M^{-1} s^{-1})[152], geometric factors will enhance the reaction with the aromatic ring in the side chain rather than with the olefinic double bond in the backbone of the polymer. The higher C−H bond strength in the CH_3 groups of t-butyl than that of allylic CH_2 groups in the 2-octyne and 2-decyne might be the reason for the moderate degradation of poly(t-butylacetylene). The γ-radiolysis of poly(1-chloro-1-alkynes) $(-CCl{=}CR-)_n$ was studied for various alkyl groups (R) in the presence or absence of oxygen[149]. Irradiation of membranes of poly(1-chloro-1-hexyne) with 40 Mrad (2.2 Mrad h^{-1}, 40 °C) in air makes them brittle. Extraction of the irradiated polymer with chloroform in a Soxhlet extractor left no gel, indicating very little cross-linking. The irradiated polymer has molecular weight of no more than a few thousands. In contrast, about 14 wt% of the product from irradiation in vacuum was a blackish gel. For larger alkyl groups the percentage of the gel fraction increases. The gel fraction was always larger in vacuum than in air. Thus for poly(1-chloro-1-octyne) the gel fraction is 20% in air and above 50% in vacuum. For poly(1-chloro-1-decyne) the gel fraction is 45% in air and 97% in vaccum. The results suggest that oxygen induces degradation of the radiation-initiated radical. For poly(1-chloro-1-hexyne) in air it was found that G(scission) is 5.4, whereas G(cross-linking) is only 0.1; G(scission) was found to be independent of the molecular weight of the original polymer ($M_n = 10^5$ to 10^6). Besides reduction of the molecular weight, the irradiation increases the ratio M_ω/M_n, indicating a random degradation process. For copolymers of 1-chloro-1-hexyne/1-chloro-2-phenylacetylene it was found that G(scission) is a linear increasing function of the mol% of 1-chloro-1-hexyne. The radiation-induced cross-linking was studied for poly(1-chloro-1-decyne) in vacuum.

At 5 Mrad, 75% of the polymer gelled. The gel fraction increases with increasing dose; a black, strong, completely cross-linked membrane was formed at 40 Mrad; G(cross-linking) was found to be 1.1 and G(scission) was 0.18. The cross-linking leads to increase of the Young modulus and to a decrease of the elongation at break. Both properties changes monotonically with dose, due to decrease in the chain length between two cross-links. The chlorine content of all polymers was found to decrease on irradiation both in the presence of air and in vacuum, suggesting that the γ-irradiation ruptures the C−Cl bonds to form allylic radicals. The irradiation in air leads to formation of OH and C=O groups (as evidenced by the IR spectra), indicating a disproportionation of hydroperoxides.

Silicon-containing mono- and di-substituted polyacetylenes (e.g. $[-CMe{=}C(SiMe_3)]-_n$) undergo radiation-induced degradation in air with high yields of main-chain scission ($G > 1$). The yield of main-chain scission is usually larger for polymers having long alkyl groups—e.g. for $[CH{=}C-CH(n\text{-}C_3H_7)SiMe_2C_6H_{13} - n]_n$ $G = 2.3$ and for $(-CMe{=}CSiEt_3-)_nG$ is 1.9 compared with 1.2 for $(-CMe{=}CSiMe_3-)_n$. No polymer degradation was found for irradiation in vacuum. The polymers irradiated in air contained C=O and Si−O groups and were soluble in polar solvents, which do not dissolve the starting polymers.

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CHAPTER **9**

Synthesis of conjugated dienes and polyenes

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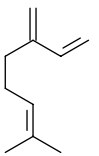
I. INTRODUCTION

Conjugated dienes and polyenes constitute an important functionality among organic compounds[1–10], discussed generally under the chemistry of alkenes. However, in recent years, they have emerged as a distinct class by themselves due to their increasing utility in organic synthesis and also due to their interesting physical properties. Dienes and polyene moieties are widely distributed among natural products[11]. Representative examples from natural products having diene and polyene moieties are gathered in Figure 1. Monoterpene, myrcene **(1)** and sesquiterpene β-farnesene **(2)** are among the simple examples of a 1,3-diene system present in nature. Retinal **(3)**, β-carotene **(4)** and lycopene **(5)** are representative conjugated polyenes from the carotenoid family, structures of which have been known for a long time[12]. Eicosinoids such as lipoxin A **(6)** are important intermediates in the biosynthetic chain between arachidonic acid and prostaglandins. Several insect pheromones, for example the alcohol dodeca-8,10-dienol **(7)**, have a diene or a polyene unit. However, isolation of several polyene macrolide antibiotics in recent years has added a new dimension to polyene chemistry. Amphoterecin B **(8)**, a 38-membered macrolide polyene, isolated from *Streptomycetes nodosus*, is a representative example from a growing number of similar antibiotics[13]. Linearmycin A 1 **(9)**, isolated recently from mycelial extract of streptomyces, sp.No. 30, is an antifungal C_{60} polyene antibiotic[14]. A C_2-symmetric anti-fungal marine natural product papuamine **(10)** is a representative example of nitrogen containing conjugated diene[15]. Dienes and polyenes have attracted a great deal of attention as they exhibit exceptional reactivity in cycloadditions and electrocyclic reactions. The most common use of dienes and polyenes is in Diels-Alder reactions (both inter- and intramolecular) and in thermal and photochemical reorganizations to furnish diverse carbo- and heterocyclic frameworks, which find application in synthesis of natural products and non-natural products[16]. Polyenes, due to their well defined architecture and delocalized π-system, are excellent substrates for energy and electron transfer. They are being explored (for example, the push-pull polyene **11**) as materials for non-linear optical applications, molecular electronics as well as photosynthesis mimics[17]. In view of such diverse applications and future potential, newer synthetic methods for assembling dienes and polyenes, under mild and efficient reaction conditions with regio- and stereocontrol, are being continually explored. Indeed, in the last few years, synthetic activity directed towards these substrates has witnessed explosive growth.

In this account, an overview of the methods employed for the synthesis of conjugated dienes and polyenes is presented. Dienes and polyenes with isolated double bonds are excluded, as they are accessed through methods usually employed for alkene synthesis[18]. Oligomerizations and polymerization reactions leading to polyenes are also not covered. Synthesis of 1,2-dienes, i.e. allenes, is excluded from the purview as there is a volume in the present series devoted to this functional group[19]. Synthesis of heterodienes, conjugated enol ethers, [*n*]-annulenes and related compounds are also not covered here. However, enynes, dienynes and enediynes syntheses have been included in a few cases in view of their emerging importance.



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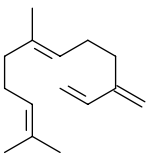

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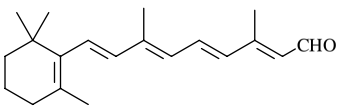

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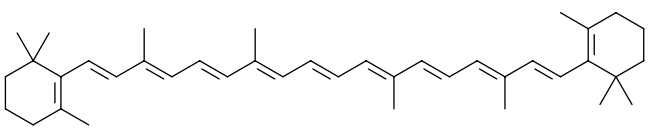

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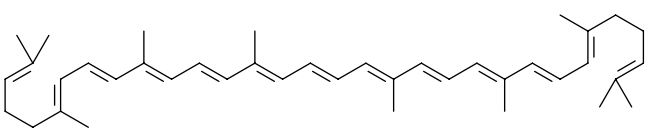

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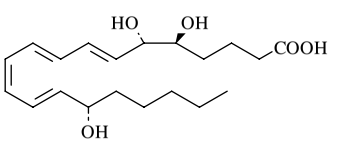

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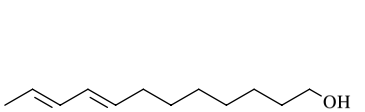
FIGURE 1



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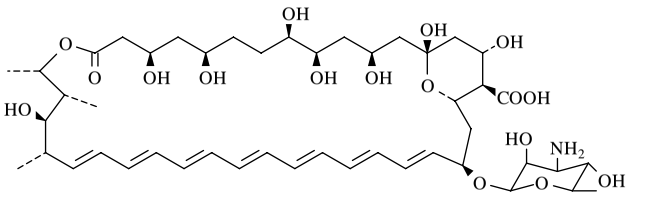

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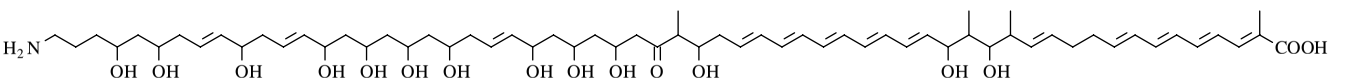
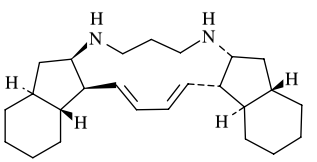


(9)



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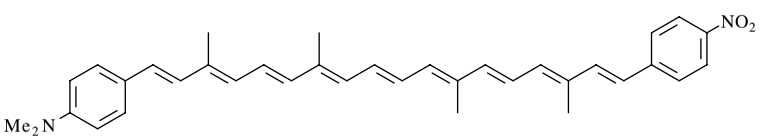


(11)

FIGURE 1. (*continued*)

The historical background to diene and polyene synthesis and literature up to 1964 has been reviewed in the earlier volume on alkenes of this series[1]. Literature up to the 70s has been reviewed exhaustively elsewhere[3] and some recent developments have been covered in *Comprehensive Organic Chemistry*[6], *Comprehensive Organic Synthesis*[8] and other monographs[4,5]. The present chapter provides a comprehensive overview with literature coverage up to mid-1995 and with emphasis on synthetic methods of preparative utility and general applicability. For the sake of convenience, various reactions leading to dienes and polyenes have been pooled together and presented under well known reaction types. Selected examples of commonly used methods, particularly of recent vintage, are gathered in the form of tables to illustrate the utility of the procedure involved. For the sake of convenience, the protecting groups have been abbreviated as 'P'.

II. ELIMINATION REACTIONS

A. General Aspects

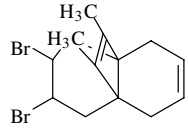
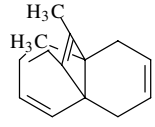
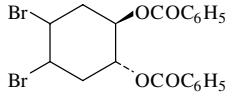
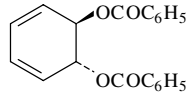
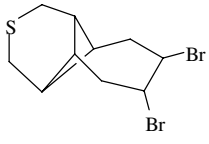
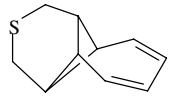
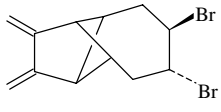
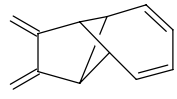
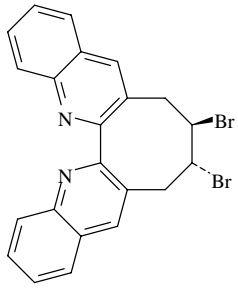
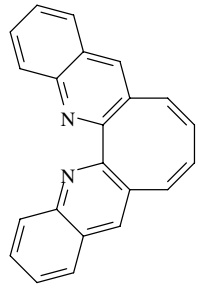
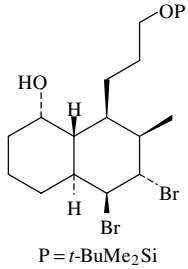
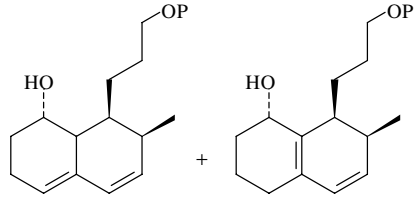
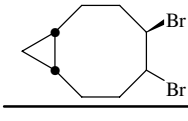
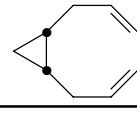
One of the simplest and classical methods for the generation of a diene moiety is through single or double elimination of appropriately functionalized alkane, alkene, allene or alkyne substrate[20]. The elimination reactions have been employed for the generation of both cyclic and acyclic dienes and polyenes. The eliminations could be either 1,2- or 1,4-. In some cases the elimination may involve rearrangements. A large number of leaving groups and reagents to facilitate the elimination process have been developed. In many of the classical elimination reactions, particularly those leading to the formation of acyclic dienes and polyenes, the reaction conditions employed are usually harsh, leading to low yields. However, more recent methods, such as palladium mediated allylic deacetylation reactions, work under milder conditions to result in products of high stereochemical purity[21]. In the following, different elimination reactions leading to the formation of dienes and polyenes with an emphasis on more recent developments is presented.

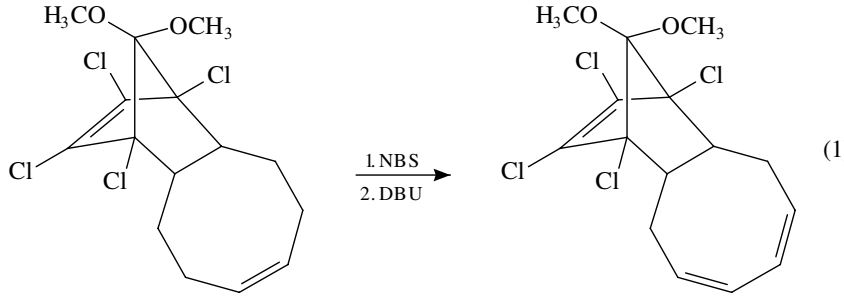
B. Dehydrohalogenations

Bromination of an olefin and double dehydrobromination of the resulting 1,2-dibromide is a classical method for the generation of 1,3-dienes (Table 1). Bromination of a double bond can be done with molecular bromine[22] or, more conveniently, with pyridinium bromide perbromide[23a]. A variety of bases has been employed for dehydrobromination. While potassium hydroxide and sodium methoxide have been used for a long time, lithium carbonate–lithium chloride in DMF or hexamethylphosphoric triamide (HMPA) works well in many cases[23a]. Double dehydrobromination with hindered bases such as potassium *t*-butoxide or diazabicyclononene (DBN) and diazabicycloundecene (DBU)[23e] give good results.

Monodehydrohalogenation of allylic halides is another classical method for diene synthesis[24]. This method is complementary to double dehydrohalogenation as both the 1,2-dihalides and allylic halides are readily accessed from alkenes. The commonly employed protocol for diene synthesis, particularly for cyclic 1,3-dienes, is through the allylic monobromination of the alkene with *N*-bromosuccinimide or related reagents followed by dehydrobromination with hindered bases such as DBN or DBU (equation 1)[25].

TABLE 1. Dienes through double dehydrobromination

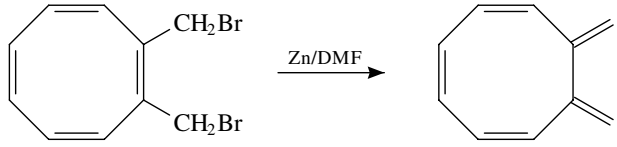
Substrate	Product	Reference
		23a
		23b
		23c
		23d
		23e
 P = *t*-BuMe$_2$Si		23f
		23g



(1)

C. Dehalogenations

Dehalogenation of 1,2- and 1,4-allylic dihalides offers another simple entry into dienes and polyenes[26] (Table 2). Dehalogenations, particularly debrominations, can be achieved by Zn/DMF (equation 2)[27], zinc amalgam[28a] or a combination of activated zinc/potassium iodide and iodine[28c]. The 1,4-dehalogenation method is particularly useful for the generation of orthoquinodimethanes from the corresponding 1,2-bisbromomethylbenzene derivatives[28c]. A high-yielding method for 1,4-elimination of 1,4-dibromo-2-enes to generate 1,3-dienes using a catalytic amount of sodium 2-thienyltellurolate has been reported[28d]. This method can also be used for 1,2-debromination to alkenes. Thus, a 1,2,3,4-tetrabromo compound has been converted to a diene in excellent yields under mild conditions (Table 2)[28d]. The *cis*- and *trans*-perfluoro-1,3,5-hexatrienes which show contrasting properties from those of the parent *cis*- and *trans*-1,3,5-hexatrienes have been synthesized by dehalogenation (Cl, Br) using zinc dust[28e].

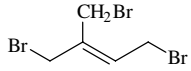
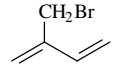
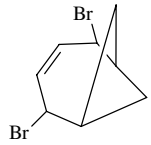
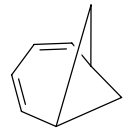
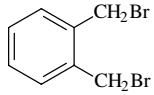
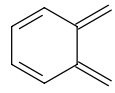
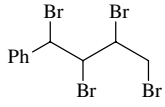
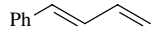
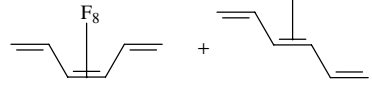


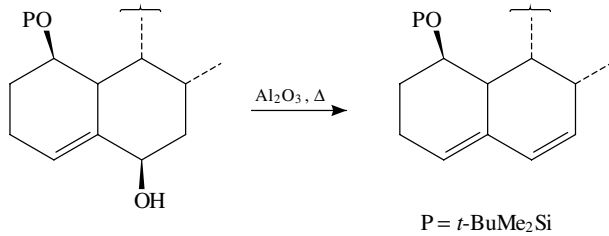
(2)

D. Dehydration and Related Reactions

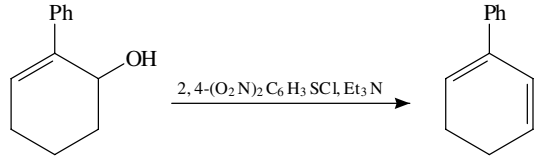
Dehydration of allylic alcohols, which are generated either by 1,2-reduction of α,β-unsaturated cabonyl compounds or by the nucleophilic addition of a vinyl group to a carbonyl compound, is a routinely employed method for the generation of 1,3-dienes and polyenes. Addition of vinyl- and polyenyl anions to a carbonyl group and subsequent dehydration will be discussed under a separate section. Allylic dehydrations can be performed by a variety of acidic reagents such as sulphuric acid, phosphoric acid, *p*-toluenesulphonic acid or Lewis acids such as $BF_3 \cdot Et_2O$, $SnCl_4$, metal oxides, metal salts as well as solid supports. Examples of diene synthesis through dehydration of allylic alcohols are well documented in the literature. However, three illustrative examples from recent literature employing alumina (equation 3)[29a,b], 2,4-dinitrobenzene sulphenyl chloride (equation 4)[29c] and methyltriphenoxyphosphonium iodide in HMPT (equation 5)[29d] as dehydrating agents are given here.

TABLE 2. Dienes through debromination

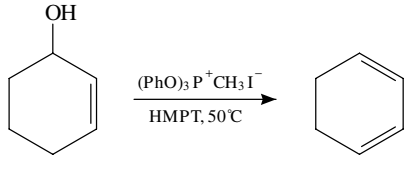
Substrate	Product	Reference
		28a
		28b
		28c
		28d
$BrCF_2CFClCF_2CFClCF_2Br$		28e



(3)

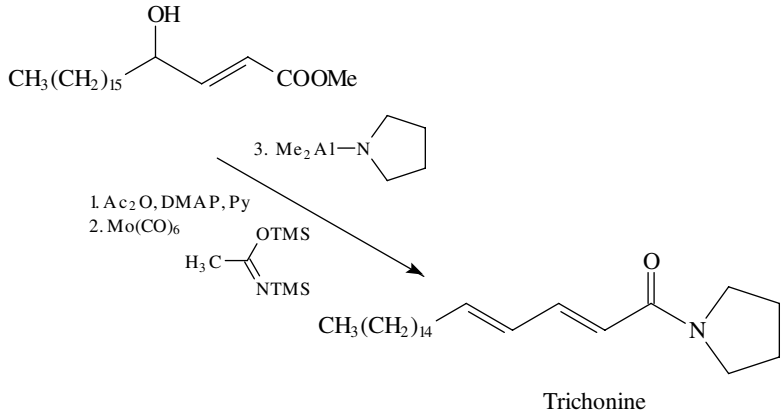


(4)



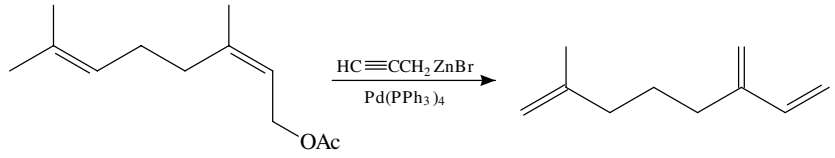
(5)

Allylic alcohols can be converted to dienes by a two-step method involving activation of the hydroxy group to a better leaving group and elimination[30]. These eliminations are commonly conducted in the presence of non-nucleophilic bases employing mesylate (OMs) or tosylate (OTs) derivatives (Table 3)[31]. Cyclic ene-1,4-diol mesylates can also be converted to dienes on treatment with sodium iodide in acetone[32]. Allylic acetates can also serve as precursors of dienes through elimination of acetic acid[33] as applied in the synthesis of the natural product trichonine (equation 6)[33a]. An interesting application is the transformation of neryl acetate to myrcene in quantitative yield in the presence of propargylzinc bromide and $Pd(PPh_3)_4$ catalyst (equation 7)[34]. Palladium catalysed 1,4-elimination in allylic carbonates also leads to dienes (equation 8)[35].



Trichonine

(6)



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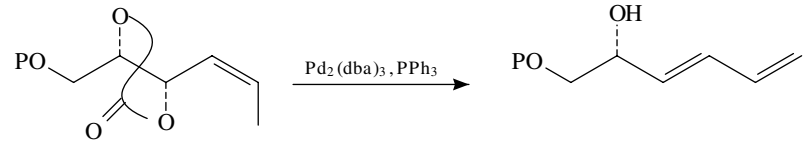


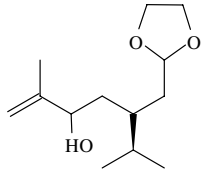
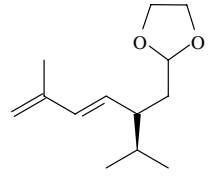
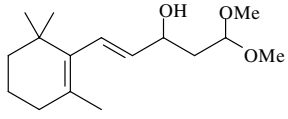
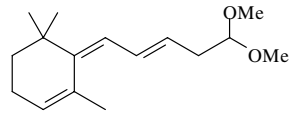
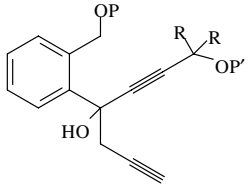
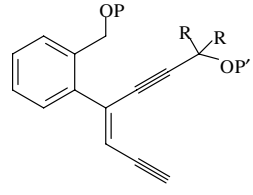
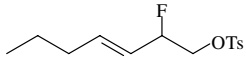
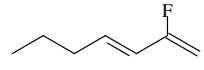
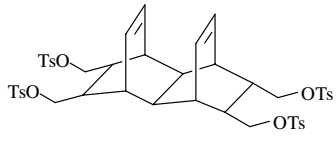
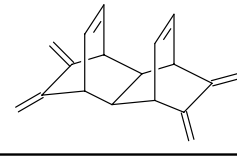
(8)

P = *p*-$MeOC_6H_4CH_2$

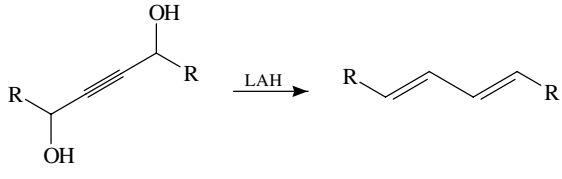
E. Reductive Deoxygenations

Reductive deoxygenation-rearrangement of 2-yne-1,4-diols to 1,3-dienes is a useful synthetic procedure since a large variety of ynediols are available in a few steps by sequential reaction at both ends of acetylene with aldehydes. Acetylenic 1,4-diols can be deoxygenated reductively by lithium aluminium hydride to form conjugated dienes of high stereoisomeric purity (equation 9)[36]. A modification to this procedure is the use of acetylenic 1,4-diol mono-THP derivative[37]. Allenic *tertiary* alcohols which are intermediates in the reaction can be separated and subjected to reductive elimination rearrangement

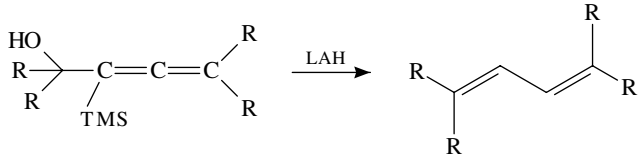
TABLE 3. Dienes via elimination of sulfonic acids

Substrate	Product	Reference
		31a
		31b
 P = $Me_2CHMe_2CMe_2Si$;	 P′ = P-$MeOC_6H_4CH_2$	31c
		31d
		31e

with LAH (equation 10)[38]. Some of the dienes and polyenes which have been synthesized following this procedure are given in Table 4[36,39].

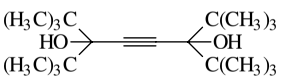
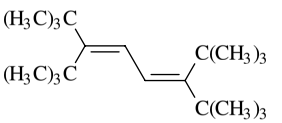
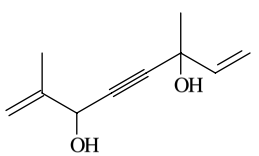
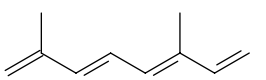
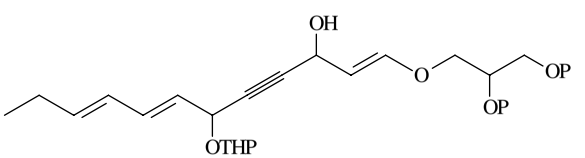
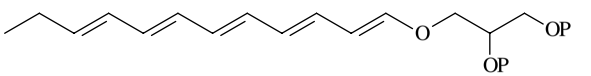


(9)

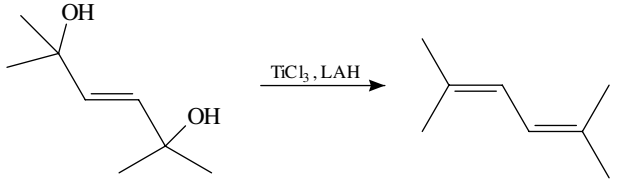


(10)

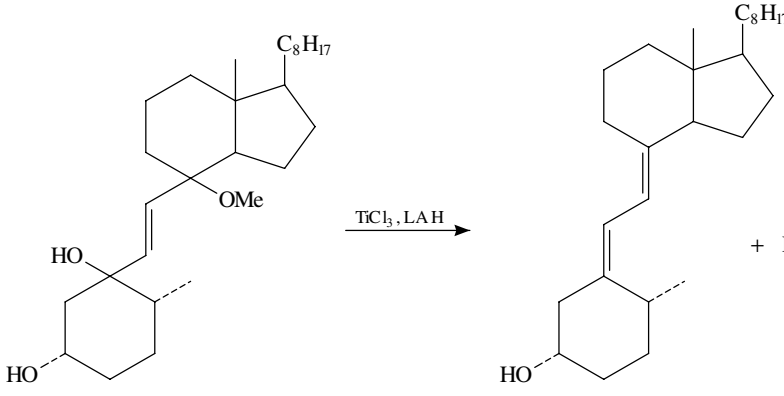
TABLE 4. Dienes and polyenes through reductive deoxygenations

Substrate	Product	Reference
		39a
	 Cosmene	36
 P = *t*-BuMe$_2$Si	 Fecapentaene derivative	39b

Walborsky and Wust found that allylic 1,4-diols or their dialkyl ethers can be reductively deoxygenated using low-valent titanium species generated *in situ* from titanium trichloride and LAH (equation 11)[40]. Reaction of both *E*- and *Z*-allylic 1,4-diols result in the formation of 1,3-dienes. It has been proposed that this reaction takes place on the titanium metal surface involving radical interemediates, like McMurry coupling reaction. Utilizing this procedure, a total synthesis of dihydrovitamin D3 (DHV3) and dihydrotachysterol (DHT3) has been devised (equation 12)[41]. A related reaction for the synthesis of conjugated all *trans*-trienes by reductive elimination of 1,6-dibenzoate-2,4-dienes (equation 13) using low-valent titanium species has been reported[42]. Under these conditions trienes are formed stereoselectively and in quantitative yield. This method was utilized for the synthesis of all *trans*-triene component of leukotriene B_4 (equation 14)[43]. As an alternative to low-valent titanium compounds, sodium amalgam has also been used as an electron transfer agent for stereospecific diene and triene synthesis[44]. Utilizing this procedure, stereospecific syntheses of *cis*- and *trans*-galbolenes have been reported (equation 15)[45].



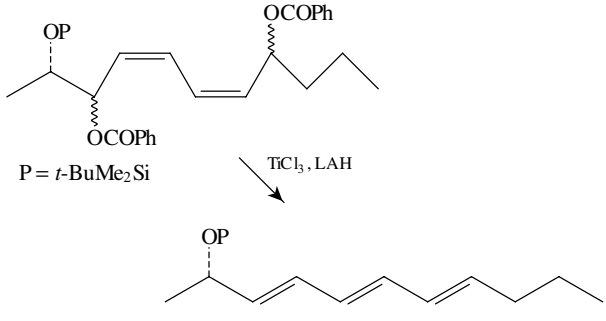
(11)



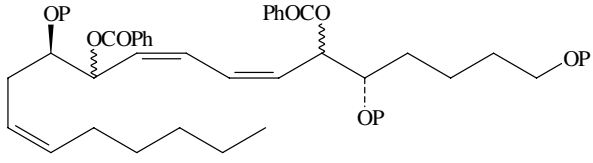
(12)

+ DHT 3

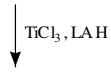
DHV 3



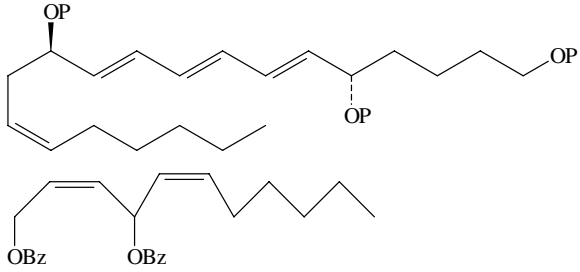
(13)



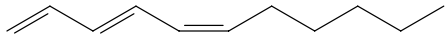
P = *t*-BuMe$_2$Si



(14)



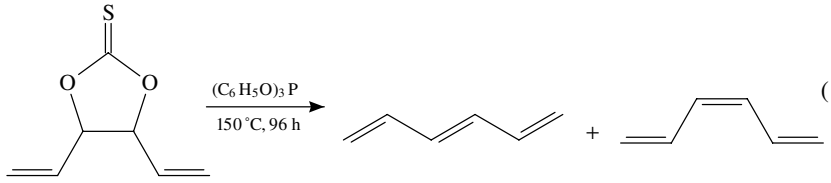
(15)



cis-Galbolene

Iodotrimethylsilane formed *in situ* from the reaction of chlorotrimethylsilane and sodium iodide, also effects the conversion of 2-ene-1,4-diols to 1,3-dienes (equation 16)[46]. Allylic thionocarbonates on heating with triphenylphosphite undergo deoxygenation (Corey–Winter reaction) to generate olefins[47]. This procedure has been used for making hexatrienes (equation 17)[47b].

(16)

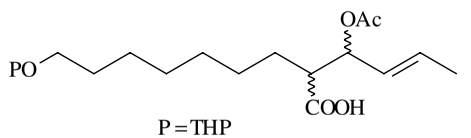
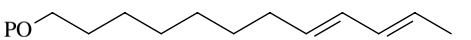
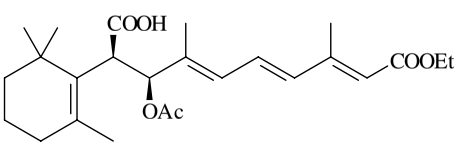
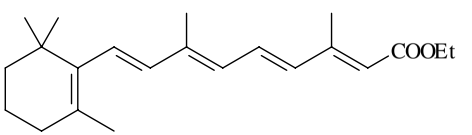


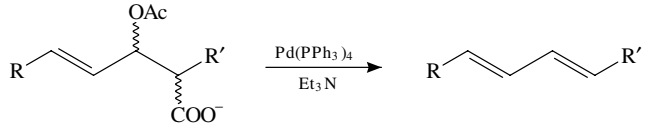
(17)

F. Decarboxylative Eliminations

Trost and coworkers have devised a stereocontrolled 1,3-diene synthesis employing a palladium-catalysed decarboxylative elimination procedure from allylic acetates carrying carboxylic acid functionality β- to the acetate group (equation 18)[48]. This decarboxylative elimination strategy has been applied to the synthesis of an insect pheromone, codlemone[48a] and the ethyl ester of vitamin A carboxylic acid (Table 5)[48b].

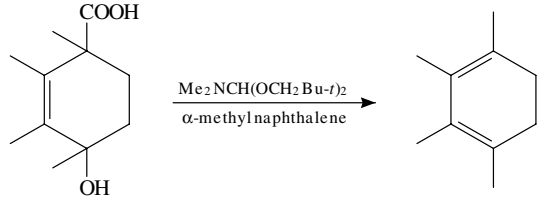
TABLE 5. Dienes and polyenes through decarboxylative elimination

Substrate	Product	Reference
 P = THP		48a
		48b



(18)

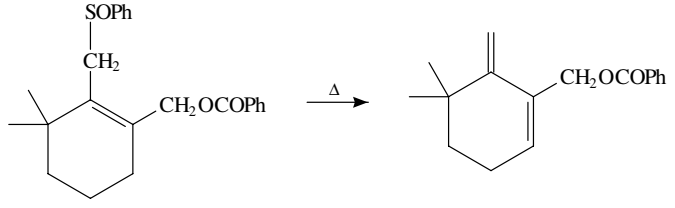
1,4-Decarboxylative elimination in 4-hydroxycyclohex-2-enecarboxylic acids with dimethylformamidedineopentylacetal has been shown to result in the formation of dienes in a regioselective manner under neutral conditions (equation 19)[49].



(19)

G. Elimination of Sulphoxides and Selenoxides

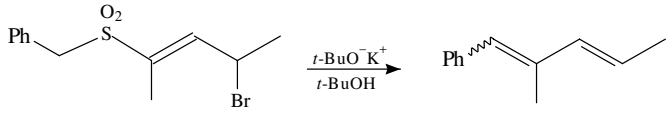
Sulphoxides and selenoxides undergo *syn* elimination under thermal conditions. A 1,4-elimination of sulphenic acid from an allyl sulphoxide leads to dienes (equation 20)[50]. Precursor sulphoxides are generated by oxidation of corresponding sulphides. This reaction, however, did not give good results when applied to more complicated systems[51].



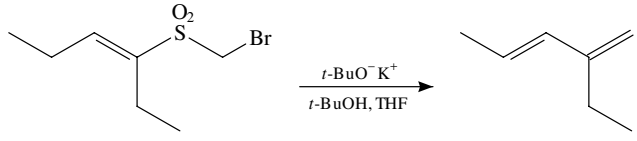
(20)

H. Ramberg–Backlund Reaction

The reaction of α-halosulphone with a base to give an olefin is known as Ramberg–Backlund reaction[52]. A vinylogous version of this rearrangement results in the formation of 1,3-dienes (equation 21)[53]. Another variation of this reaction is shown in equation 22[54]. These rearrangements proceed with moderate stereoselectivity.

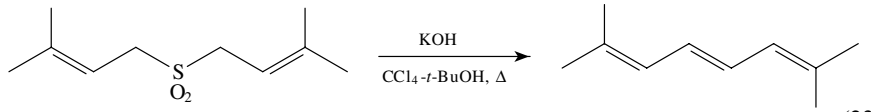


(21)

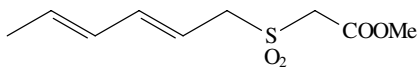


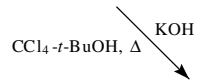
(22)

Bisallylic sulphones can be converted to trienes stereospecifically by treatment with potassium hydroxide in CCl_4–*t*-BuOH (equation 23)[55,56]. This method has been extended for the synthesis of trienoic acids by starting with dienyl β-sulphonyl esters (equation 24)[57]. β-Carotene has been prepared by treating the α,α'-dianion generated from starting sulphone with bromine or iodine followed by rearrangement (equation 25)[55]. Utilizing the Ramberg–Backlund reaction, an interesting cyclic enediyne has been made (equation 26)[58].

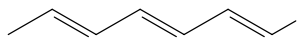


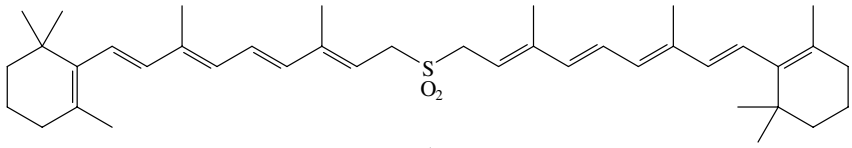
(23)

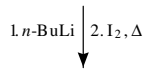




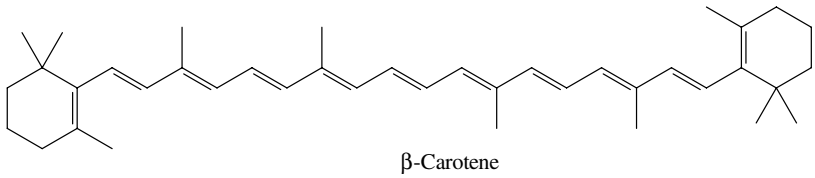
(24)



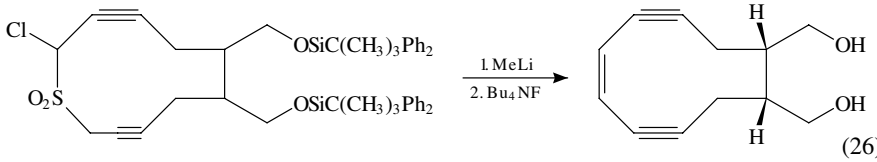




(25)



β-Carotene

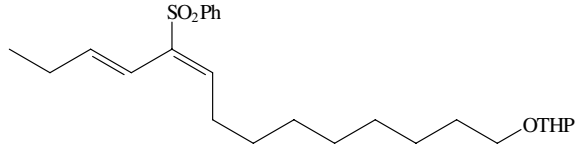


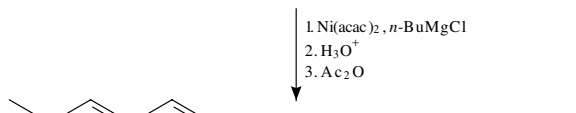
(26)

I. Reductive Desulphonylations

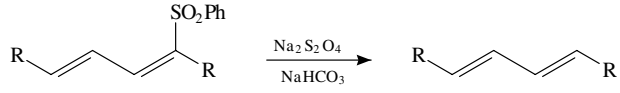
In general, reductive removal of a sulphonyl group from vinyl sulphones is not a stereospecific reaction. However, two methods, both developed by Julia, result in stereospecific products. The first one involves reaction of the vinyl sulphone with *n*-BuMgCl in the presence of a transition metal catalyst such as $Ni(acac)_2$. This method was used to synthesize a pheromone having a (*Z*,*E*)-diene (equation 27)[59]. Palladium catalysts can also be used for

reductive desulphonylation reaction provided that appropriate ligands are used. The other method for vinyl sulphone hydrogenolysis is to treat it with sodium dithionite and sodium bicarbonate in aqueous DMF (equation 28)[60]. The mechanism of this reaction involves conjugate addition of HSO_2^- followed by the loss of sulphur dioxide and sulphinate moiety[61].





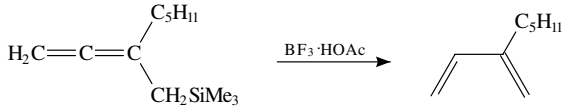
(27)



(28)

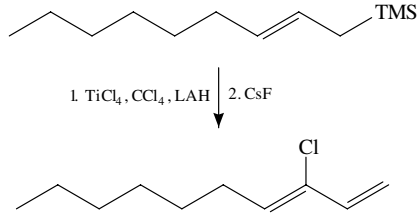
J. Elimination of Silyl Groups

Dienes can be obtained from silylallenes by protodesilylation using boron trifluoride–acetic acid complex (equation 29)[62]. Since silylallenes can be obtained by the reaction of propargyl acetate with cuprous reagent derived from chloromethyltrimethylsilane, this reaction sequence constitutes conversion of propargylic acetate to butadiene through one carbon homologation.



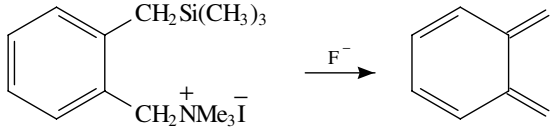
(29)

Allylic silanes react with dichlorocarbenes, generated from dechlorination of carbon tetrachloride with low valent titanium species, to furnish dichlorocyclopropanes, which in turn get desilylated with CsF in DMF to generate 3-chloro-1,3-butadienes (equation 30)[63].

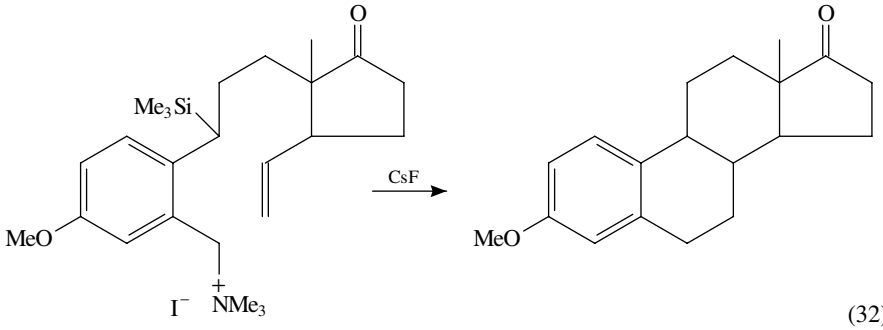


(30)

An efficient method for the generation of *o*-quinodimethanes via desilylation reaction involves treatment of a 2-[(trimethylsilylmethyl)benzyl]trimethylammonium iodide with fluoride ion (equation 31)[64]. This reaction was applied by Saegusa and coworkers for the synthesis of estrone in which an intramolecular Diels-Alder reaction of an *o*-quinodimethane, generated *in situ*, served as the key reaction (equation 32)[65].



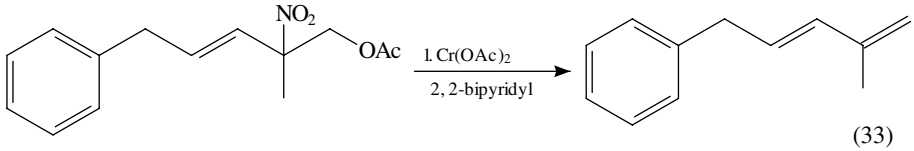
(31)



(32)

K. Reductive Elimination of Nitroacetates

Zard and coworkers have developed a synthesis of substituted dienes by reductive elimination of allylic nitroacetates (equation 33)[66]. Allylic nitroacetates can be prepared by condensation of nitromethane with the carbonyl compound followed by addition of formaldehyde and acetylation[67]. Reductive elimination can be carried out by employing either chromous acetate or samarium iodide.

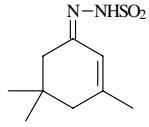
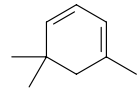
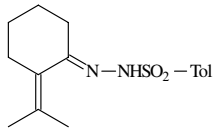
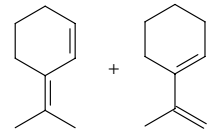
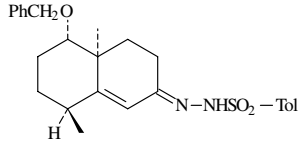
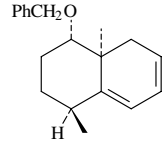


(33)

L. The Shapiro Reaction

Ketone *p*-toluenesulphonyl hydrazones can be converted to alkenes on treatment with strong bases such as alkyl lithium or lithium dialkylamides. This reaction is known as the Shapiro reaction[68]. When α,β-unsaturated ketones are the substrates, the products are dienes. This reaction is generally applied to the generation of dienes in cyclic systems where stereochemistry of the double bond is fixed. A few examples where dienes have been generated by the Shapiro reaction have been gathered in Table 6[69].

TABLE 6. Dienes through the Shapiro reaction

Substrate	Product	Reference
		69a
	 80% + 9%	69b
		69c

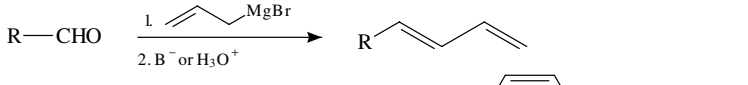
III. ADDITION–ELIMINATION REACTIONS

A. General Aspects

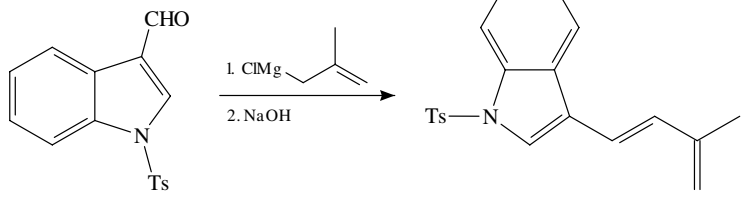
Nucleophilic additions to carbonyl groups lead to alcohols which on dehydration, furnish alkenes[70,71]. This two-step protocol has been extremely useful for diene and polyene synthesis with wide variation in the carbonyl substrate and the nucleophilic addendum. Diene synthesis using aldol-type condensation as well as phenyl sulphonyl carbanion (the Julia reaction) are also discussed in this section.

B. Allyl and Vinyl Organometallics

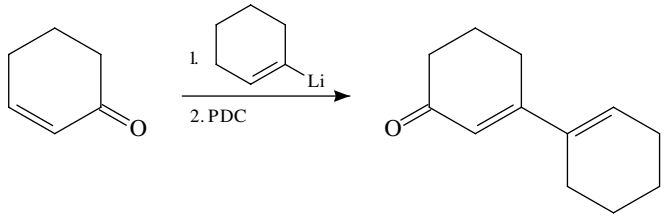
A simple two-step protocol for the generation of a terminal diene is to add allyl magnesium bromide to an aldehyde or a ketone and subsequent acid or base catalysed dehydration (equation 34)[72]. Cheng and coworkers used this sequence for the synthesis of some indole natural products (equation 35)[72a]. Regiospecific dienones can be prepared by 1,2-addition of vinyllithium to α,β-unsaturated carbonyl compounds and oxidative rearrangement of the resulting dienols with pyridinium dichromate (equation 36)[73].



(34)



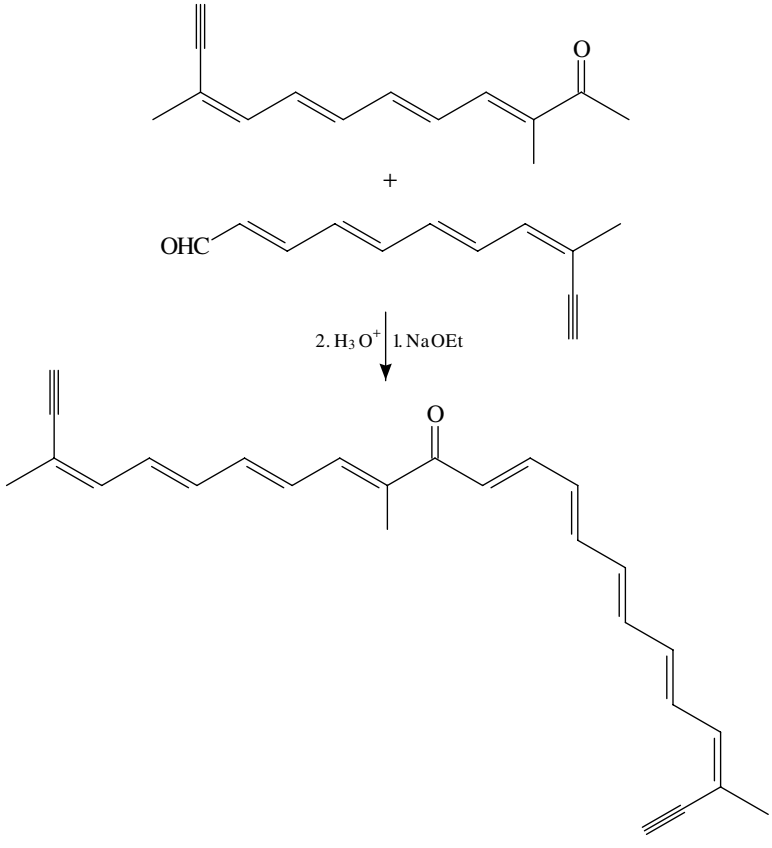
(35)



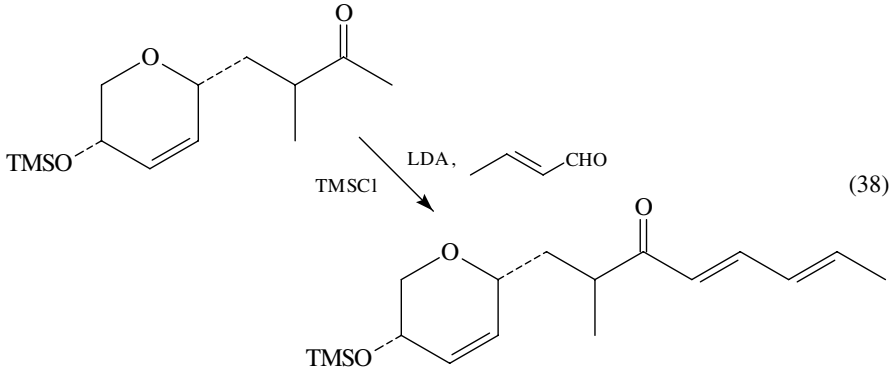
(36)

C. Aldol Condensation-dehydration (Knoevenagel Reaction)

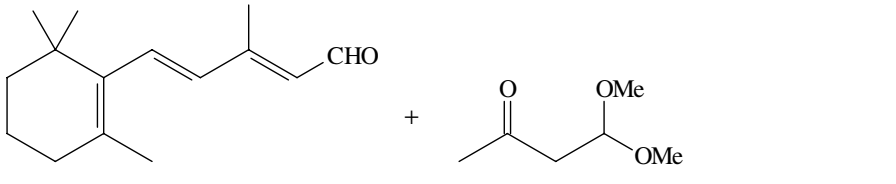
The nucleophilic addition of a carbanion to an aldehyde or a ketone having a conjugated double bond and the subsequent dehydration sequence (Knoevenagel reaction) is a popular method for generating dienes and polyenes (equation 37)[74]. This reaction takes place efficiently and stereoselectively, when LDA is used as a base in the presence of chlorotrimethylsilane (equation 38)[75]. Knoevenagel condensation was a key reaction during many classical carotenoid syntheses[76]. Recently, Seltzer and coworkers used the dimethyl acetal of acetylacetaldehyde for aldol condensation with a C_{15}-aldehyde, to generate the tetraenyl ketone acetal (equation 39)[77].

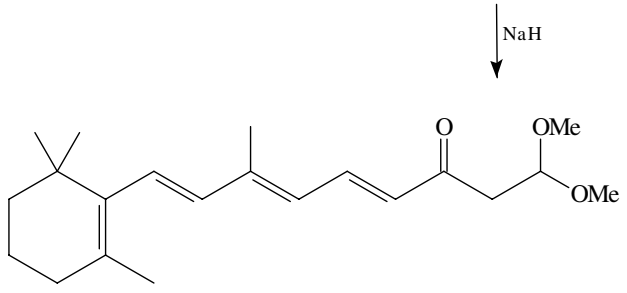


(37)



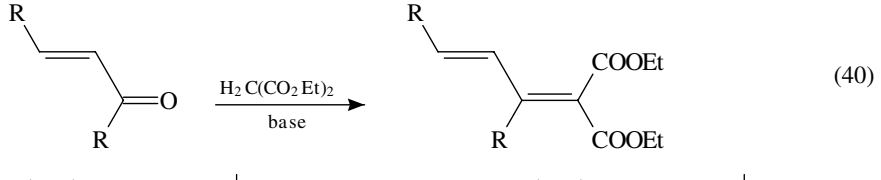
(38)



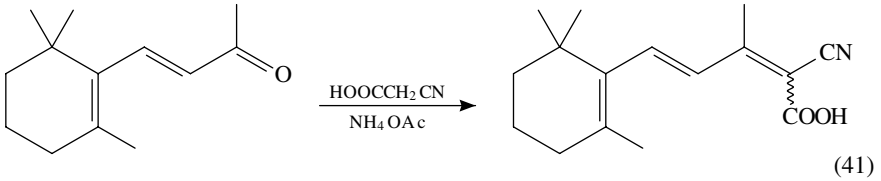


(39)

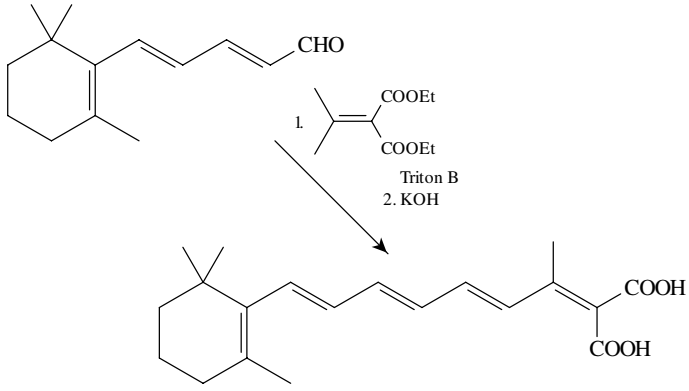
Knoevenagel condensation of diethyl malonate or related compounds with α,β-unsaturated aldehydes and ketones results in diene esters (equation 40)[78]. This condensation reaction has been used to extend the polyene chain length of vitamin A related compounds (equations 41[79] and 42[80]).



(40)

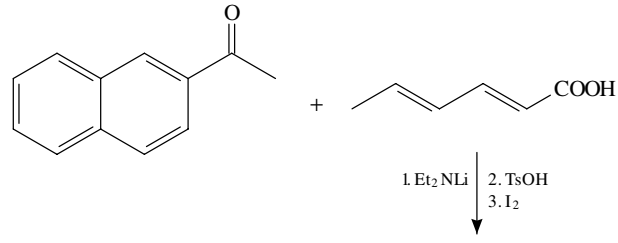


(41)

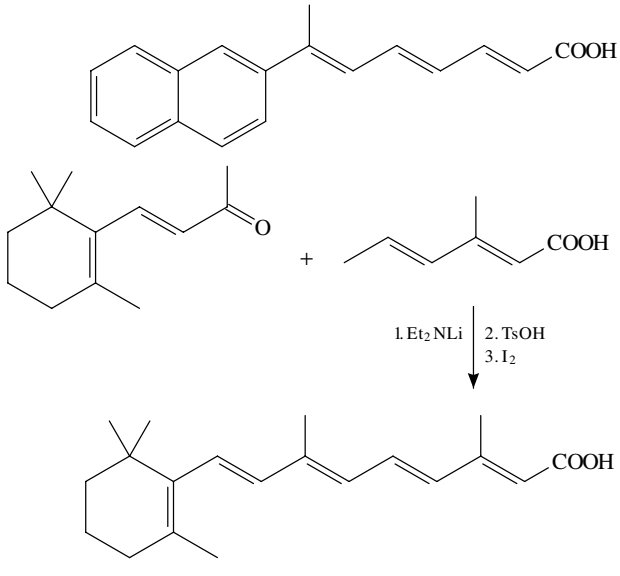


(42)

A convenient way of six-carbon homologation of aldehydes and ketones is the nucleophilic addition of the dianion generated from sorbic acid, (2*E*,4*E*)-hexa-2,4-dienoic acid and subsequent dehydration to form the corresponding trienoic acid (equation 43)[81]. The 3-methyl analogue of sorbic acid has been used in a similar fashion for a short synthesis of vitamin A carboxylic acid (equation 44)[82].



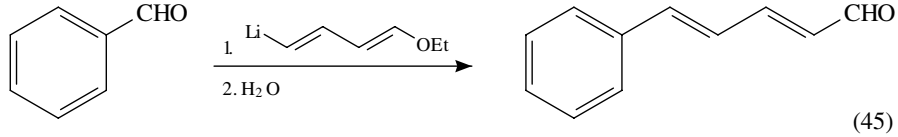
(43)



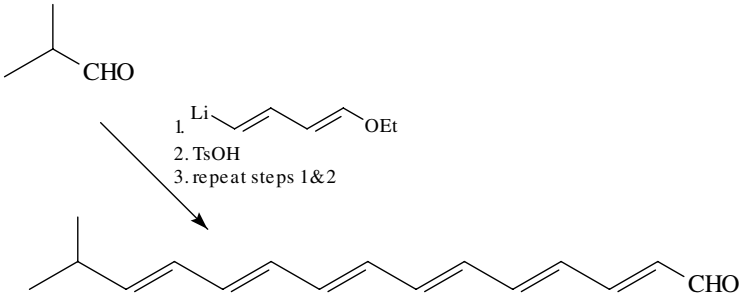
(44)

D. Wollenberg Method

Wollenberg introduced 4-lithio-butadienyl ethyl ether as a versatile reagent for four-carbon homologation of carbonyl compounds to the corresponding dienals (Table 7)[83]. This reagent, which is obtained *in situ* by transmetallation of 4-(tri-*n*-butylstannyl)butadienyl ethyl ether, adds to carbonyl compounds to generate intermediate alcohols which, on dehydration and hydrolysis of the enol ether, result in dienals (equation 45)[83a]. The advantage of this method is the generation of the aldehyde function at the end of the reaction so that it can be subjected to iterative Wollenberg reaction for polyene synthesis (equation 46)[83b]. Rychnovsky and coworkers found this methodology to be specially useful for the synthesis of polyene portions of macrolide antibiotics such as roflamycoin[83c] and roxaticin[83d] (Table 7).

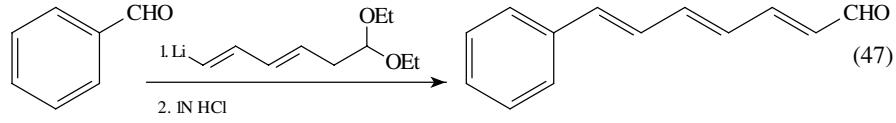


(45)



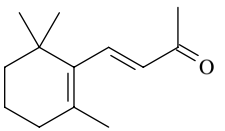
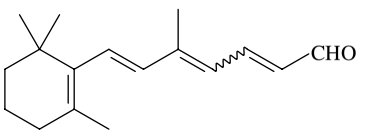
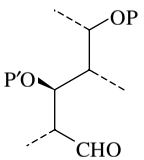
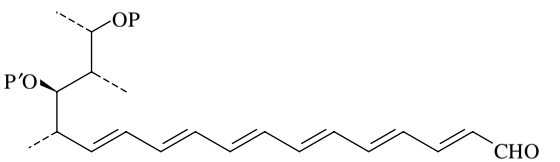
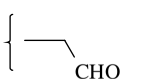
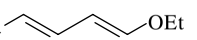
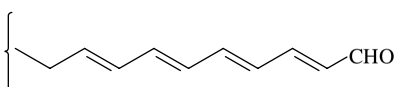
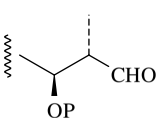
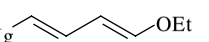
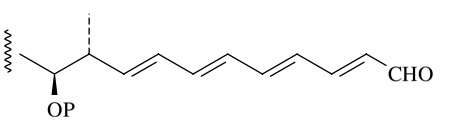
(46)

Duhamel and coworkers introduced a convenient isoprenylating reagent, 1-lithio-2-methyl-4-trimethylsiloxybutadiene, for five-carbon homologation of a carbonyl group[83g]. Utilizing this reagent, in a reiterative fashion, retinal was synthesized in good yields starting from β-ionylideneacetaldehyde[83g]. In a related study, Duhamel and coworkers developed the dimethy; acetal derivative of ω-lithiosorbaldehyde for six-carbon homologation[84] (equation 47) and 4-lithio-1-trimethylsiloxybutadiene for four-carbon homologation[85] (equation 48) of carbonyl compounds. Simultaneously, the same group also introduced C_7 reagents, 1-lithio-6-methoxy-4-methylhexatriene and 1-lithio-4-methyl-6-trimethylsiloxyhexatriene for a seven-carbon homologation of carbonyl compounds[83g]. These C_7 units were utilized for a short $C_{13} + C_7$ synthesis of retinal, starting from abundantly available β-ionone (equation 49). Extending further, 1-lithio-2,6-dimethyl-8-methoxyoctatetra-1,3,5,7-ene was introduced as C_{10} reagent for $C_{10} + C_{10}$ synthesis of vitamin A aldehyde, retinal (equation 50)[86,87].



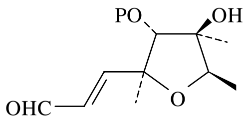
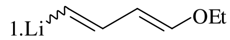
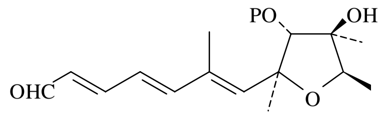
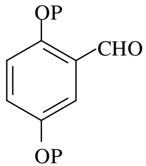
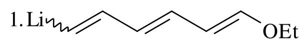
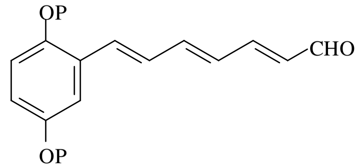
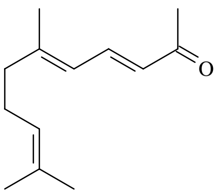
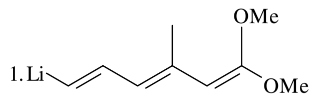
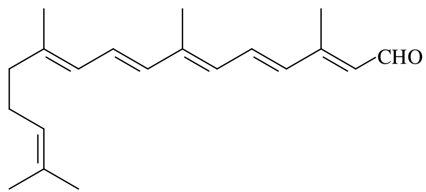
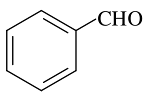
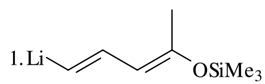
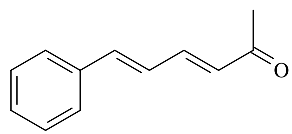
(47)

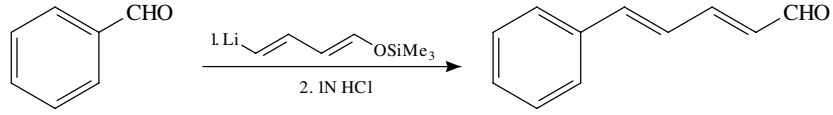
TABLE 7. Dienes and polyenes through the Wollenberg method

Starting ketone	Reagents	Product	Reference
	1. Li CH=CH—CH=CH—OEt 2. TsOH		83a
 P = $MeOCH_2$;	1. Li CH=CH—CH=CH—OEt 2. TsOH 3. repeat steps 1 & 2 P′ = TBS	 (Amphotericoin B fragment)	83b
	1. BrMg  2. MsCl, Et_3N 3. repeat steps 1 & 2	 (Roflamycoin fragment)	83c
 P = 1,3-Benzodithiolan-2-yl	1. BrMg  2. MsCl, Et_3N 3. repeat steps 1 & 2	 (Roxaticin fragment)	83d

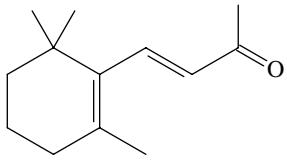
continued overleaf

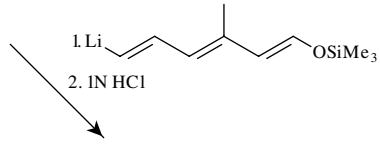
TABLE 7. (*continued*)

Starting ketone	Reagents	Product	Reference
 P = $MeOCH_2$	 2. SiO_2		83e
	 2. 1N HCl P = *t*-$BuMe_2Si$		83f
	 2. 1N HCl		83g
	 2. H_3O^+		83h

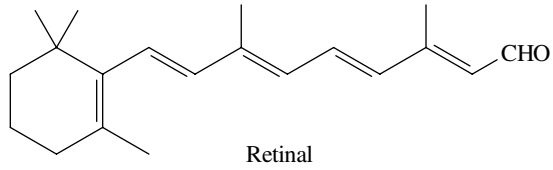


(48)

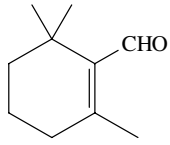


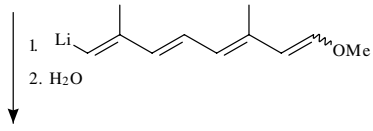


(49)

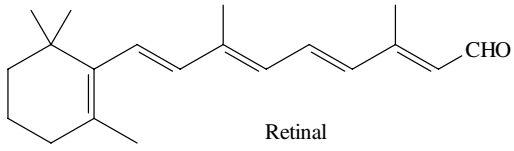


Retinal



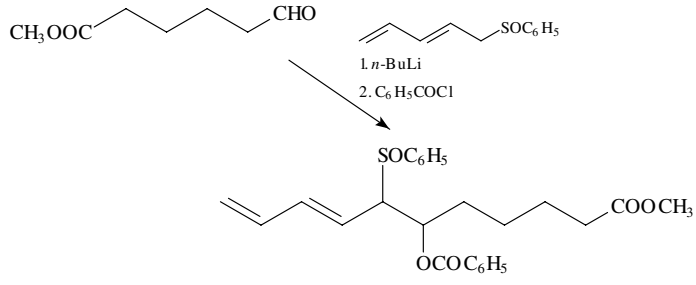


(50)

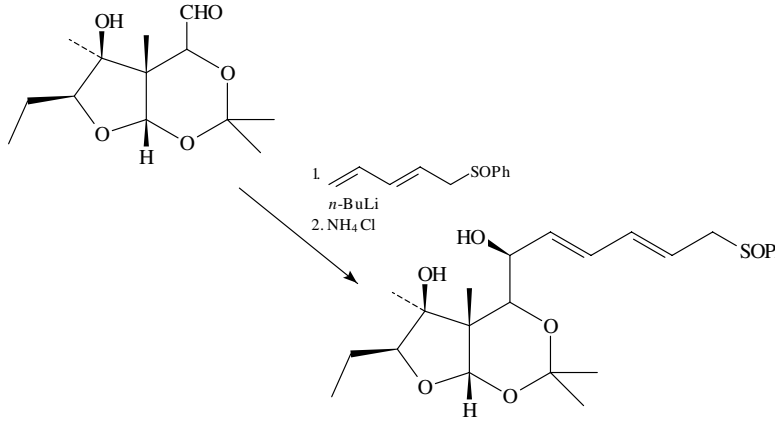


Retinal

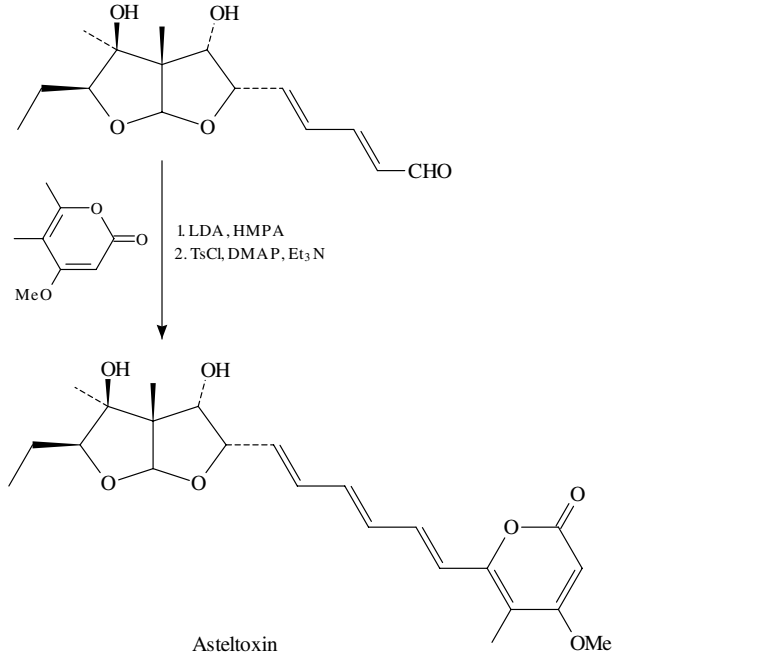
Corey and coworkers used the anion from *E*-1-phenylsulfinylmethyl-1,3-butadiene as an equivalent of the 4-formyl-(*E*,*E*)-1,3-butadienyl anion for the synthesis of 5-desoxyleukotriene D. Thus, the lithio derivative of pentadienyl sulphoxide reacts with methyl 5-formylpentanoate to result in the aldol, which on double [3.2]sigmatropic rearrangement furnishes diene product (equation 51)[88]. Conversion of phenyl sulphoxide to aldehyde was achieved through the Pummerer rearrangement-hydrolysis pathway. The dienal so formed was ready for Wittig reaction to generate the (*E*,*E*,*Z*)-triene moiety present in the target molecule. Schreiber and Satake also made use of lithiated pentadienyl sulphoxide as 4-formyl-(*E*,*E*)-1,3-butadienyl anion equivalent and subsequent Pummerer rearrangement, aldol condensation and dehydration led to the total synthesis of polyene antibiotic asteltoxin (equations 52 and 53)[89].



(51)



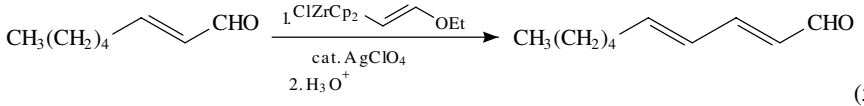
(52)



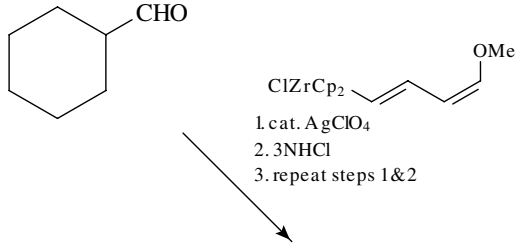
(53)

Asteltoxin

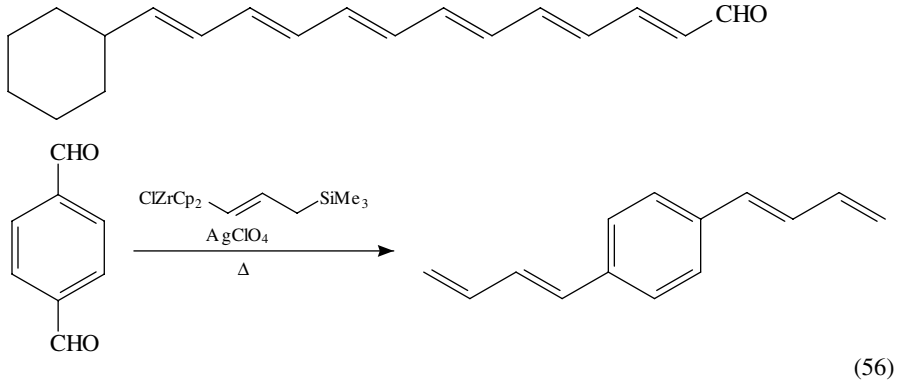
Alkenylzirconocene reagents add to carbonyl compounds in the presence of a catalytic amount of silver perchlorate to give allylic alcohols which, on dehydration, give dienes (equation 54)[90]. Since alkenylzirconocene intermediates are accessible readily from alkynes by reacting with Schwartz reagent $[Cp_2Zr(H)Cl]$[91], this sequence is of immense practical importance. An application of this reaction in an iterative fashion for the preparation of polyenals is shown in equation 55[92]. Trimethylsilyl-1-propenylzirconocene chloride also adds to carbonyl compounds leading to allylic alcohols which, on Peterson-type elimination, give predominantly *E*,*E*-1,3-dienes (equation 56)[93].



(54)

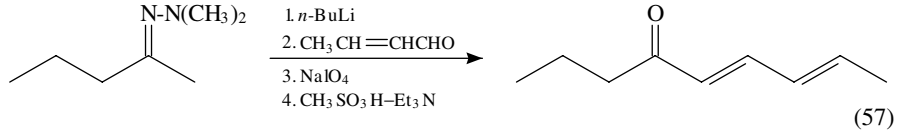


(55)



(56)

Crossed aldol condensation of an anion generated α- to a ketone equivalent with α,β-unsaturated aldehyde, dehydration and release of the ketone is an effective way of generation of dienones. Corey and Enders found that α-lithiated *N*,*N*-dimethylhydrazones undergo 1,2-addition to the aldehydes and ketones to form β-hydroxy derivatives. Sequential treatment of the intermediate with sodium periodate and methanesulphonyl chloride-triethylamine furnishes *E*,*E*-2,4-dienone derivative (equation 57)[94].

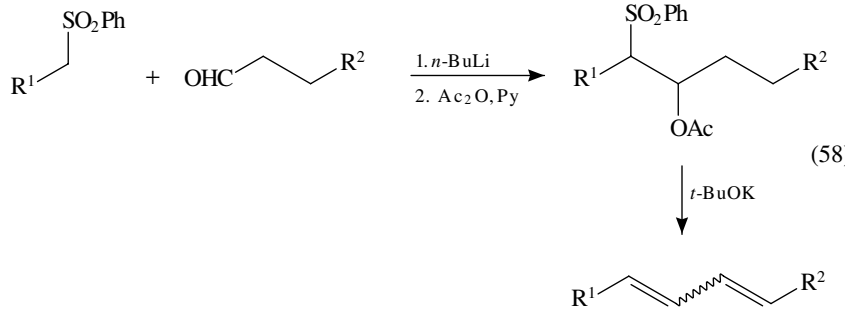


(57)

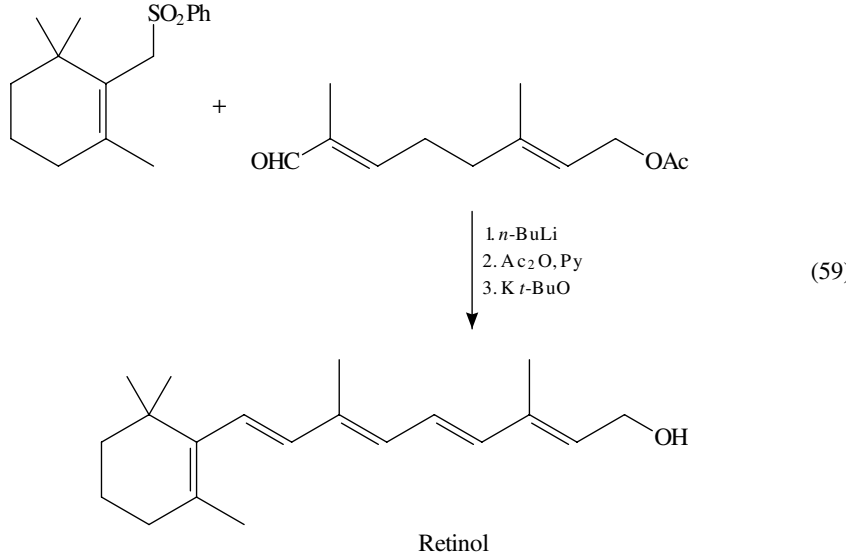
E. Sulphones (Julia and Related Reactions)

α-Sulphone carbanions add to aldehydes and ketones to generate β-hydroxy sulphones. Concomitant reductive removal of the hydroxy group and sulphenic acid results in alkene formation[95]. Since the alkene formation in this reaction (Julia reaction) is equilibrium controlled, E/Z selectivity is usually high, favouring the E-isomer. When one of the reacting partners, either the sulphone or the carbonyl compound, has a double bond already present, then the product is a diene. Julia coupling methodology has been used extensively for the generation of conjugated diene (Table 8)[96] and polyene (Table 9)[97] moieties.

Otera and coworkers developed an alternative procedure to the Julia method for generating dienes or alkynes in the same reaction by the double elimination of β-acetoxy or β-alkoxy sulphones with potassium t-butoxide (equation 58)[98,99]. The reaction pathway leading to the diene or an alkyne depends on the substrate structure and the reaction conditions. If an allylic hydrogen is present in the substrate then diene is formed; otherwise, the alkyne is the product of the reaction. This modified Julia methodology has been applied to the synthesis of vitamin A (equation 59)[100], alkaloids piperine (equation 60)[101] and trichonine (equation 61)[102].



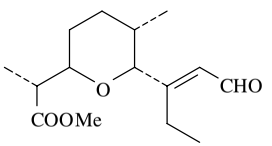
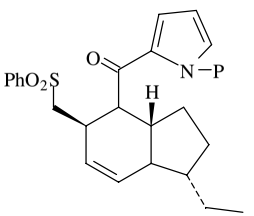
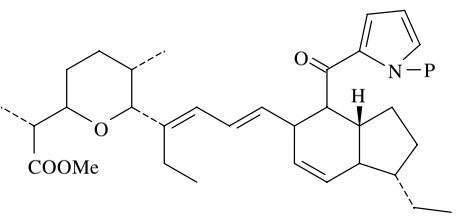
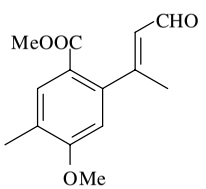
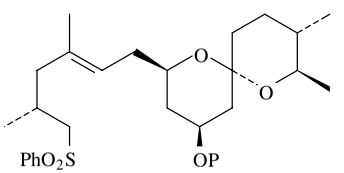
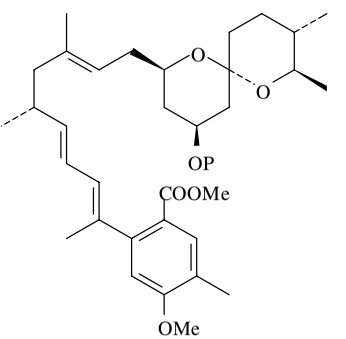
(58)



(59)

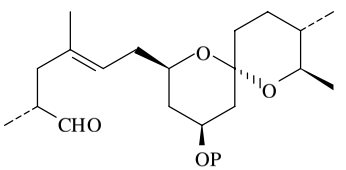
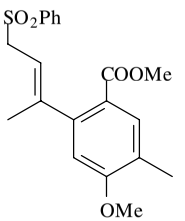
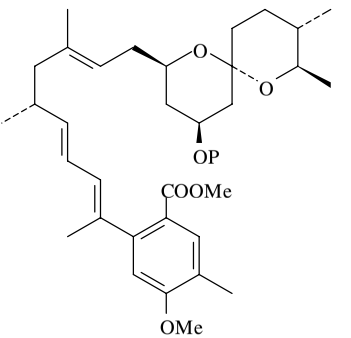
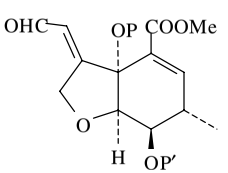
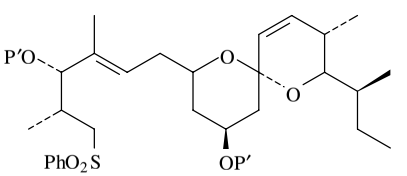
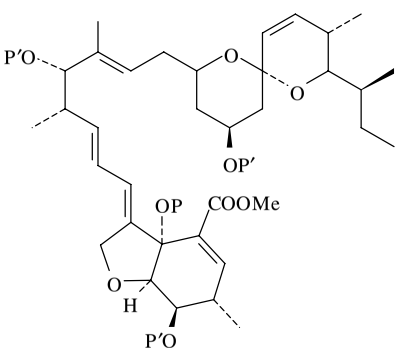
Retinol

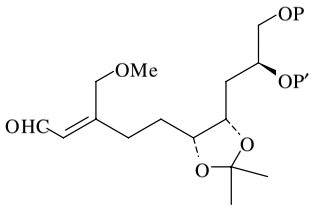
TABLE 8. Dienes through the Julia reaction

Aldehyde	Sulphone	Product	Reference
 P = $Me_3SiCH_2CH_2O$			96a
	 P = *t*-$BuPh_2Si$		96b

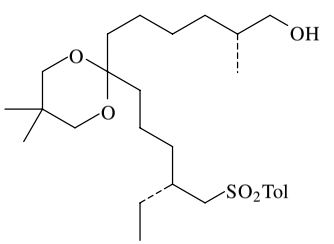
continued overleaf

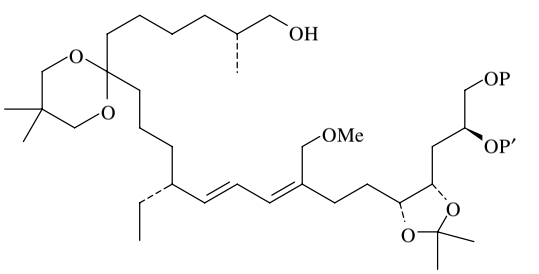
TABLE 8. (*continued*)

Aldehyde	Sulphone	Product	Reference
 P = *t*-BuMe$_2$Si			96c
 P = Me$_3$Si; P′ = *t*-BuMe$_2$Si			96d



P = *t*-BuMe$_2$Si; P′ = MeOCH$_2$





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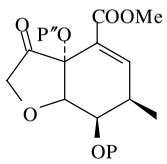
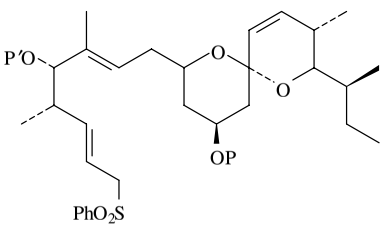
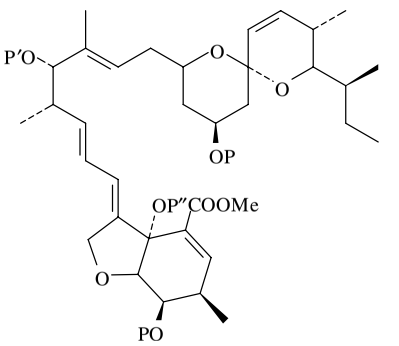


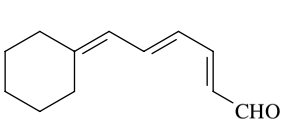
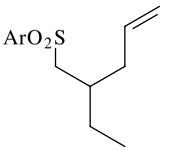
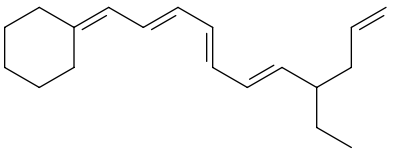
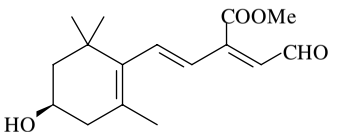
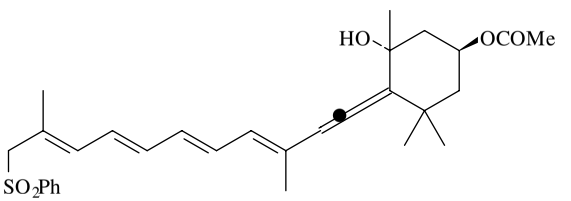
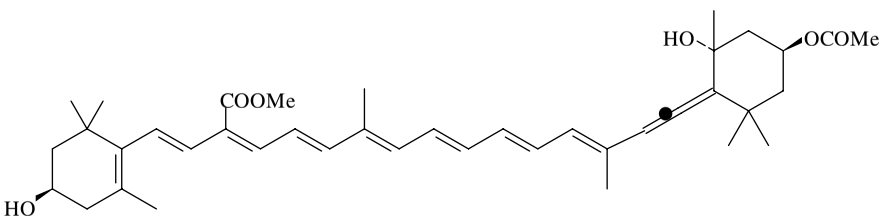
P = *t*-BuMe$_2$Si; P′ = SEM; P″ = TES

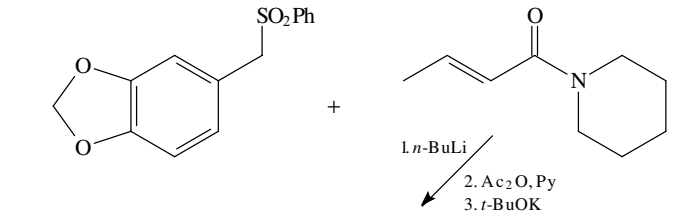




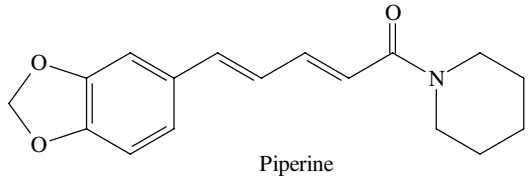
96f

TABLE 9. Polyenes through the Julia reaction

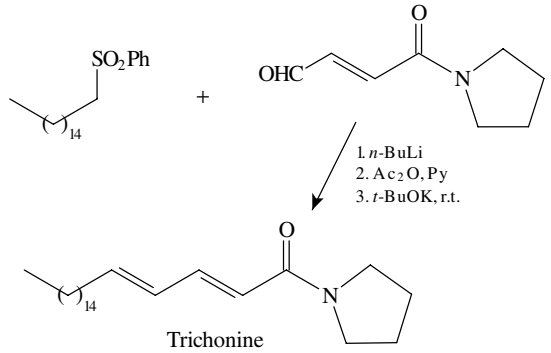
Aldehyde	Sulphone	Product	Reference
			97a
			
			97b



(60)



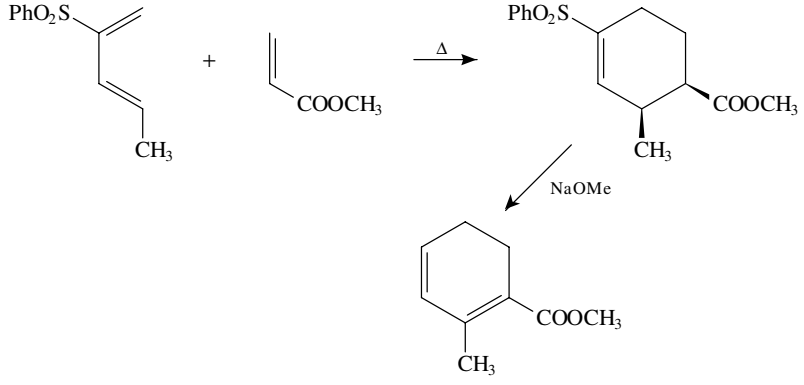
Piperine



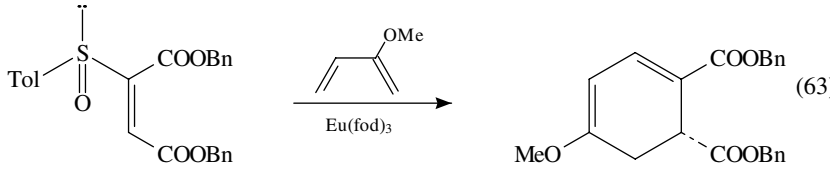
(61)

Trichonine

Backvall and Juntunen and Fuchs and Braish have developed (*E*)-2-phenylsuphonyl-1,3-dienes prepared under Julia conditions as versatile synthones for a variety of organic transformations[103]. These dienes undergo facile Diels–Alder reaction and subsequent 1,4-elimination of sulphinic acid by base to generate a new diene (equation 62)[103a]. An elegant extension of this method is to use chiral sulfinylmaleate which, on Diels–Alder reaction and elimination of the sulfinyl group, generates an optically active diene for further applications (equation 63)[104].

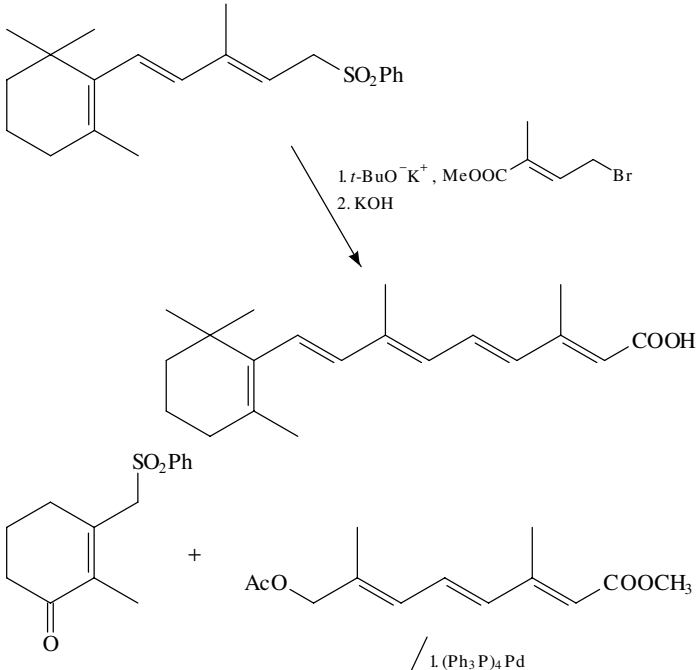


(62)



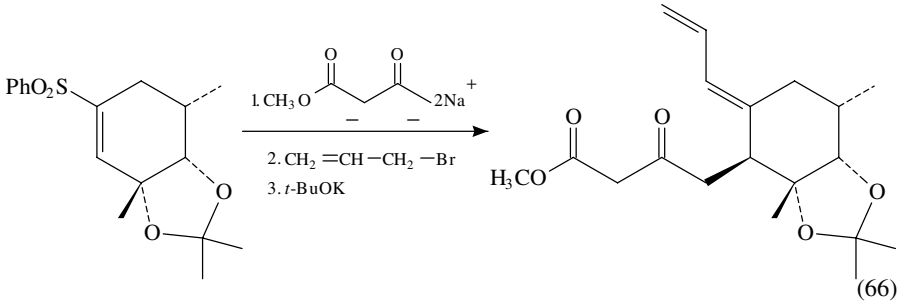
(63)

Allyl sulphones can be converted to dienes by alkylation and elimination of sulphinic acid under basic conditions (equation 64)[105]. Several vitamin A related polyenes have been synthesized following this two-step protocol (Table 10)[106]. The poor leaving-group ability of the arylsulphonyl group requires treatment with strong base for elimination. However, elimination of the allylsulphonyl group takes place readily under palladium catalysis (equation 65)[107]. Vinyl sulphones can be converted to dienes via Michael addition, alkylation with allyl halides and elimination of sulphinic acid sequence (equation 66)[108].



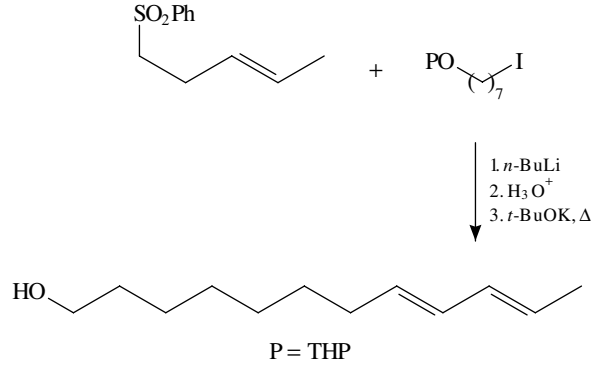
(64)

(65)



(66)

An alternative approach to the synthesis of 1,3-dienes is by elimination of benzenesulphinic acid from homoallylic sulphones under basic conditions. This method has been used for the synthesis of a pheromone constituent of the codling moth (equation 67)[109].



(67)

IV. CONCERTED REACTIONS

A. General Aspects

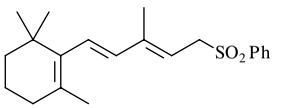
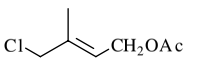
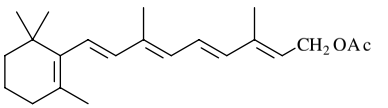
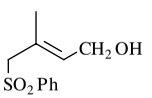
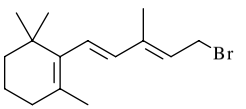
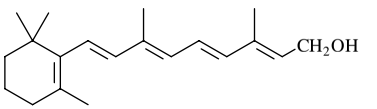
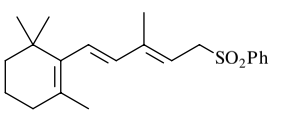
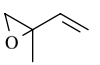
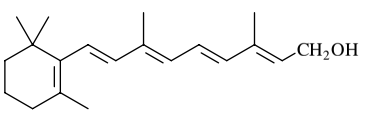
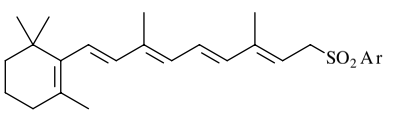
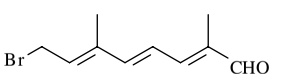
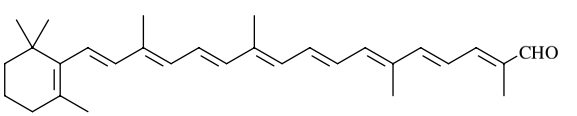
Symmetry-allowed concerted reactions such as retro Diels–Alder reactions and electrocyclic ring-opening reactions are popular methods for releasing the diene component for further manipulations[110]. As the reactions take place via symmetry-allowed processes[111], the diene products can be obtained with high stereochemical purity. Extrusion of molecules such as sulphur dioxide, nitrogen, oxygen and carbon dioxide from cyclic substrates is another commonly used methodology for the stereoselective generation of dienes.

B. Extrusion of Neutral Species

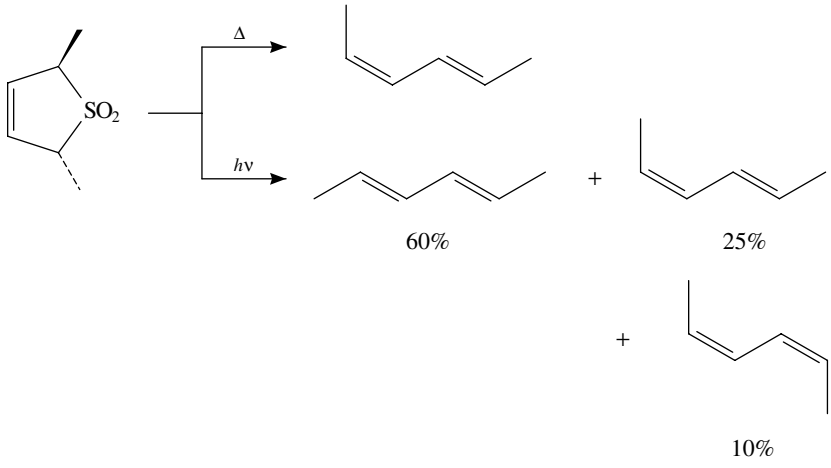
1. Sulphur dioxide

Extrusion of sulphur dioxide from cyclic systems leading to dienes has proved to be a synthetically useful reaction[112]. Thermolysis of *cis*- and *trans*-2,5-disubstituted sulpholenes, which can be readily obtained through regio- and stereoselective alkylation, proceeds in a stereospecific manner affording 1,3-dienes of high stereochemical purity, as predicted by symmetry rules (equations 68 and 69)[113]. On the other hand, a photochemical process is not completely stereospecific (equation 68)[114]. 2,5-Dialkylative cyclization

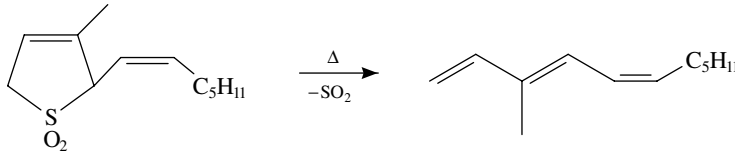
TABLE 10. Synthesis of vitamin A and related compounds through allyl sulphones

Allyl Sulphone	Electrophile	Product	Reference
			106a
			106b
			106c
 Ar : $C_6H_5OC_6H_4$	 		106d

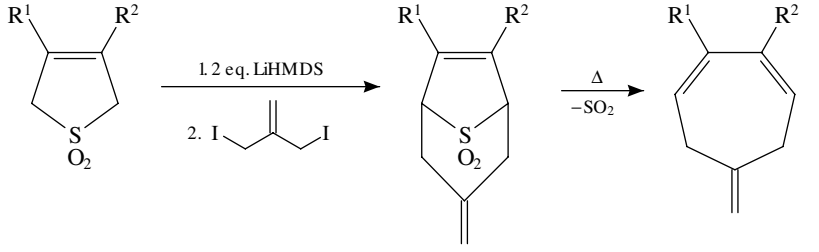
can be performed on 3-sulpholene with 3-chloro-2-(chloromethyl)propene and sulphur dioxide extrusion from the [3.2.1]bicyclic product results in a seven-membered cyclic diene (equation 70)[115]. Regioselective monoalkylation of sulpholene derivatives can be performed via their 2-stannyl or 2-manganese derivatives with vinyl iodides in the presence of a Pd^0 complex[116]. Sulphur dioxide extrusion from the products result in trienes with well-defined stereochemistry (equation 71).



(68)

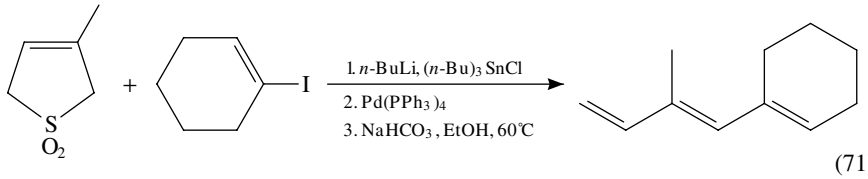


(69)



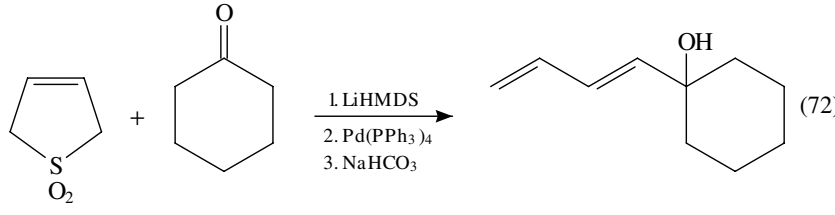
(70)

LiHMDS = lithium hexamethyldisilazide



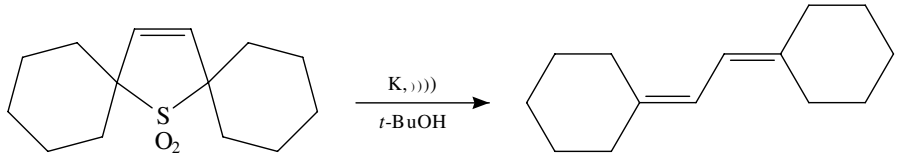
(71)

The carbanion generated from deprotonation of the α-carbon atom of sulpholene reacts with aldehydes and ketones to give alcohols. Sulphur dioxide extrusion from the products results in (*E*)-α-hydroxy-1,3-dienes (equation 72), or dehydration followed by thermal desulphonylation results in trienes[117]. Dienones can be obtained if the initial condensation is conducted with an aldehyde, followed by oxidation and sulphur dioxide removal[117].



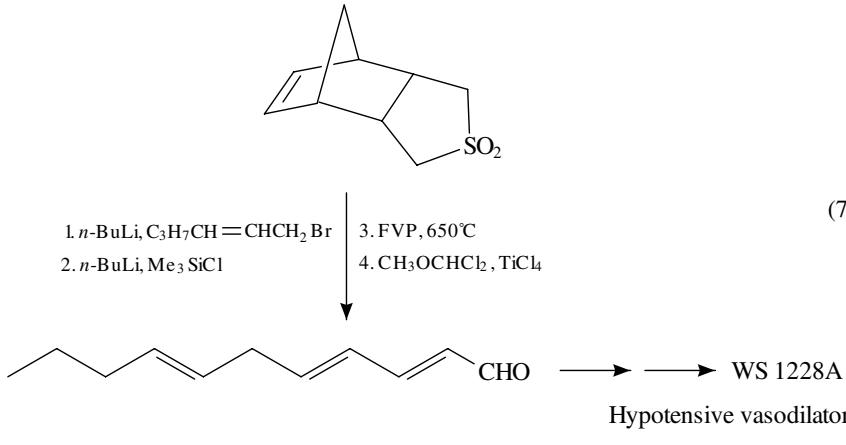
(72)

Even though sulphur dioxide extrusion from sulpholene derivatives is generally conducted either by heating in a non-polar solvent or in the presence of base[118], alternative reagents such as LAH[119], and finely dispersed potassium metal[120] are also used. Syntheses of some tetrasubstituted butadienes were achieved by treating the corresponding sulpholenes with ultrasonically dispersed potassium metal in the presence of water (equation 73)[120b].

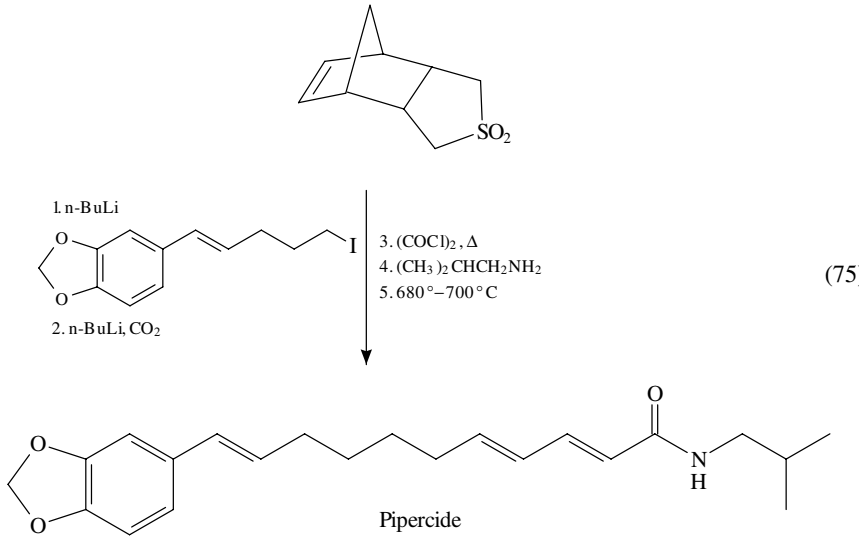


(73)

The Diels–Alder adduct of sulpholene and cyclopentadiene is a useful starting material for substituted diene synthesis[121]. The diene moiety is unmasked by retro-Diels–Alder reaction and sulphur dioxide extrusion under flash vacuum pyrolysis conditions (equations 74 and 75)[122,123].

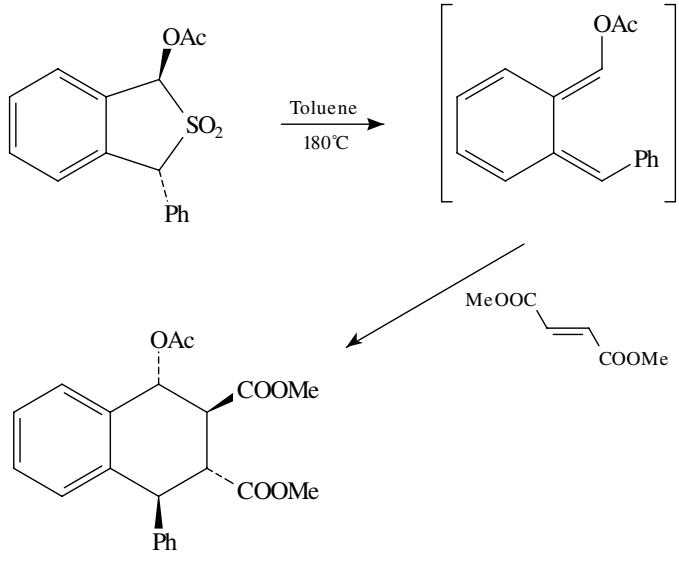


(74)

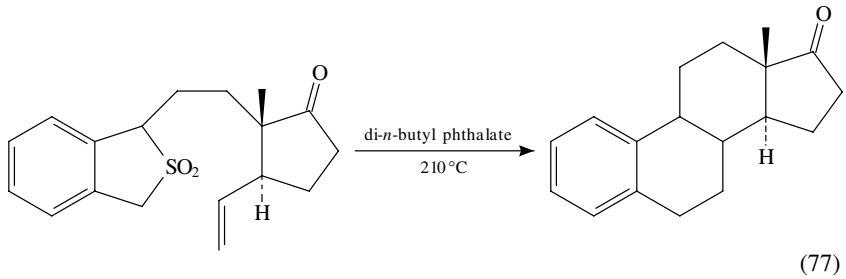


(75)

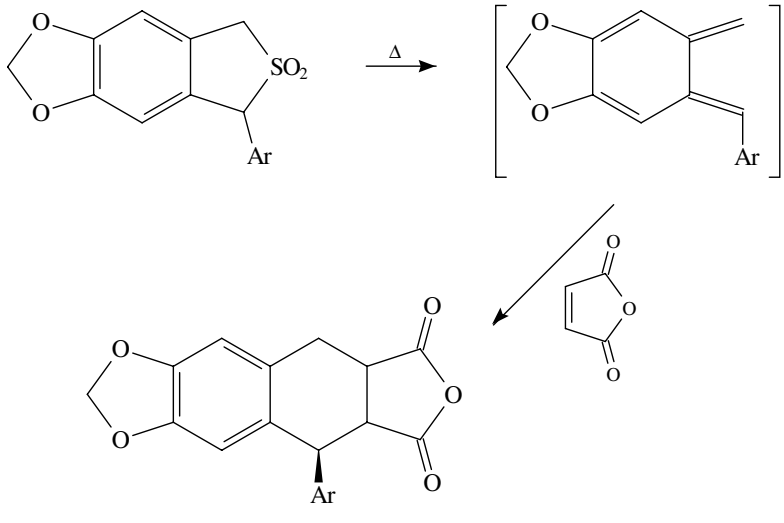
o-Quinodimethanes can be made *in situ* by sulphur dioxide extrusion from 1,3-dihydro-4,5-benzo[*c*]thiophene-2,2-dioxide derivatives (equation 76)[124,124*j*]. *o*-Quinodimethanes undergo facile intramolecular Diels–Alder reaction with an internal alkene to result in polycyclic compounds. An expedient synthesis of estrone derivative, an enantioselective synthesis of (+)-esterdiol and a short synthesis of a lignane: were achieved following this strategy (equations 77 and 78)[125,126]. Heteroaromatic *o*-quinodimethanes can be prepared *in situ* by sulphur dioxide extrusion from the appropriate sulpholene precursors which readily undergo Diels–Alder reactions (equation 79)[127].



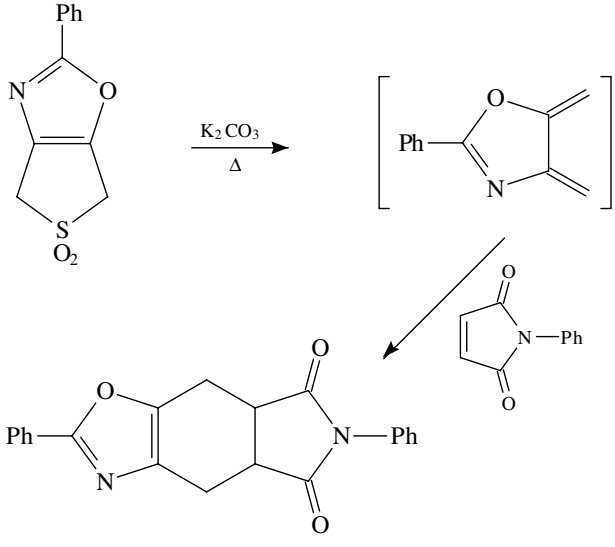
(76)


O
SO2
H
di-n-butyl phthalate
210 °C
O
H

(77)


O
O
SO2
Ar
Δ
O
O
Ar
O
O
O
O
O
O
O
O
Ar

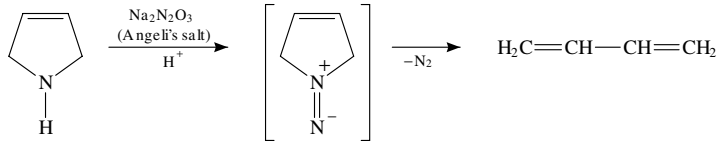
(78)


Ph
N
O
S
O2
K2 CO3
Δ
O
Ph
N
O
N—Ph
O
Ph
N
O
N—Ph
O
O

(79)

2. Nitrogen

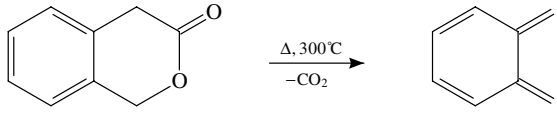
Butadiene can be obtained by thermal extrusion of a nitrogen molecule from a cyclic diazene (equation 80)[128]. However, this reaction has found only limited synthetic applications.



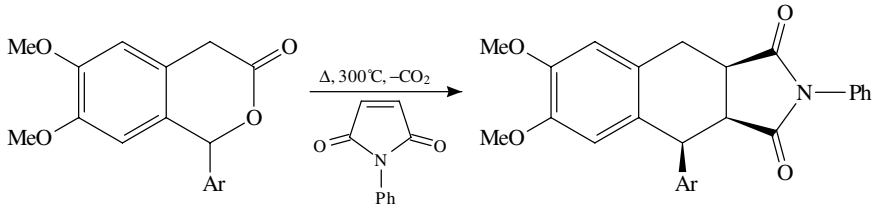
(80)

3. Carbon dioxide and carbon monoxide

Isochromones lose carbon dioxide on heating via retro-Diels–Alder pathway to result in *o*-quinodimethanes (equation 81)[124i,129]. An isochromone route to podophyllotoxin derivative has been described (equation 82)[130]. Diels–Alder adducts of α-pyrone readily extrude carbon dioxide on thermal activation to furnish cyclohexadienes, which are useful substrates in tandem Diels–Alder reactions (equation 83)[131].

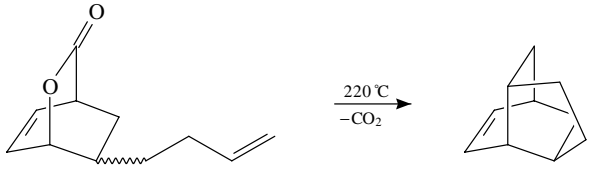


(81)



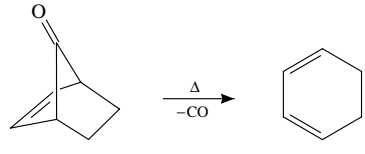
Ar = 3, 4, 5-$(MeO)_3$ C_6H_2

(82)



(83)

Photo- and thermal decarbonylation of cyclic unsaturated ketones leads to the formation of cyclic 1,3-dienes. Such decarbonylations are commonly observed in 7-ketonorbornenes and related bridged bicyclic systems to give cyclohexadienes (equation 84)[132].

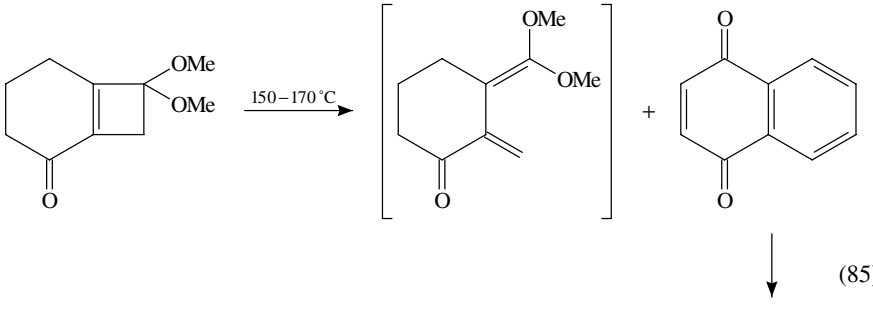


(84)

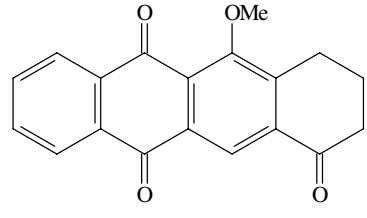
C. Ring Opening of Cyclobutenes

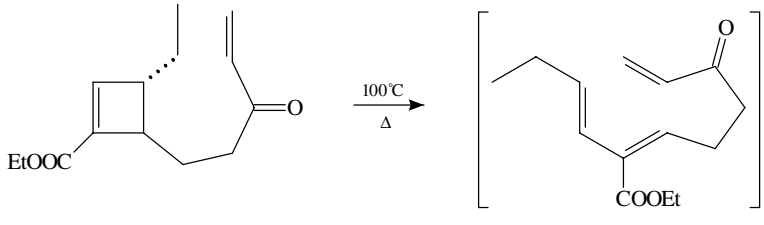
Cyclobutenes undergo facile, thermally induced conrotatory ring opening to generate 1,3-dienes[133]. Highly oxygenated butadienes are useful in Diels–Alder and hetero-Diels–Alder reactions. A number of such oxygenated 1,3-butadienes can be readily prepared from the corresponding cyclobutenes by thermal ring opening. Examples are given in Table 11.

1,3-Dienes generated in this fashion can be trapped with dienophiles, either intramolecularly or intermolecularly, and this strategy has been exploited for the synthesis of natural products (equations 85 and 86)[135,136].



(85)





(86)

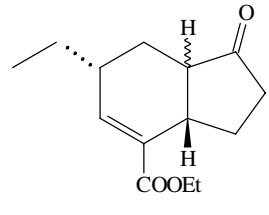
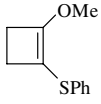
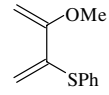
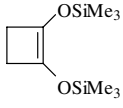
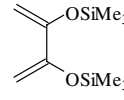
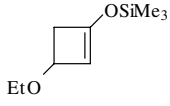
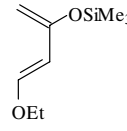
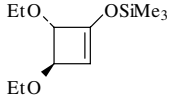
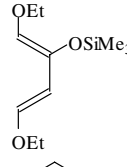
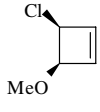
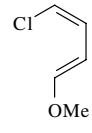
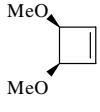
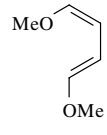
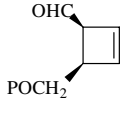
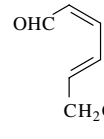
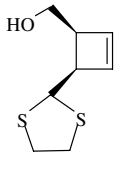
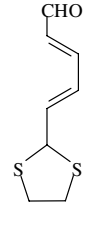
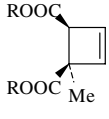
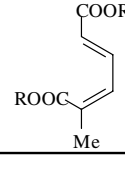


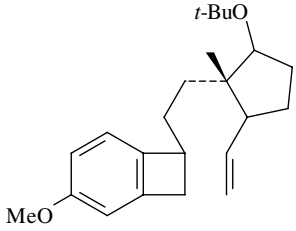
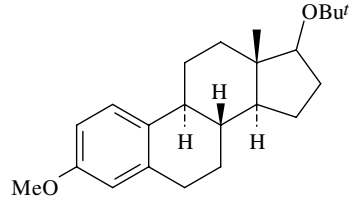
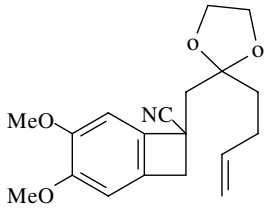
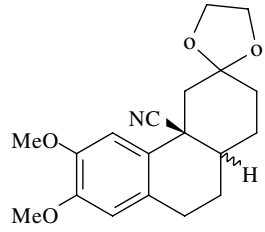
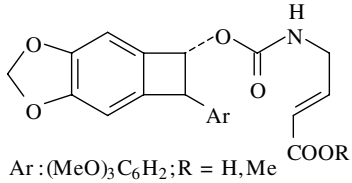
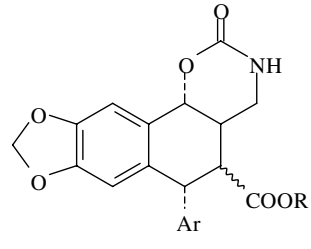
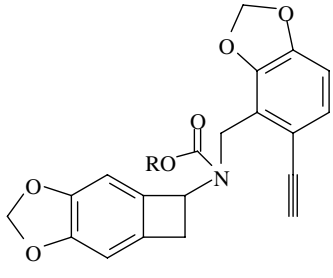
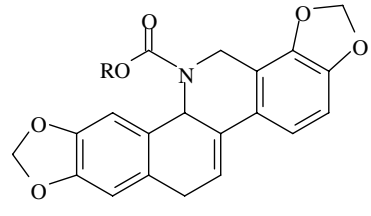
TABLE 11. Substituted butadienes through cyclobutene ring-opening reactions

Substrate	Conditions	Product	Reference
	340 °C		134a
	180 °C		134b
	25 °C		134c
	25 °C		134c
	80 °C		134d
	80 °C		134d
	−78 °C		134e
	P = 4-MeOC$_6$H$_4$CH$_2$		
	PCC, RT		134e
	Δ		134f

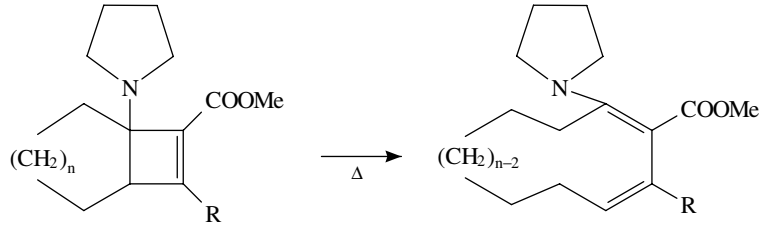
Several ingenious syntheses of natural products have been developed by exploiting benzcyclobutene ring opening to *o*-quinodimethane. Particularly, the intramolecular Diels–Alder strategy employing *o*-quinodimethane intermediates has been very effective for the construction of polycyclic structures. Selected examples are gathered in Table 12.

[*n*.2.0]Bicyclic butenes having a dialkylamino substituent on the bridge head carbon undergo facile ring opening to result in 2-carbon ring enlarged cyclic 1,3-dienes (equation 87)[138]. This approach has been utilized for the synthesis of several natural

TABLE 12. Polycycles through benzocyclobutene ring opening

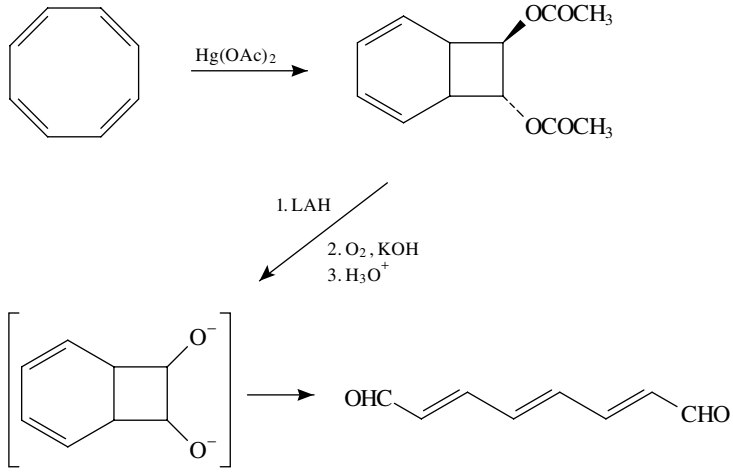
Substrate	Product	Reference
		137a
		137b
 Ar : $(MeO)_3C_6H_2$; R = H, Me		137c
 R = C_7H_7	 Chelidonine intermediate	137d

products which contain medium or large rings such as steganone[139], muscone[140] and velleral[141].



(87)

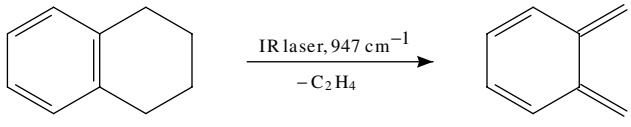
trans-7,8-Diacetoxy[4.2.0]octa-2,4-diene derived from cyclooctatetraene, on reduction with lithium aluminium hydride and oxidative ring opening of the cyclobutane ring, results in octa-2,4,6-triene-1,8-dial (equation 88)[142]. This synthon has been used for the construction of the heptaene portion of the macrolide antibiotic amphotericin B[143].



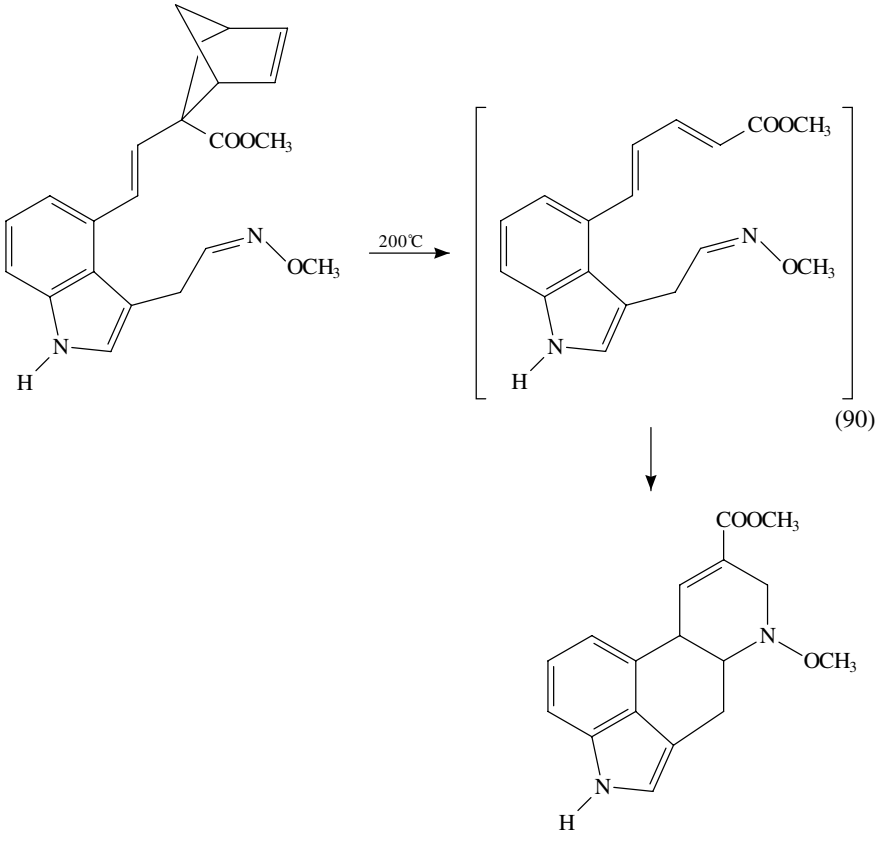
(88)

D. Retro-Diels–Alder Reactions

Retro-Diels–Alder reactions can be used to regenerate dienes or alkenes from 'Diels–Alder protected' cyclohexene derivatives under pyrolytic conditions[144]. Most of the synthetic utility of this reaction comes from releasing the alkene by diene-deprotection. However, tetralin undergoes cycloreversion via the retro-Diels–Alder pathway to generate *o*-quinodimethane under laser photolysis (equation 89)[145]. A precursor of lysergic acid has been obtained by deprotection of the conjugated double bond and intramolecular Diels Alder reaction (equation 90)[146].



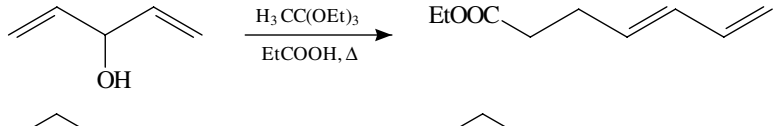
(89)



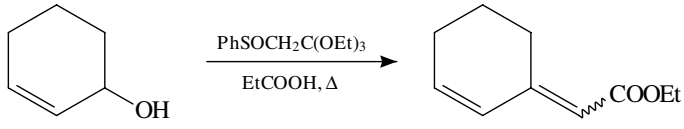
(90)

E. Orthoester Claisen Rearrangements

Allylic alcohols undergo symmetry-allowed orthoester Claisen rearrangement, when treated with trialkyl orthoacetate in the presence of an acid catalyst. When this reaction is applied to 2-butyne-1,4-diols, one of the products formed is a 1,3-diene[147]. 1,3-Dienes also result when this reaction is performed on bisallylic alcohols (equation 91)[148]. Regiospecific conversion of allylic alcohols to two-carbon extended dienoate esters, by performing an orthoester Claisen rearrangement with phenylsulfinyl orthoacetate, has been described (equation 92)[149].



(91)



(92)

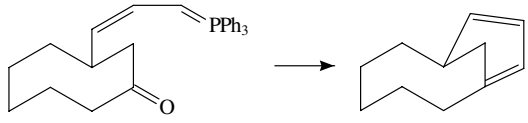
V. WITTIG AND RELATED REACTIONS

A. The Wittig Reaction

The Wittig reaction is a classical method for the transformation of a carbonyl group to an olefin[150]. The stereoselectivity of the olefin formation in the Wittig reaction depends highly on the ylide structure and the reaction conditions[151]. Generally, non-stabilized ylides give predominantly the *Z*-alkenes and stabilized ylides give higher selectivity of *E*-alkenes. The nature of the base also plays a role in stereoselectivity of olefins derived from unsaturated ylides[152]. Wittig carbonyl olefination is used extensively in olefin, diene and polyene synthesis and has found new areas of application in industrial practice. Application of the Wittig reaction for the synthesis of natural products, especially carotenoids, has been extensively reviewed[150c,153].

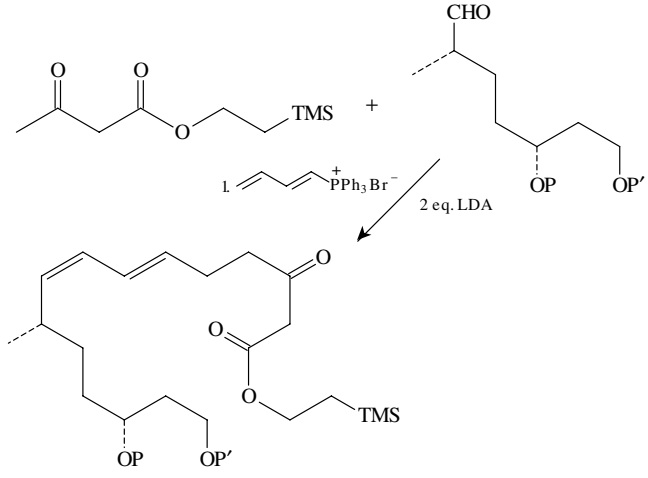
When one of the reacting partners of the Wittig reaction, i.e. the carbonyl compound or the ylide, has a double bond already present in it, the resulting product is a diene. Usually, when polyenes are synthesized following the Wittig method, a mixture of stereoisomers is formed. However, all *trans*-polyenes can be obtained by equilibrating the mixture with a catalytic amount of iodine, or under photolytic conditions. Examples of dienes and polyenes generated via a Wittig reaction are given in Tables 13 and 14, respectively.

The Wittig methodology can also be employed for diene synthesis in an intramolecular version. Propenylidinephosphoranes having a carbonyl group undergo intramolecular Wittig reactions to generate cyclic dienes (equation 93)[156].



(93)

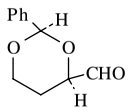
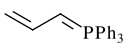
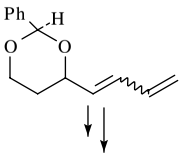
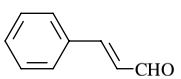
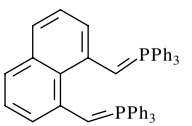
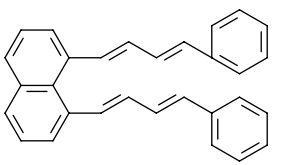
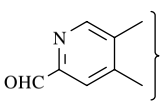
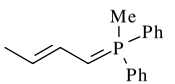
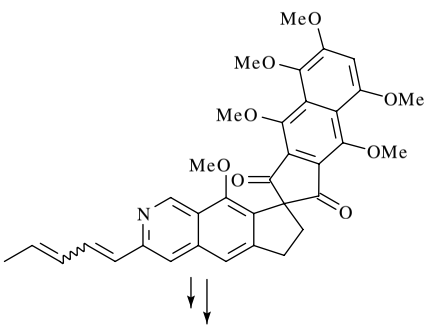
The butadienylphosphonium salt reacts with dianions on the end-carbon atom to result in an intermediate Wittig ylide, which undergoes normal olefination to generate (*E*,*Z*)-dienes of high stereoselectivity. This reaction is in effect a three-component coupling of a nucleophile, Wittig salt and an electrophile[157]. This strategy of three-component coupling was utilized for the diene construction of macrolide latrunculin A (equation 94)[158].

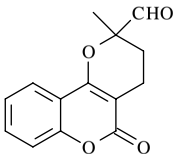


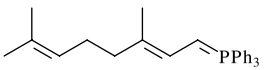
(94)

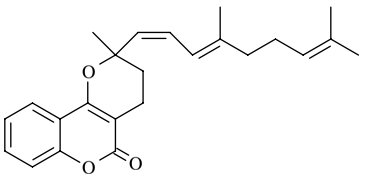
P = [2-(trimethylsilyl) ethoxy] methyl; P′ = *t*-BuMe$_2$Si

TABLE 13. Dienes through Wittig reaction

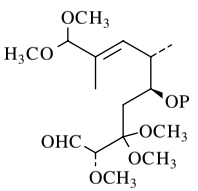
Carbonyl Compound	Wittig Yilide	Product	Reference
		 Swainsonine	154a
			154b
		 Fredericamycin	154c



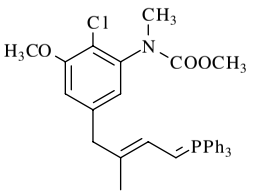


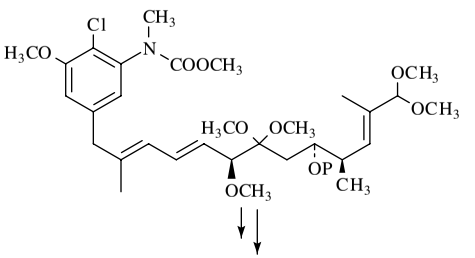


154d



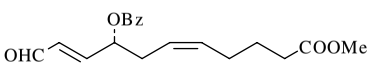
P = *t*-BuMe$_2$Si

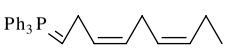


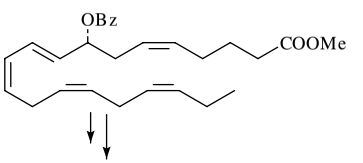


Maytansinoids

154e



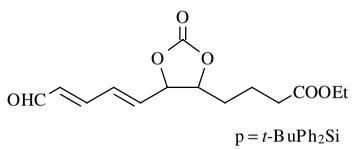
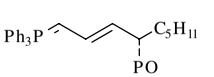
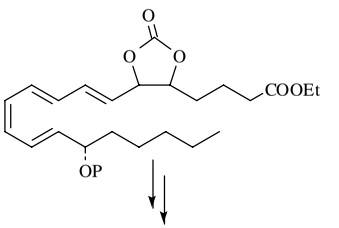
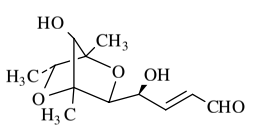
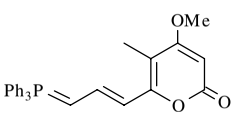
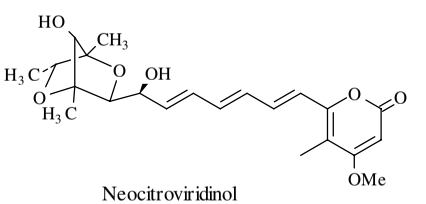
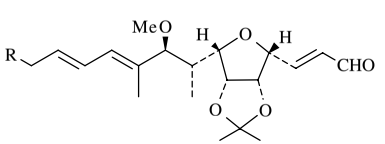
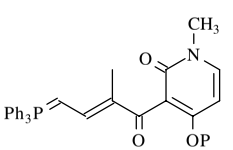
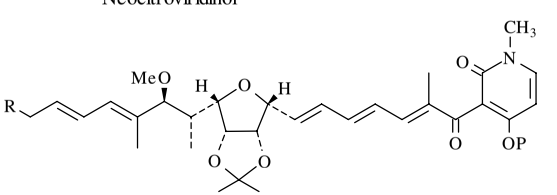


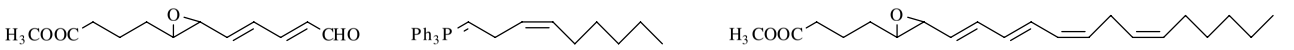


eicosinoid monohydroxy fatty acid

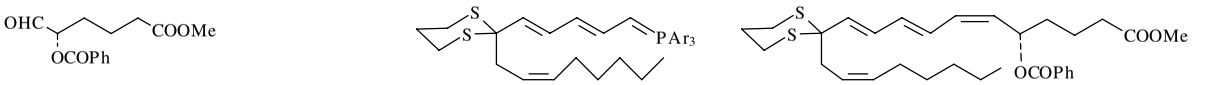
154f

TABLE 14. Polyene synthesis through the Wittig reaction

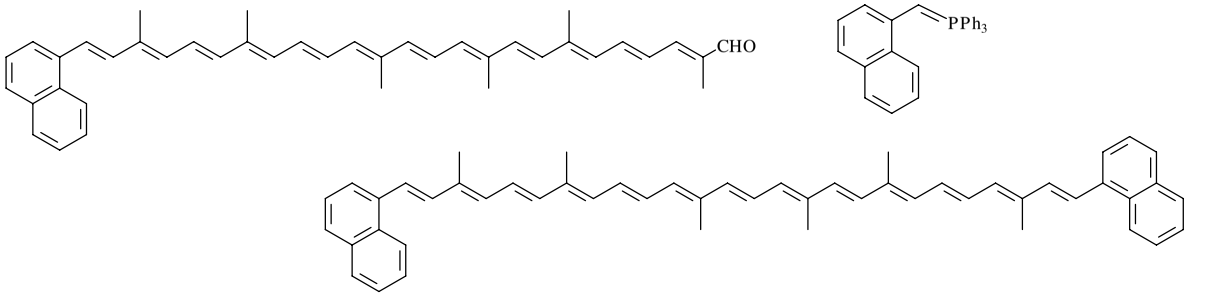
Ketone	Wittig ylide	Olefinic compound	Reference
 p = *t*-BuPh$_2$Si		 Lipoxin A	155a
		 Neocitroviridinol	155b
 R = NHCOOCH$_2$CCl$_3$; P = PhCH$_2$			155c



155d



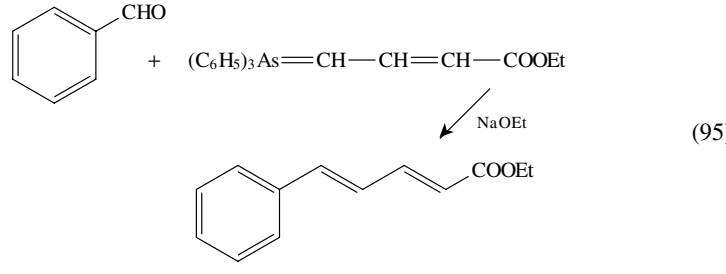
155e



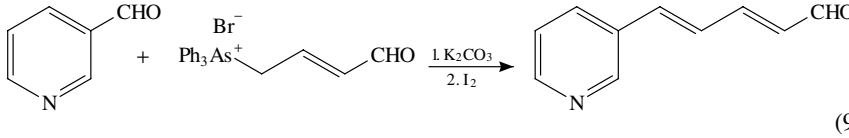
155f

B. Arsenic Ylides

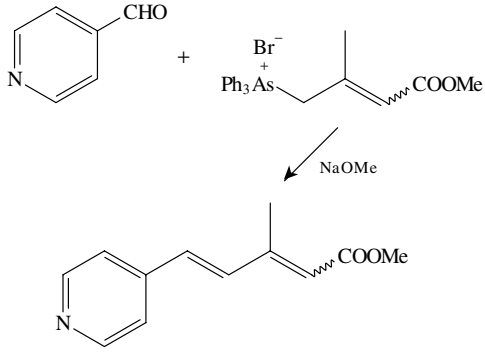
Stabilized arsenic ylides are more reactive than the corresponding phosphorus (Wittig) ylides[159]. In many cases where phosphorus ylides failed to react with carbonyl compounds, the corresponding arsenic ylides have been applied in the olefin forming reactions. Huang and coworkers developed the chemistry of arsenic ylides for the synthesis of dienes and polyenes[160]. Thus, 3-ethoxycarbonylallylidenetriphenylarsone reacts with a variety of aldehydes and ketones to afford diene esters (equation 95). This reagent reacts with aromatic aldehydes stereospecifically leading to the formation of *E*, *E*-products. Another reagent of high synthetic potential is formylallyltriphenylarsonium bromide[161]. This reagent reacts with aldehydes to give dienals, which can again be subjected to olefination in an iterative fashion (equation 96). In a similar manner, an isoprenoid arsone reagent, 3-methoxycarbonyl-2-methyl-2-propenylidenetriphenylarsorane, for appending isoprenoid unit to aldehydes, has been developed (equation 97)[161b]. Applications of arsenic ylides for the synthesis of dienes and polyenes are given in Table 15[160,161a,162].



(95)



(96)

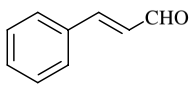
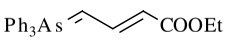
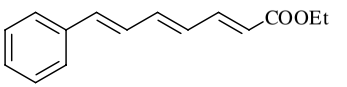
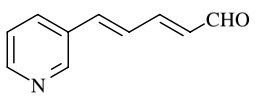
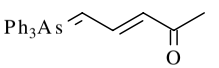
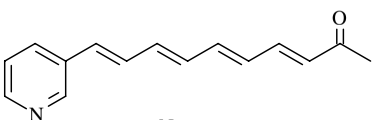
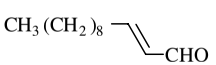
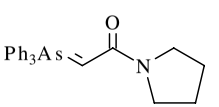
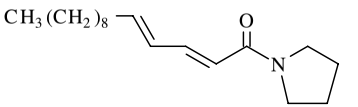


(97)

C. The Horner–Wadsworth–Emmons (HWE) Reaction

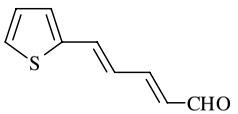
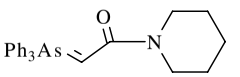
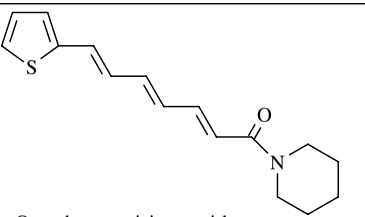
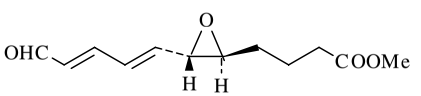
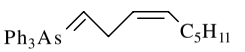
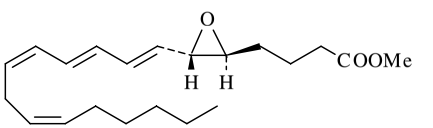
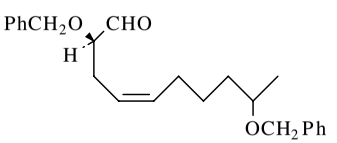
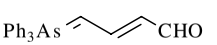
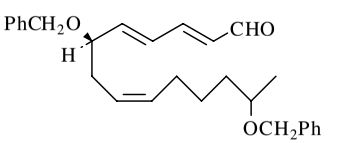
An important modification to the Wittig reaction is the use of stabilized phosphonate carbanions in olefin synthesis. This reaction, originally discovered by Horner but developed by Wadsworth and Emmons, is used extensively for transformation of a carbonyl

TABLE 15. Dienes and polyenes with arsenic ylides

Substrate	Arsenic ylide	Product	Reference
			160
		 Navenone	161a
		 Achillea amide	162a

continued overleaf

TABLE 15. (*continued*)

Substrate	Arsenium ylide	Product	Reference
		 Otanthus maritina amide	162a
		 Leukotriene A_4 (LTA_4) methylester	162b
			162c

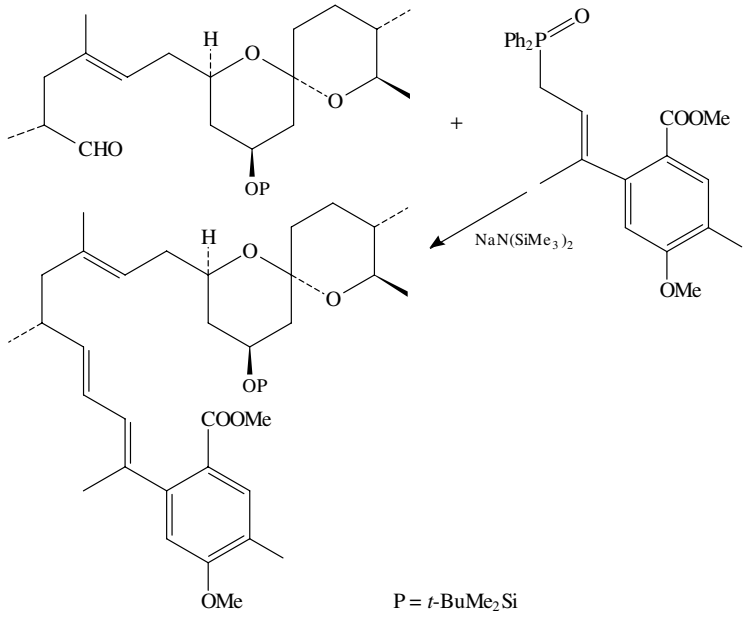
group to an olefin[163]. Phosphonate carbanions are more nucleophilic than the corresponding Wittig ylides, and therefore are more reactive towards carbonyl compounds, especially when the substituent on the phosphonate reagent is an electron-withdrawing group. When the substituent on the phosphonate reagent is an electron-withdrawing group such as an ester or ketone, the product in the olefination reaction is predominantly *E*.

HWE reaction has been used extensively for the synthesis of dienes and polyenes. Examples from recent literature are shown in Table 16 (dienes) and Table 17 (polyenes). HWE reaction also has been used for intramolecular cyclizations leading to polyene macrolides (Table 18).

D. The Wittig–Horner Reaction

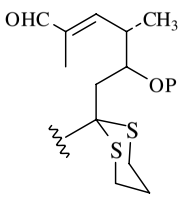
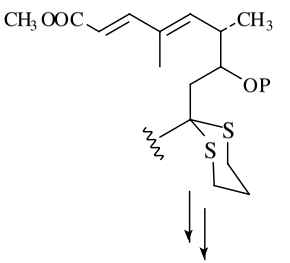
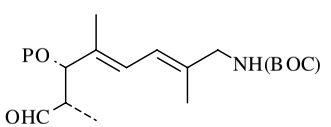
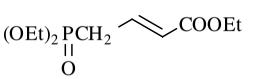
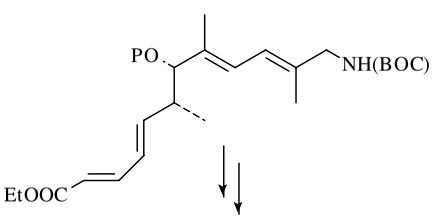
Another variation of the Wittig reaction is the Wittig–Horner reaction, in which the anion generated α- to phosphine oxide is used as a nucleophile to react with carbonyl compounds[167]. The intermediate formed in this reaction, β-hydroxyphosphine oxide, is isolable particularly when bases with lithium counterion are used for deprotonation. Since the β-hydroxyphosphine oxides are diastereomers, they can be separated and subjected to elimination to form the corresponding alkenes[168]. Since the elimination of phosphonate moiety is *syn*, stereospecific alkenes are obtained from the elimination step[169]. As expected, the generation of *erythro* and *threo* isomers is dependent on the solvent and the reaction conditions.

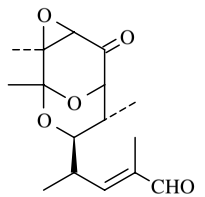
When one of the reacting partners in the Wittig–Horner reaction, either the phosphine oxide or the carbonyl compound, has a double bond, the product is a diene. The Wittig–Horner reaction was utilized by Smith and coworkers in the total synthesis of milbemycin (equation 98)[170]. They found that when sodium hexamethyldisilazide was employed as a base, the desired *E*-diene selectivity is high (85%). Some examples from the literature where the Wittig–Horner reaction has been utilized for the construction of *E*-double bonds present in dienes and polyenes are given in Table 19[171].

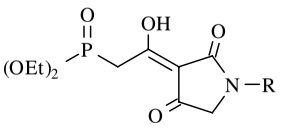


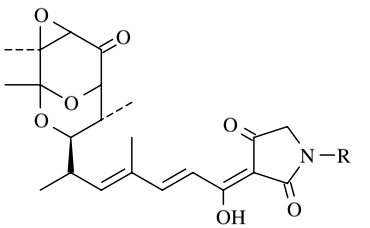
(98)

TABLE 16. Diene synthesis through HWE reaction

Starting aldehyde	Phosphonate	Product	Reference
 P = $MeOCH_2$		 Methylmaysenine	164a
 P = *t*-$BuMe_2Si$		 lejimalides	164b



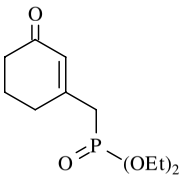


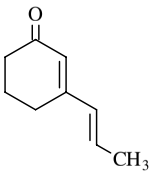


164c

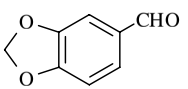
R = $(MeO)_2C_6H_3CH_2$

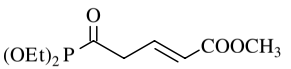
CH_3CHO

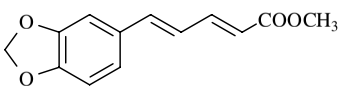




164d

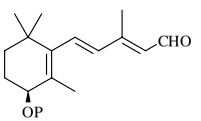
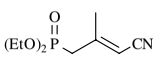
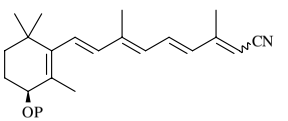
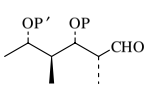
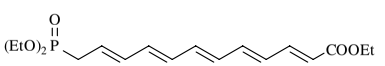
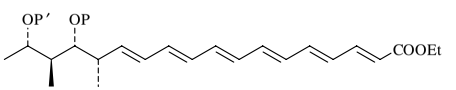
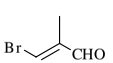
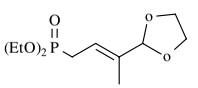
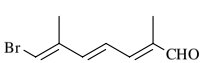
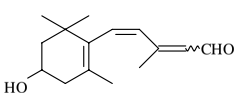
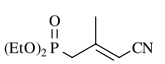
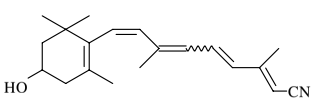
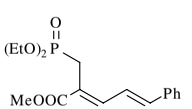
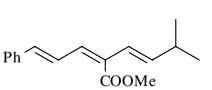


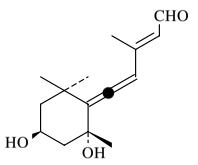


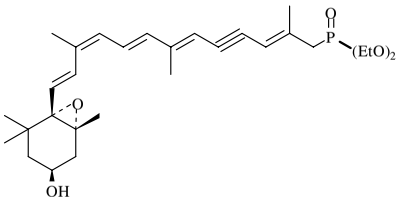


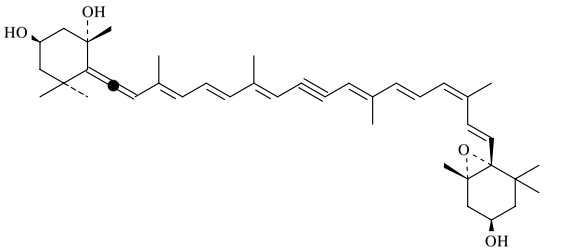
164e

TABLE 17. Polyene synthesis through HWE reaction

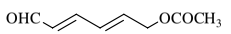
Aldehyde	Phosphonate	Product	Reference
 P = t-BuMe$_2$Si			165a
 P = t-BuMe$_2$Si; P′ = Et$_3$Si		 (Amphotericin fragment)	143
			86
			165b
			165c



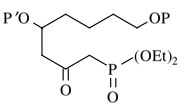


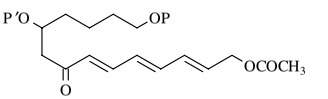


165d

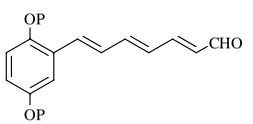


P = $PhCH_2$; P′ = *t*-$BuMe_2Si$

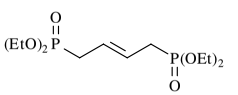


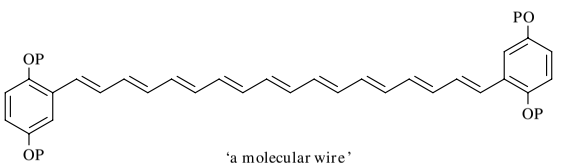


165e



P = *t*-$BuMe_2Si$





'a molecular wire'

83f

TABLE 18. Intramolecular HWE reactions for macrocyclizations

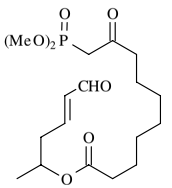
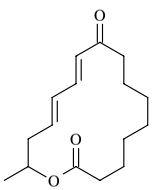
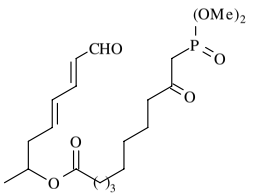
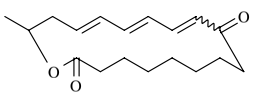
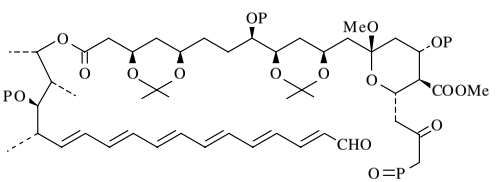
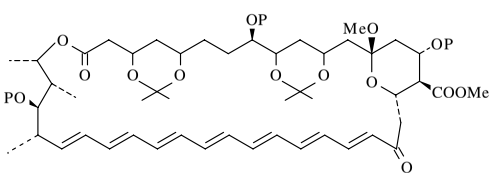
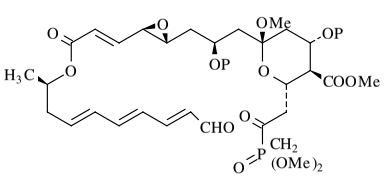
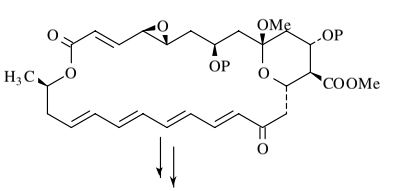
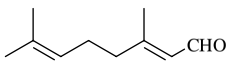
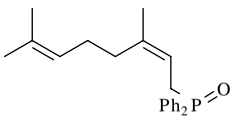
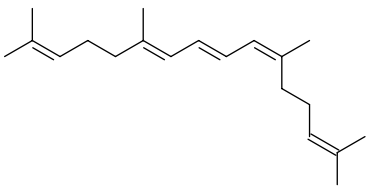
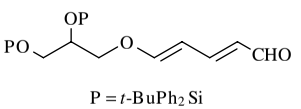
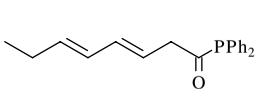
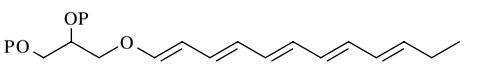
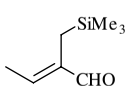
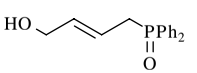
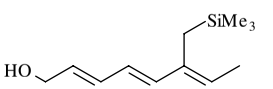
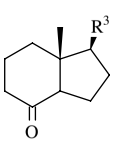
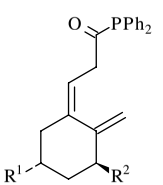
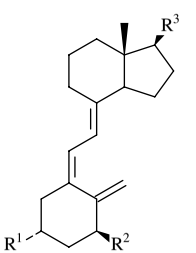
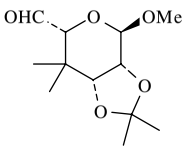
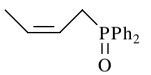
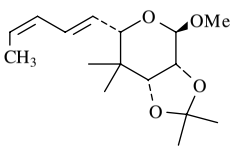
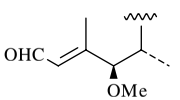
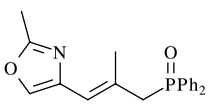
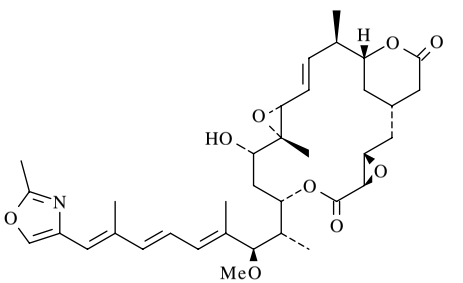
Substrate	Product	Reference
		166a
		166a
 P = *t*-BuMe$_2$Si		166b
 P = *t*-BuMe$_2$Si	 Pimarolide methylester	166c

TABLE 19. Dienes and polyenes through the Wittig–Horner reaction

Substrate	Phosphine oxide	Product	Reference
			171a
			171b
			171c
			171d

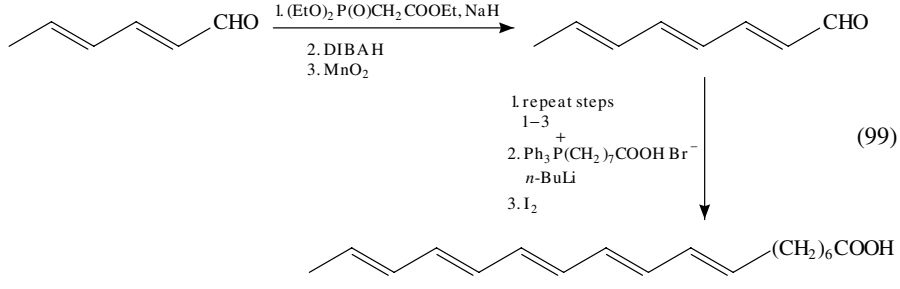
continued overleaf

TABLE 19. (*continued*)

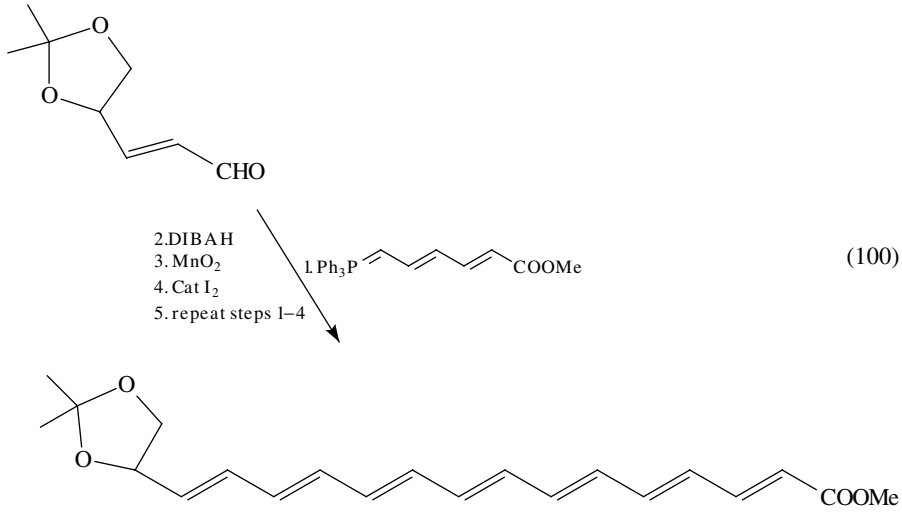
Substrate	Phosphine oxide	Product	Reference
			171e
		 Rhizoxin	171f

E. Iterative Wittig-type Reactions

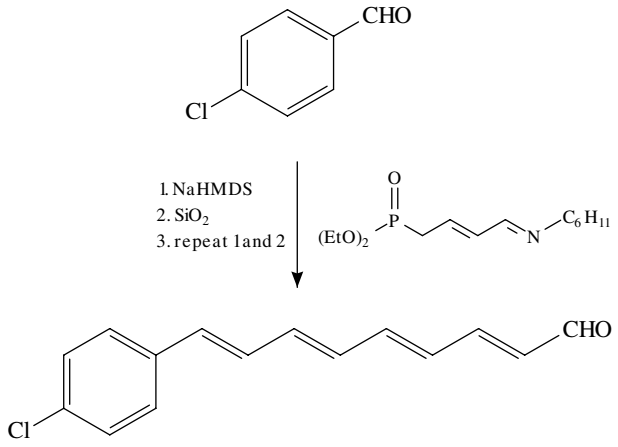
When the HWE reaction is performed with anylide having a functional group such as an ester or a masked aldehyde on the terminal carbon, the olefin generated can be set to perform another HWE reaction in an iterative fashion by generating the aldehyde group through simple chemical manipulations. This methodology is very popular for polyene synthesis. Various functionalized ylides for specific homologation of carbonyl compounds are available. For example, triethylphosphonoacetate is a two-carbon homologating agent. The ylide generated from this reagent reacts with aldehydes readily to give an α,β-unsaturated ester, which on reduction and controlled oxidation sequence generates α,β-unsaturated aldehyde which is ready for the HWE reaction again (equation 99)[172]. Similarly, a dienic ylide has been introduced for six-carbon homologation (equation 100)[173]. Polyenes having up to seven-conjugated double bonds have been prepared utilizing this iterative protocol[173c]. Four- and five-carbon bifunctional HWE ylides having an imine functionality have also been developed[174,175]. These synthons react with aldehydes and ketones in the presence of base, in Wittig fashion, and on work-up release aldehyde group (equation 101)[175]. The iterative HWE protocol has been used for the synthesis of the polyene portion of cyclophane-based trienic esters[176] and the natural product, roxaticin[177].



(99)



(100)

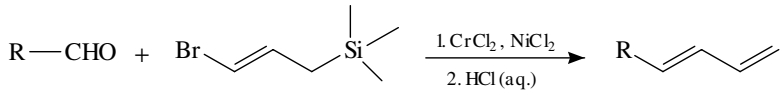


(101)

F. Peterson and Related Reactions

The Peterson olefination reaction involves the addition of an α-silyl substituted anion to an aldehyde or a ketone followed by the elimination of silylcarbinol either under acidic (*anti*-elimination) or basic (*syn*-elimination) conditions to furnish olefins[178]. Thus, Peterson olefination, just like Wittig and related reactions, is a method for regioselective conversion of a carbonyl compound to an olefin. Dienes and polyenes can be generated when the Peterson reaction is conducted using either an α,β-unsaturated carbonyl compound or unsaturated silyl derivatives as reaction partners (Table 20)[179].

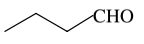
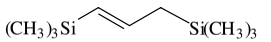
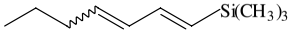
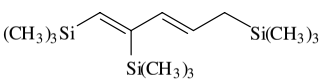
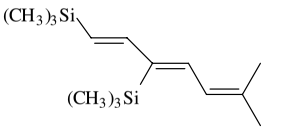
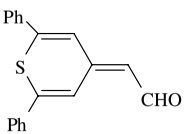
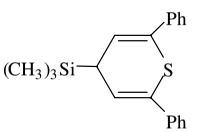
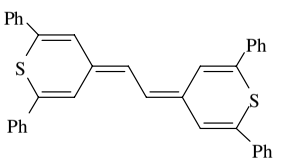
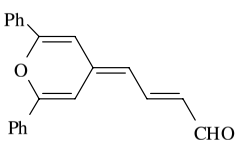
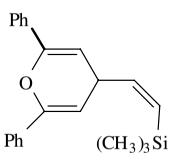
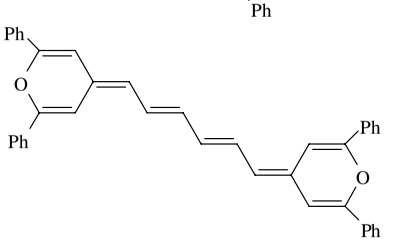
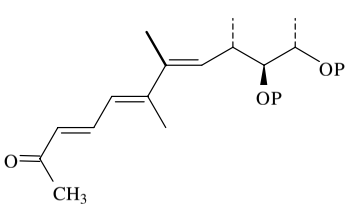
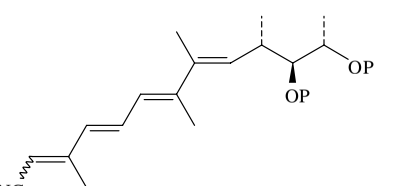
Several strategies closely related to the Peterson synthesis have been developed for diene and polyene generation. Angell, Parsons and coworkers reported a mild method for the diene installation on a carbonyl group using a γ-bromoallylsilane reagent in the presence of excess chromous chloride and a catalytic amount of nickel(II) chloride (equation 102)[180].

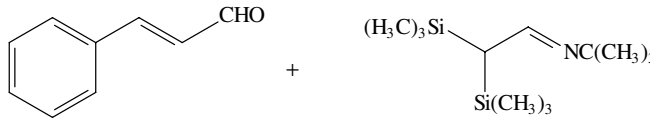


(102)

Bellassoued and Majidi introduced a two-carbon homologation reagent, α,α-bis(trimethylsilyl)-*N*-*tert*-butylacetaldimine, the anion of which reacts with an aldehyde in the presence of a catalytic amount of zinc bromide to afford two-carbon homologated α,β-unsaturated aldehyde (equation 103)[181]. This sequence in an iterative mode provides access to polyenes. A four-carbon homologation reagent has also been introduced by the same group[182]. Anion generated from trimethylsilylcrotanaldimine reacts with aldehydes smoothly in the presence of a catalytic amount of caesium fluoride to furnish a dienal (equation 104)[182]. Wang and coworkers have described the synthetic utility of γ-trimethylsilyl substituted allyl boranes for stereospecific generation of terminal 1,3-dienes (equation 105)[183]. Ring opening of epoxysilanes with alkenyl cuprate reagents in the presence of $BF_3 \cdot Et_2O$ affords β-hydroxysilanes which, on Peterson elimination, give stereospecific dienes[183].

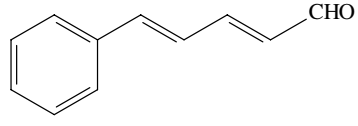
TABLE 20. Dienes and polyenes through the Peterson reaction

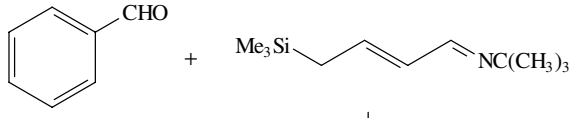
Substrate	Silane	Product	Reference
			179a
			179b
			179c
			179d
			179e
P = *t*-BuMe$_2$Si		Calyculin fragment	



1. $ZnBr_2$
2. H_3O^+

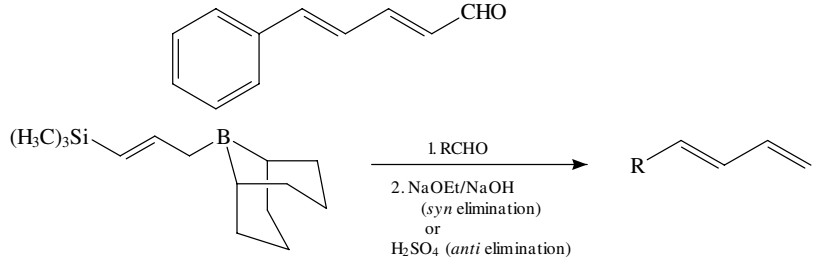
(103)





1. CsF, DMSO
2. $ZnCl_2$, H_2O

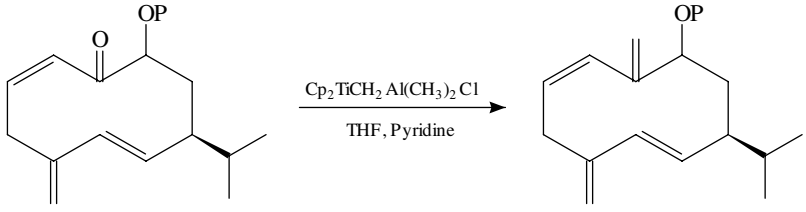
(104)



(105)

G. Organotitanium Reagents

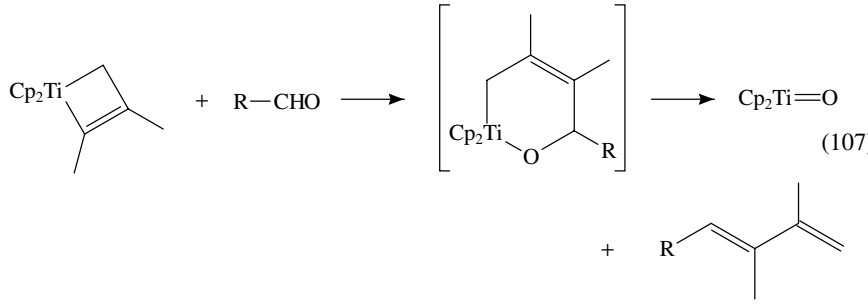
Tebbe's reagent, $Cp_2TiCH_2Al(CH_3)_2Cl$, converts carbonyl compounds to methylenes[184]. This reagent when applied to α,β-unsturated aldehydes and ketones generates dienes (equation 106)[184c]. Synthetic utility of the reagent for generation of dienes and polyenes is limited because of the difficulty in the preparation and incompatibility with other functional groups such as esters etc.



(106)

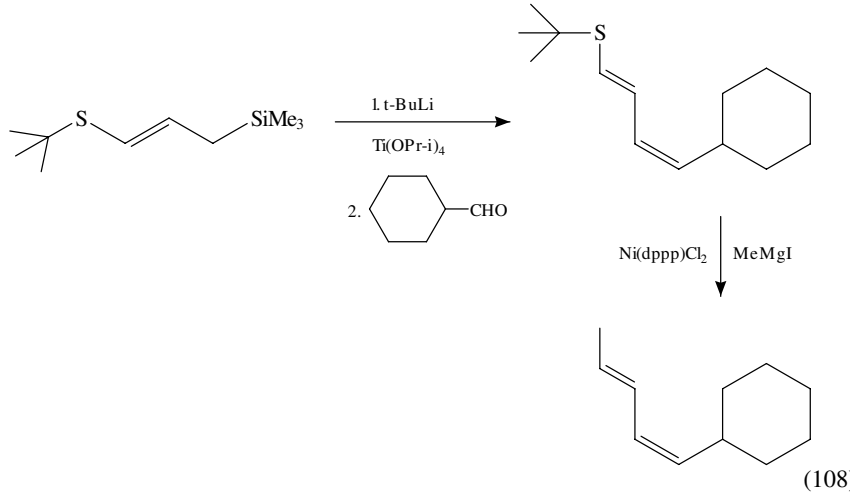
P = *t*-$BuMe_2Si$

Titanacyclobutenes, prepared readily from Tebbe reagent and alkynes, react with aldehydes and ketones to form insertion products which undergo facile retro-Diels-Alder reaction to afford substituted 1,3-dienes (equation 107)[185].



(107)

Organotitanium reagent generated from 1-*tert*-butylthio-3-trimethylsilyl-1-propene condenses with aldehydes to give 1-*tert*-butylthio-(*E*, *Z*)-1,3-alkadienes, via *β*-hydroxysilane intermediates[186]. The *tert*-butyl sulphide group on the diene can be replaced by an alkyl group by a cross-coupling reaction with a Grignard reagent in the presence of nickel catalyst (equation 108). The utility of this method was illustrated by an application to the synthesis of spilanthol, a naturally occurring insecticide[186].



(108)

VI. COUPLING REACTIONS

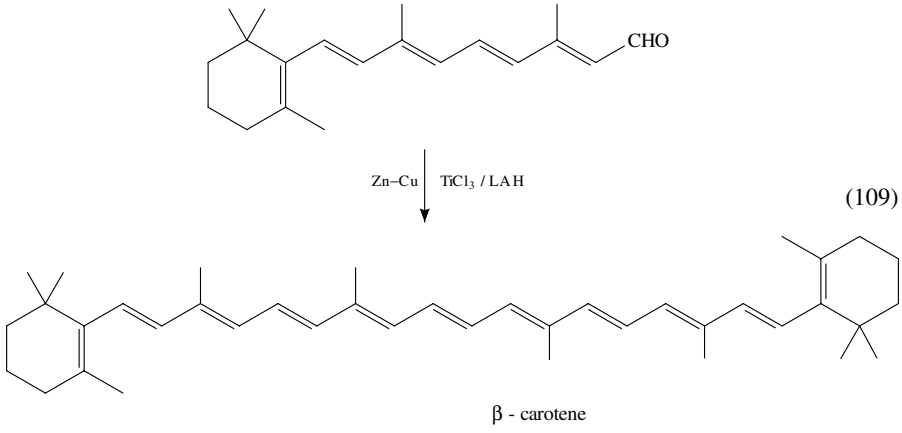
A. General Aspects

Though coupling reactions are among one of the earliest known C−C bond forming reactions, they have found only limited synthetic applications owing to lack of control and unsatisfactory yield. However, during the past two decades development in organometallic chemistry had a profound impact on revising the coupling process as an important synthetic reaction. Employing a variety of organometallic catalysts and intermediates it is now possible to carry out diverse coupling reactions in good yield, under mild conditions and with high stereocontrol.

B. Reductive Carbonyl Coupling Reactions

1. The McMurry coupling reaction

The McMurry reaction involving low-valent titanium species accomplishes coupling of two carbonyl groups to furnish alkenes[187]. The low-valent titanium species is generated either from $TiCl_3$/LAH[187a], $TiCl_3$/Mg[188] or $TiCl_4$/Zn–Cu[189]. When one or both carbonyl substrates carry one or more additional double bonds, dienes or polyenes result from this reaction (equation 109)[187a]. The McMurry coupling reaction is remarkably selective and a wide variety of functionalities are tolerated. This reaction can be carried out in both inter- and intramolecular modes to furnish a variety of dienes and polyenes. Synthesis of dienes and polyenes where McMurry coupling has been a key reaction is given in Table 21[190].



(109)

β - carotene

TABLE 21. Dienes and polyenes through McMurry coupling

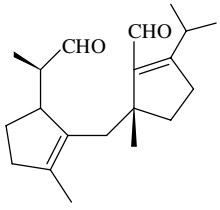
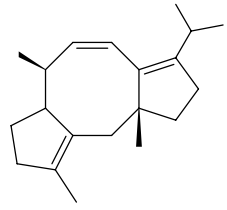
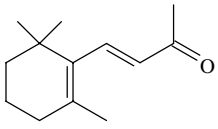
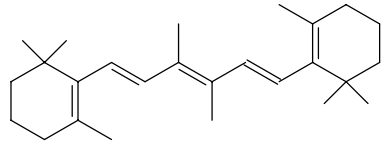
Substrate	Product	Reference
	 Fusicoccane type	190a
	 A minicarotene	190b

TABLE 21. (*continued*)

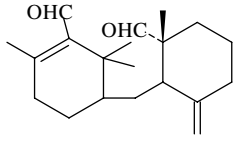
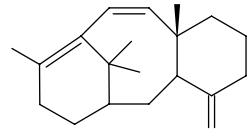
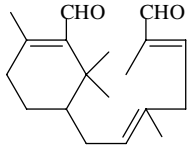
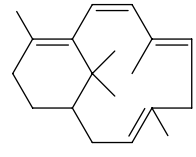
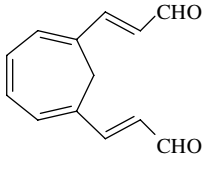
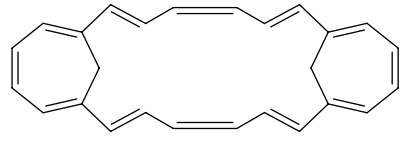
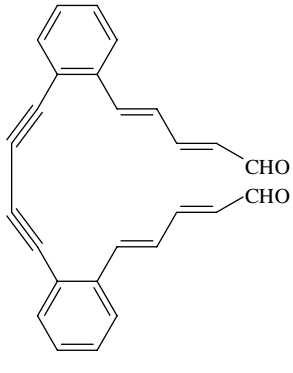
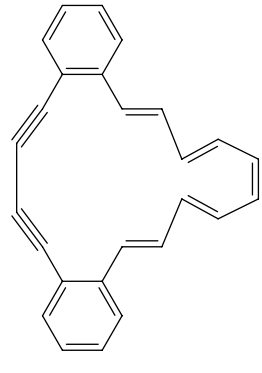
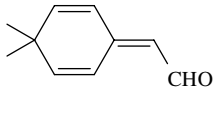
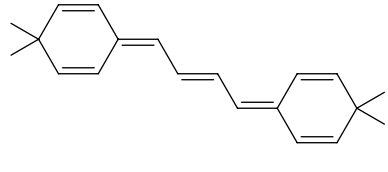
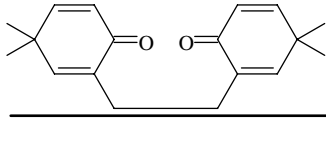
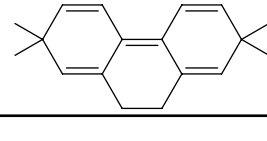
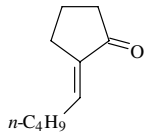
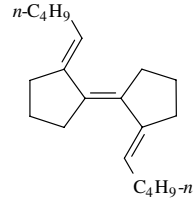
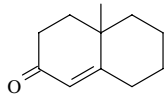
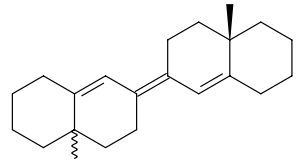
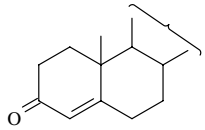
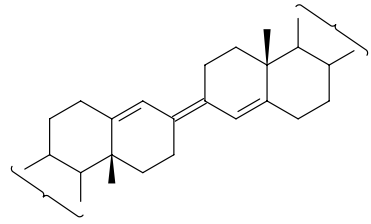
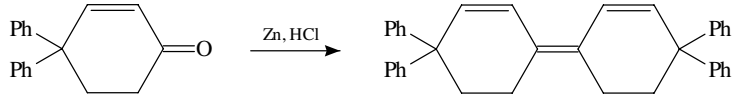
Substrate	Product	Reference
	 Taxane skeleton	190c
		190d
		190e
		190f
		190g
		190h

TABLE 22. Polyenes through reductive coupling with zinc

Substrate	Product	Reference
		193a
		193b
 Chlost-4-ene-3-one		193b

2. Organozinc intermediates

α,β-Unsaturated carbonyl compounds undergo a reductive coupling reaction to generate trienes on the surface of the reactive zinc metal (equation 110)[191]. Zn–HCl[191], Zn–Hg–HCl[192], Zn–TMSCl or Zn–1,2-bis(chlorodimethylsilyl)ethane[193] have been employed for carrying out this reaction (Table 22)[193]. When Zn–HCl is employed, coupled products as well as Clemmensen reduction products are formed.



(110)

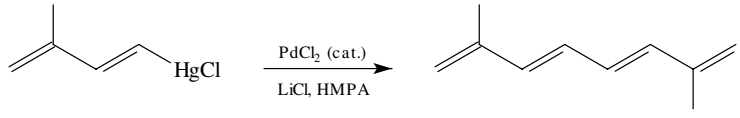
C. Homo-coupling Reactions

1. Organopalladium intermediates

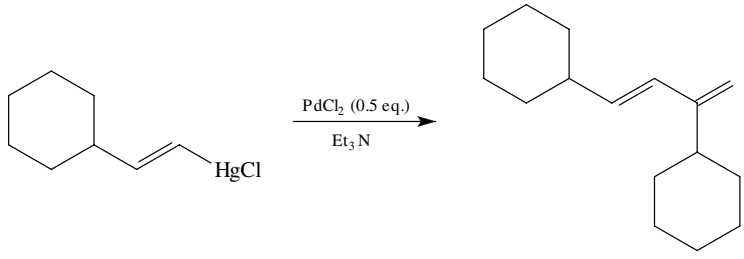
1,3-Dienes can be obtained by direct coupling of alkenes with palladium acetate[194]. However, this reaction is seldom applied as a synthetic procedure, since the yields are low and side products due to oxidation of the double bond also contaminate the reaction.

Homo-coupling of vinylic mercurials occurs readily under palladium[195] or rhodium[196] catalysis, but with the stoichoimetric amount of a reagent (equation 111)[195]. Divinylpalladium intermediates may be involved in this reaction. This reaction is also of limited synthetic scope since organomercurials are usually prepared via vinylboranes, which

themeselves are known to undergo coupling under palladium catalysis. Moreover, a stoichiometric amount of palladium has to be used to effect these reactions. However, surprisingly, when the reaction of trans-2-cyclohexylethenylmercuric chloride was carried out with 0.5 equivalent of palladium chloride, an unsymmetrical 'head-to-tail' coupling took place (equation 112)[197].

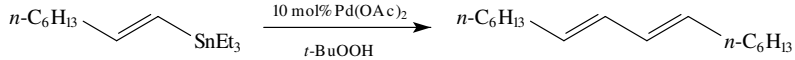


(111)

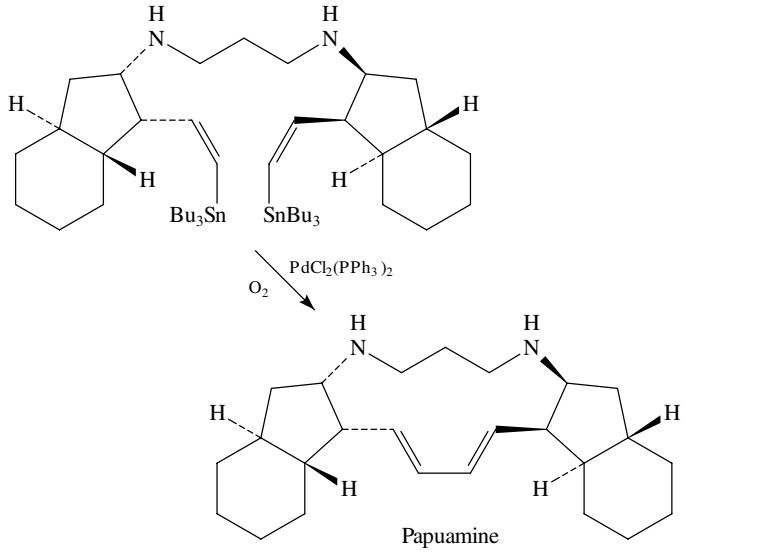


(112)

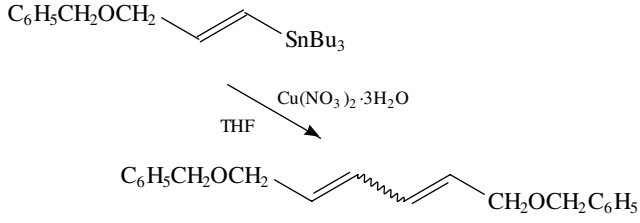
Vinyl stannanes also undergo oxidative homo-coupling under transition metal catalysis to result in dienes (equation 113)[198]. An intramolecular version of this method was employed for the macrocyclization-coupling reaction leading to the synthesis of papuamine (equation 114)[199]. Homo-coupling of vinylstannanes also takes place readily under the mediation of copper(II) nitrate to result in dienes in moderate to good yields (equation 115)[200]. This reaction is analogous to copper-mediated dimerization of terminal alkynes[201].



(113)



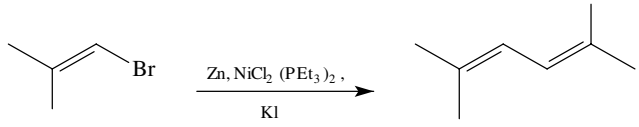
(114)



(115)

2. Organonickel intermediates

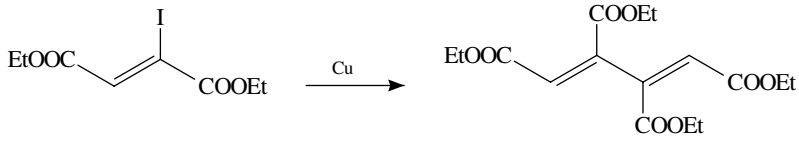
Direct homo-coupling of vinyl halides is a simple way of generating 1,3-dienes. This transformation can be achieved employing various transition metal catalysts such as nickel(0) reagent in the presence of phosphine ligand[202] or a nickel(0) reagent in the presence of potassium iodide and thiourea (equation 116)[203].



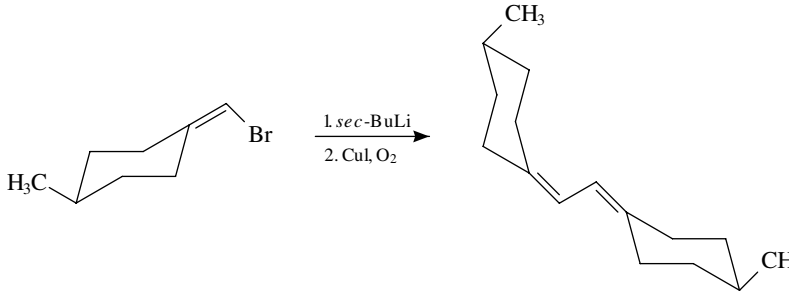
(116)

3. Organocopper intermediates

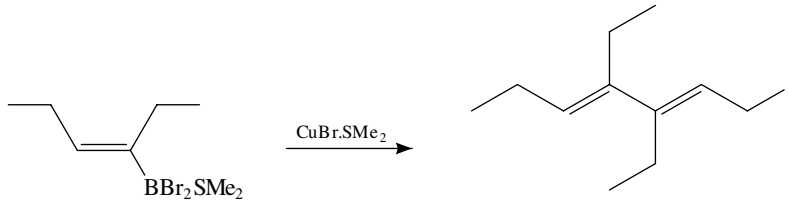
Vinyl halides, particularly vinyl iodides and bromides, dimerize readily in the presence of activated copper (equation 117)[204]. This reaction is analogous to classical Ullmann biphenyl synthesis. A general method for self-coupling of vinyl halides consists of conversion to the corresponding lithium divinyl cuprate followed by heating[205] or treatment with oxygen[206] (equation 118). Vinyl boranes and vinylzirconium derivatives in the presence of copper reagents undergo stereospecific dimerization to furnish (*E*,*E*)-1,3-butadiene or (*Z*,*Z*)-1,3-butadiene depending on the stereochemistry of the vinyl metal intermediate (equation 119)[207]. Alkenyl cuprates prepared by hydrocupration of terminal alkynes decompose to give (*E*,*E*)-1,3-dienes in good yields (equation 120)[201].



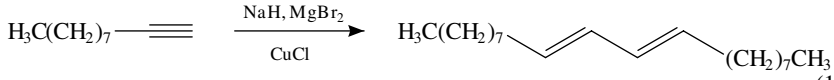
(117)



(118)



(119)

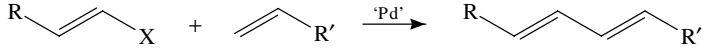


(120)

D. Cross-coupling Reactions

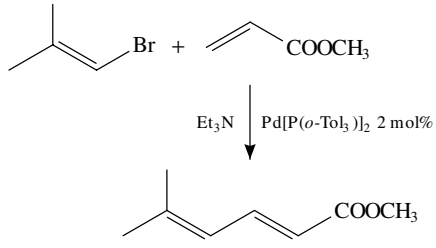
1. The Heck reaction

a. Alkene–alkene coupling. The palladium(0) catalysed arylation or alkenylation of alkenes is known as the Heck reaction[21,208] (equation 121) and has found extensive applications in synthesis (Table 23). Several variations of the Heck reaction have also been reported.



(121)

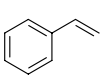
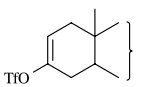
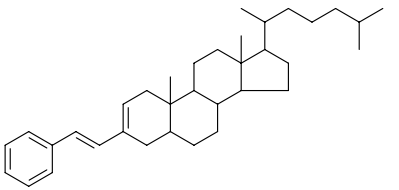
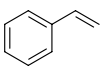
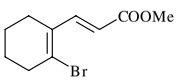
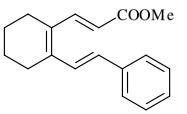
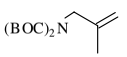
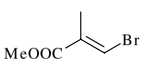
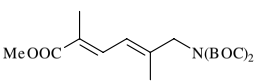
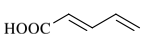
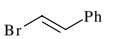
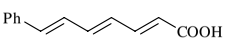
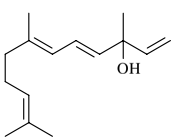
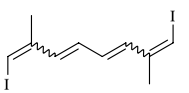
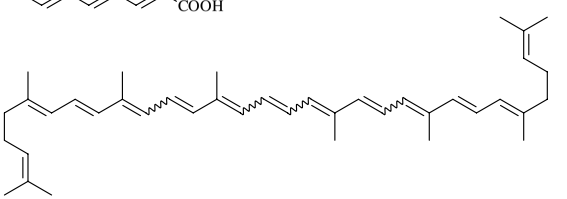
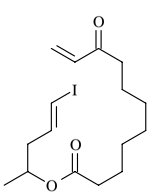
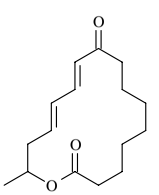
The reaction involves insertion of Pd(0) species in vinyl halides, generating reactive species which undergo *cis*-addition to alkenes to form a new carbon–carbon bond; subsequent *syn* elimination of the palladium species generates the diene. The regiochemistry of the addition of the organopalladium intermediate to the alkene appears to be sterically controlled, with the organic group acting as the largest part of the reagent and therefore adding to the least substituted carbon of the double bond. If an electron-withdrawing group is present on one of the carbons of the alkene, then the vinylic group adds exclusively to the other carbon (equation 122). A Heck reaction is generally conducted in aqueous acetonitrile[210] since water is found to accelerate the reaction. In many cases the reaction is also accelerated by the presence of silver(I)[211] or thallium(I) salts[212]. Recent reports indicate that Heck reactions can be carried out at room temperature either employing high pressure[213] or phase transfer catalysis[214].

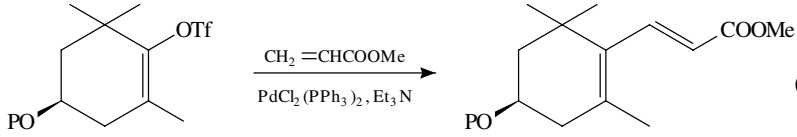


(122)

Alkenyl trifluoromethanesulphonates (enol triflates) undergo Heck coupling with alkenes efficiently (equation 123)[209a,215]. This reaction is a useful variation of the use of vinyl halides not only because they are easy to prepare from the corresponding carbonyl compounds, but also because yields are good, and the stereochemistry of the triflate is largely maintained.

TABLE 23. Dienes and polyenes through the Heck reaction

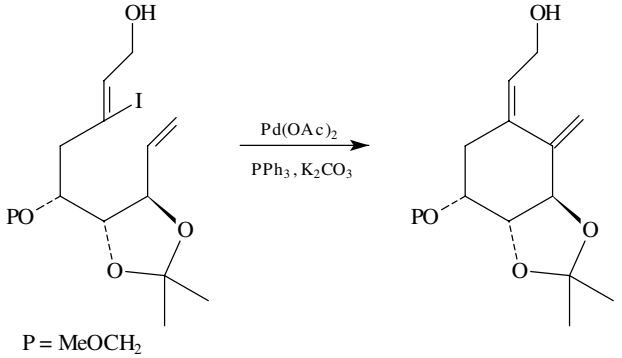
Substrate-1	Substrate-2	Product	Reference
			209a
			209b
			209c
			209d
			209e
			209f



(123)

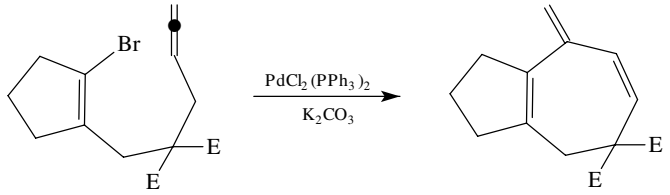
P = *t*-BuMe$_2$Si

Suitably positioned vinyl halide can undergo Heck-type intramolecular coupling to generate dienes (equations 124 and 125)[216,217]. When one of the reacting partners in the Heck reaction is a diene, trienes are obtained (equation 126)[218]. Heck coupling of allylic alcohols and alkenyl iodides has been employed for the synthesis of vitamin A and related compounds (equation 127)[219,220]. A similar double Heck reaction on a C_{10}-diiodide with a C_{15}-allylic alcohol leads to β-carotene as a mixture of isomers (equation 128)[209e].



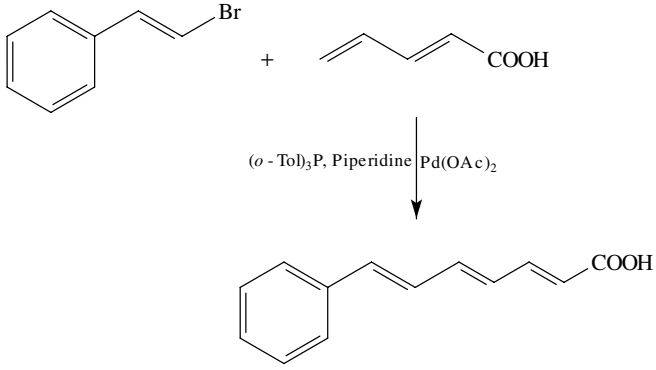
(124)

P = MeOCH$_2$

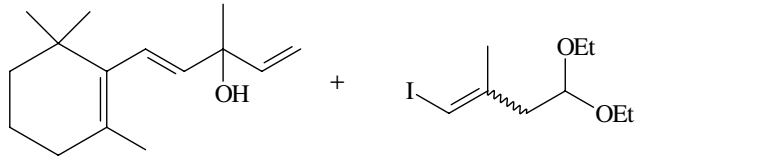


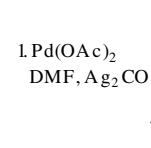
(125)

E = COOEt

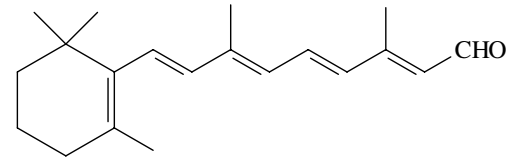


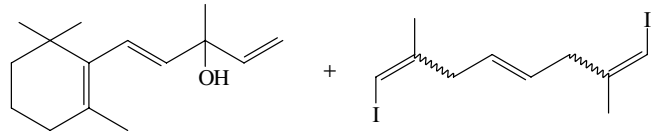
(126)



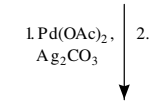


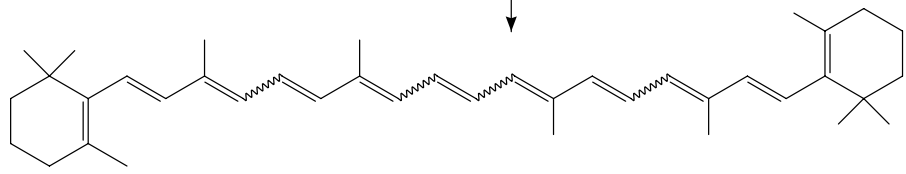
(127)



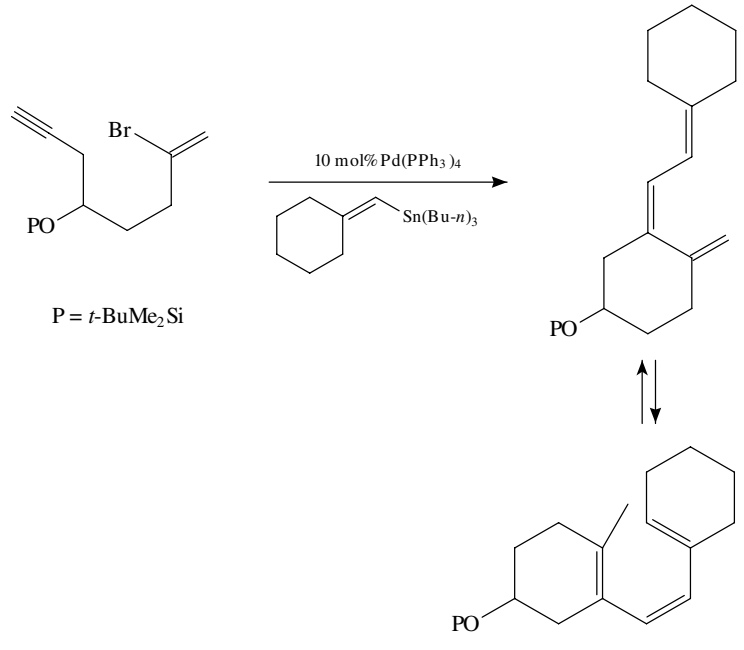


(128)

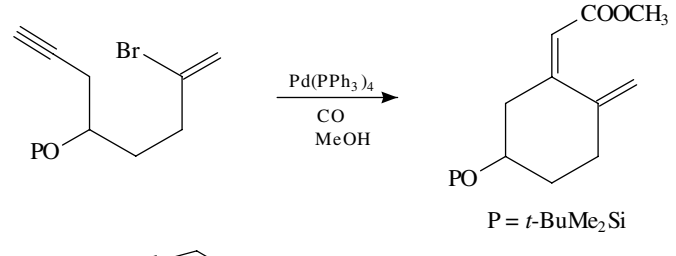




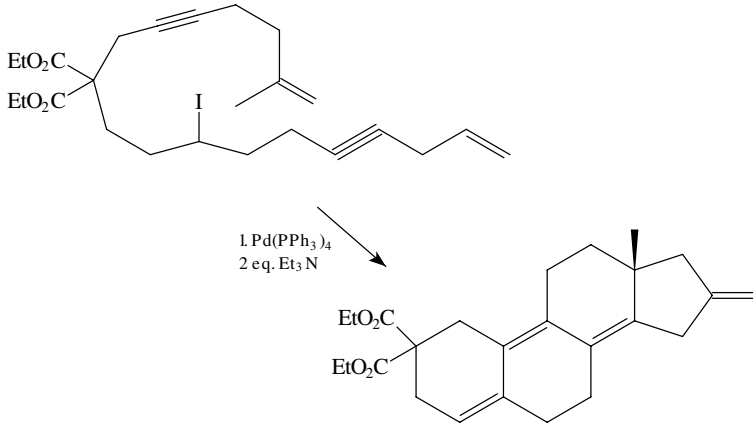
b. Alkene–alkyne reductive coupling. Intramolecular Heck coupling involving appropriately positioned alkenyl halide and an alkyne leads to a vinylpalladium intermediate which reacts with nucleophiles readily to furnish cyclic products[221]. This strategy was applied by Nuss and coworkers for the synthesis of triene unit of vitamin D_3 (equation 129)[222]. Alternatively, organopalladium intermediates can be carbometallated to yield diene ester, which is a suitable intermediate for vitamin D_3 synthesis (equation 130)[222]. Alkenyl palladium intermediates generated by intramolecular addition of haloalkane to a triple bond may also be captured by alkenes to form polycyclic compounds. An elegant example of intramolecular cascade cyclization is the synthesis of steroidal polyene generated from an acyclic precursor (equation 131)[223]. Two more examples of palladium-mediated cascade cyclizations and subsequent pericyclic reactions leading to the formation of polycyclic diene products are given in equations 132[224] and 133[225].



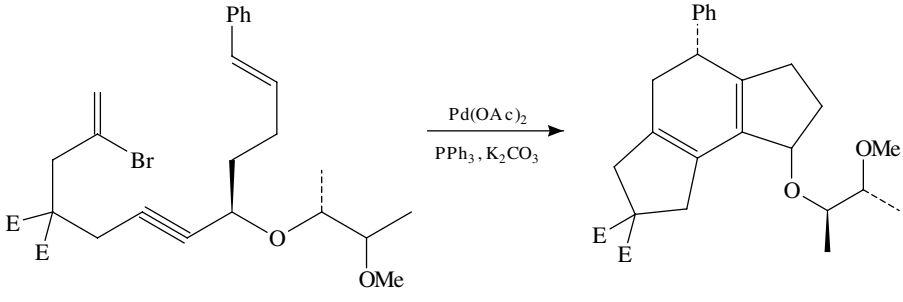
P = *t*-BuMe$_2$Si (129)



P = *t*-BuMe$_2$Si (130)

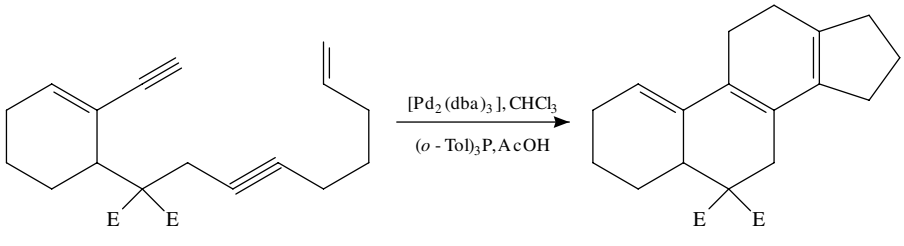


(131)



E = COOEt

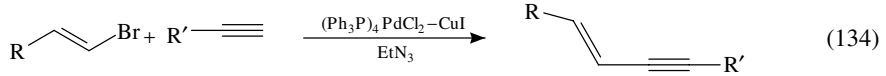
(132)



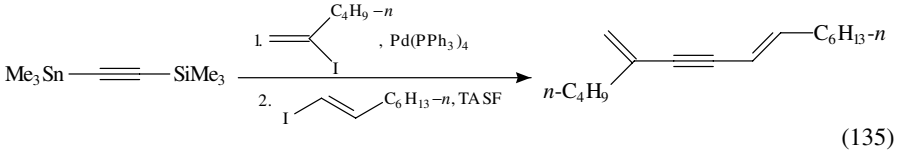
E = COOMe

(133)

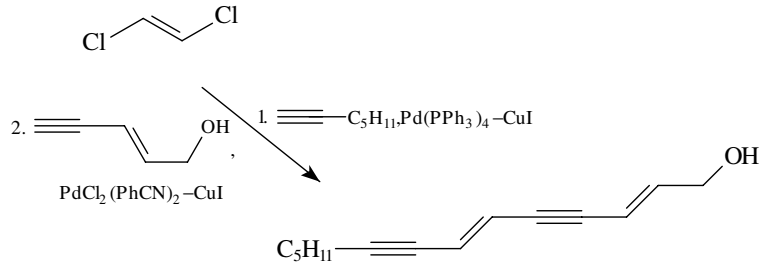
c. Alkene–alkyne oxidative coupling. Enynes and enediynes are important structural fragments present in several natural products, especially in enediyne antibiotics[226]. Enynes can be prepared stereospecifically by coupling of alkynes with alkenyl halides in the presence of catalytic amount of palladium complex and copper(I) salt (equation 134)[227,228,232]. Several alkynyl derivatives such as alkynylmagnesium bromides[229], alkynylzinc chloride[230], alkynylsilanes[231] and alkynylstannanes (discussed under the Stille reaction) participate in this reaction effectively. Palladium-catalysed one-pot sequential cross-coupling of trimethylstannyl(trimethylsilyl)ethyne, first with one alkenyl iodide and then with another alkenyl iodide in the presence of newly added *tris*(diethylamino)sulphonium trimethyldifluorosilicate (TASF), affords conjugated dienynes (equation 135)[231]. When either *E*- or *Z*-1,2-dihaloalkenes are used as substrates, enediynes result from the reaction (equation 136)[233]. A few examples from recent literature on the synthesis of some enynes and enediynes are presented in Table 24[234].



(134)



(135)

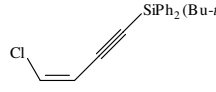
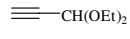
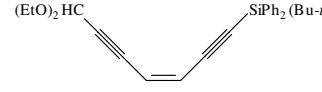
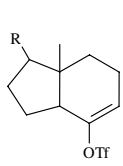
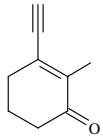
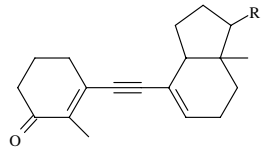
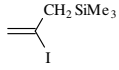
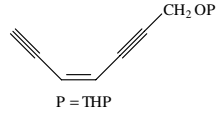
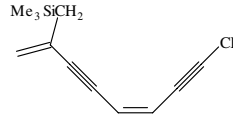
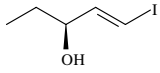
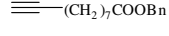
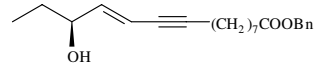


(136)

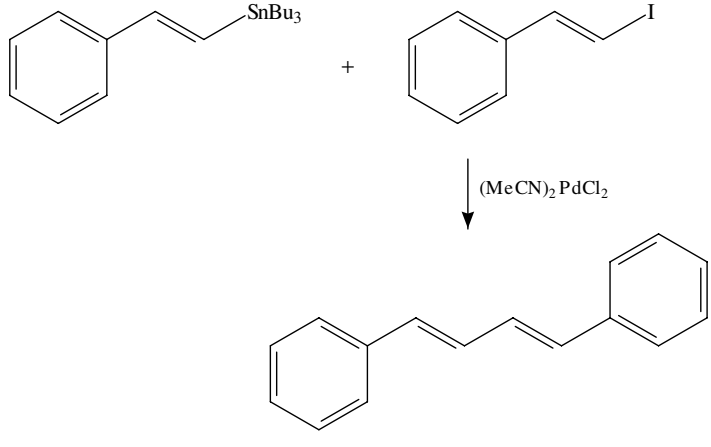
2. Stille coupling

a. Alkene–alkene coupling. The cross-coupling reaction of alkenyltin reagents with alkenyl electrophiles catalysed by palladium complexes to generate dienes of high stereoselectivity is known as Stille coupling (equation 137)[235]. When leaving group on the alkenyl electrophile is iodide (or iodonium salt)[236], triflate or a mesylate[237], the reaction works at room temperature, whereas with vinyl bromides, heating up to 100 °C is required. Vinylstannanes can be prepared by a variety of methods such as transmetallation of vinyllithium[238], vinylaluminium[239], vinylcuprate[240a] or reaction of vinyl halides with a tin cuprate[240b]. They can also be prepared by the stereospecific addition of a tin–metal bond across a carbon–carbon triple bond[241,242]. Palladium catalysts such as $Pd(PPh_3)_4$, $PdCl_2(MeCN)_2$, $PdCl_2(PPh_3)_2$ and $Pd_2(dba)_3$ are commonly employed. However, the presence of a palladium catalyst for this coupling is not always necessary. Piers and

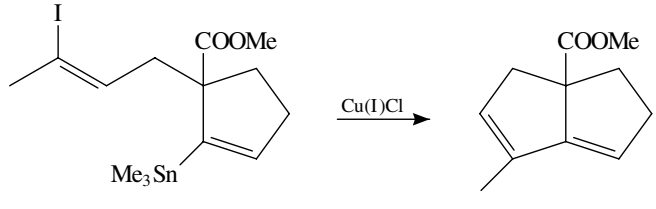
TABLE 24. Enynes through alkyne–alkene coupling

Alkene component	Alkyne component	Enediyne/dieneyne/eneyne	Reference
			234a
			234b
			234c
			233

Wong reported that stoichiometric amounts of copper(I) chloride alone can promote the intramolecular Stille coupling (equation 138)[243]. In fact, copper(I)-mediated reaction was cleaner and faster compared with that catalysed by Pd(0) species. Selected examples of intermolecular Stille coupling reactions leading to dienes (Table 25)[236a,242b,244], polyenes (Table 26)[245] and macrocyclizations (Table 27)[246] are given in the respective tables.

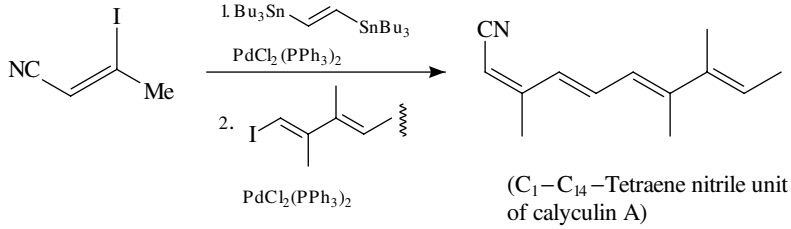


(137)



(138)

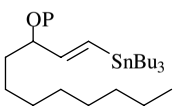
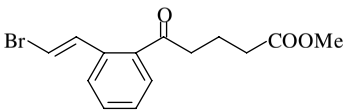
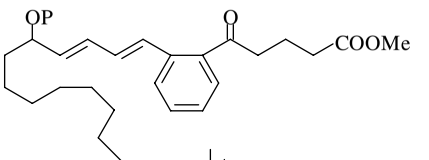
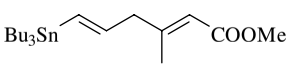
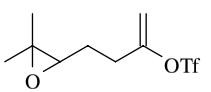
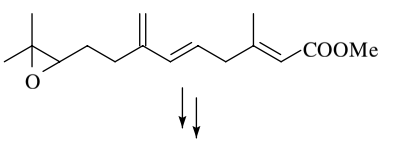
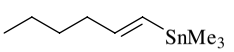
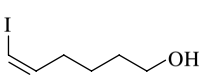
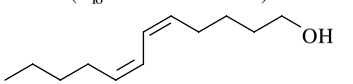
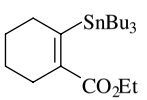
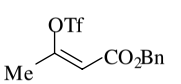
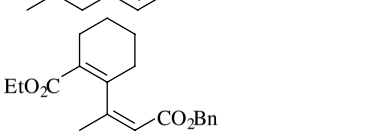
trans-1,2-Bis(tri-*n*-butylstannyl)ethylene, prepared from *trans*-dichloroethylene in a two-step process via tri-*n*-butylchloroethenylstannane[247], is a versatile substrate for double Stille coupling in a sequential manner. Barrett employed it to generate the required dienyl stannane in the first step and later employed it for further coupling with another alkenyl iodide during the synthesis of tetraene portion of calyculin A (equation 139)[248]. Extraordinary versatility of Stille coupling was demonstrated by Nicolaou and coworkers during the total synthesis of rapamycin. A double Stille coupling was employed for the macrocycle construction and the formation of a triene unit in the total synthesis of this polyene macrolide antibiotic (equation 140)[249].



(139)

(C_1-C_{14}–Tetraene nitrile unit of calyculin A)

TABLE 25. Synthesis of dienes through a Stille coupling reaction

Stannane	Vinyl halide/triflate	Product	Reference
 P = THP		 (benzoleukotriene B_3)	244a
		 (C_{16} Juvenile hormone)	244b
			236a
			244c

continued overleaf

TABLE 25. (*continued*)

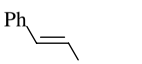
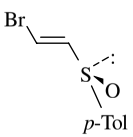
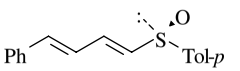
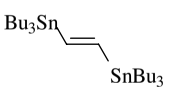
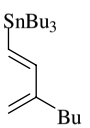
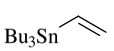
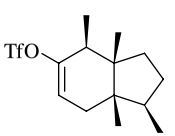
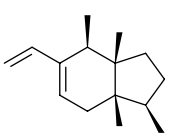
Stannane	Vinylhalide/triflate	Product	Reference
			244d
			242b
			244e

TABLE 26. Synthesis of polyenes through Stille coupling

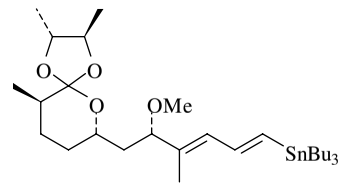
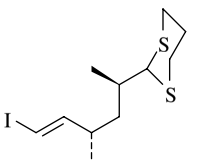
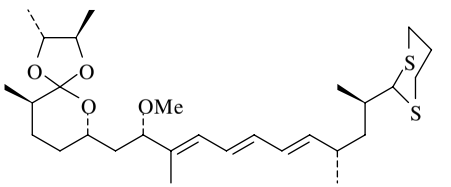
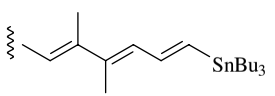
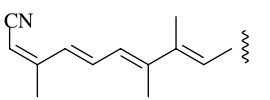
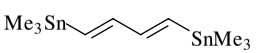
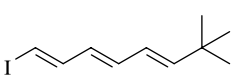
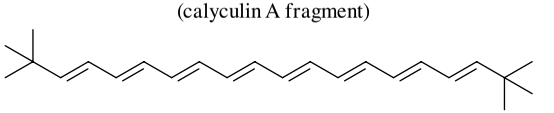
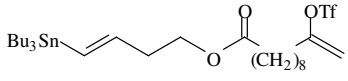
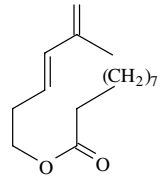
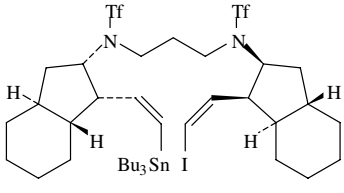
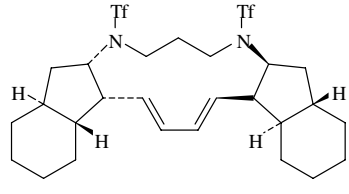
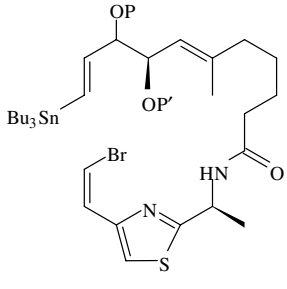
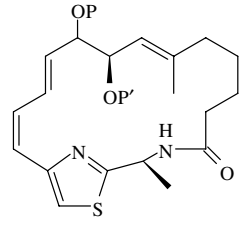
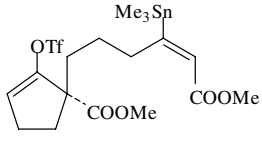
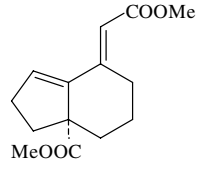
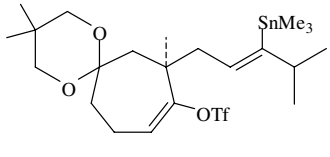
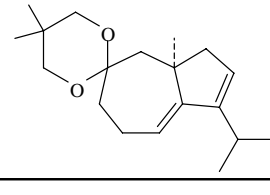
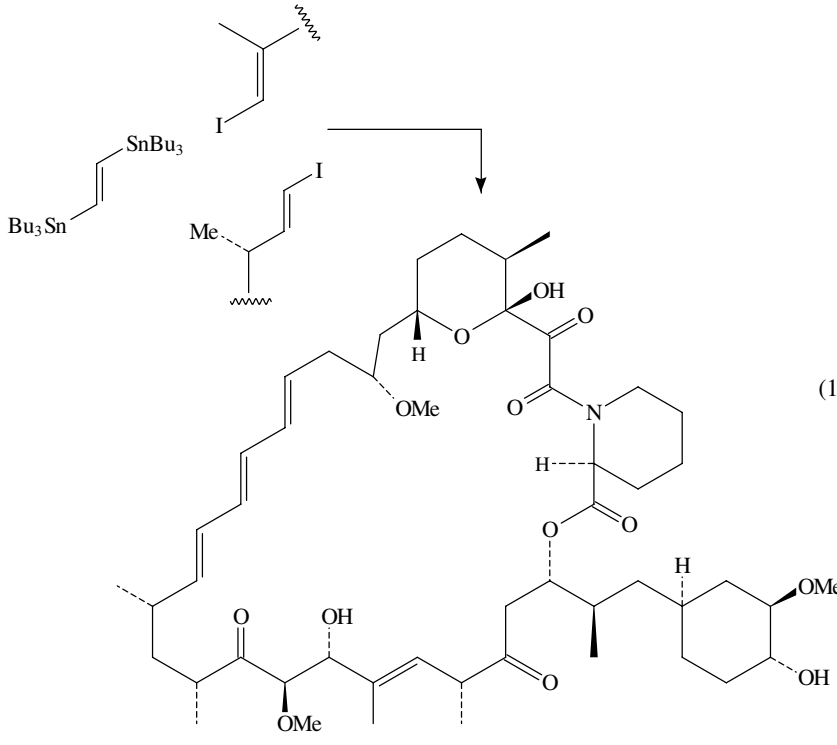
Stannane	Alkenyl iodide	Product	Reference
		 (rapamycin fragment)	245a
		 (calyculin A fragment)	245b
			245c

TABLE 27. Intramolecular cyclizations through Stille coupling

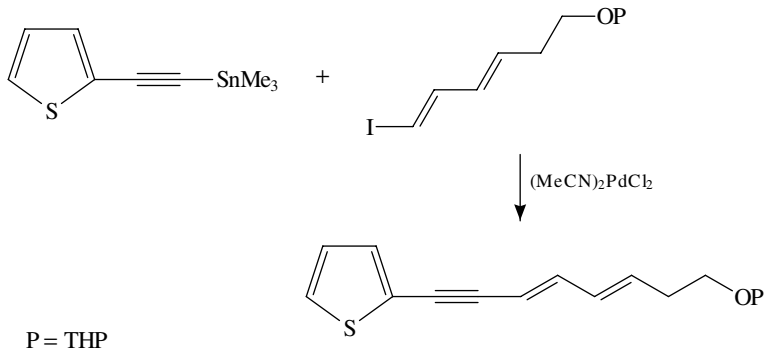
Substrate	Product	Reference
		246a
	 Papuamine	246b
 P = *t*-BuMe$_2$Si; P′ = MeOCH$_2$		246c
		246d
		246e



(140)

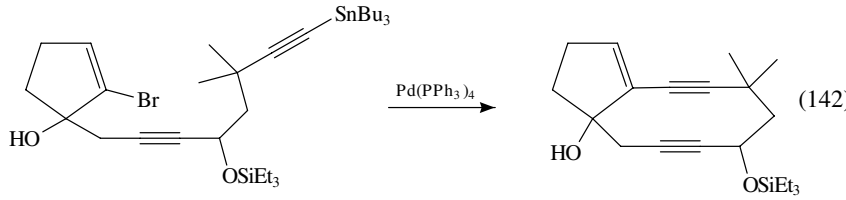
Rapamycin

b. Alkene–alkyne coupling. Alkynyl tin compounds couple with vinyl iodides or vinyl bromides under palladium catalysis to result in conjugated enynes stereospecifically[250]. This reaction has been employed for the enyne formation leading to the synthesis of a tetrahydropyranyl derivative of a natural insecticide, (3*E*,5*E*)-8-(2-thienyl)-3,5-octadien-7-yn-1-ol (equation 141)[250]. An intramolecular version of this reaction generates a 10-membered ring analogue of the chromophore of the antitumer antibiotic neocarzinostatin (equation 142)[251].



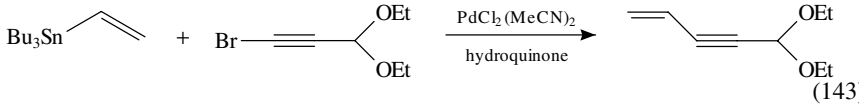
(141)

P = THP

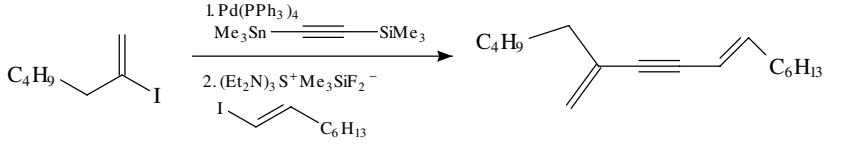


(142)

Bromoalkynes also couple with vinylstannanes readily to result in enynes. Synthesis of protected enynals via cross-coupling of vinylstannanes with 1-bromoalkynes in the presence of a catalytic amount of Pd(II) has been reported (equation 143)[252]. Hiyama and coworkers extended the Stille methodology for sequential three-component coupling of trimethylstannyl(trimethylsilyl)acetylene with a vinyl iodide in the first step and cross-coupling of the intermediate trimethylsilylethyne with another alkenyl iodide in the presence of tris(diethylamino)sulphonium trimethyldifluorosilicate in the second step to generate a dienyne (equation 144)[253]. Both steps occur under palladium catalysis, in one-pot, to result in stereodefined 1,5-dien-3-ynes.



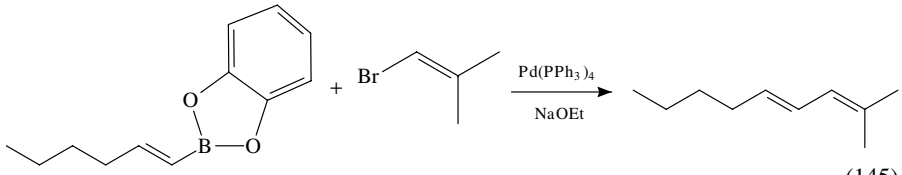
(143)



(144)

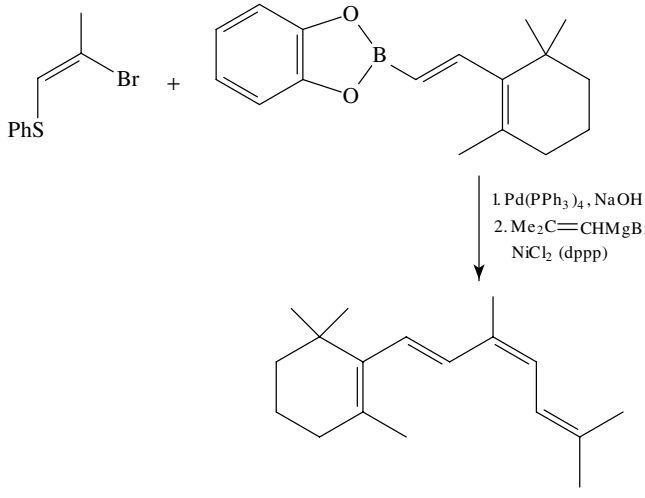
3. Suzuki coupling and related reactions

Coupling of 1-alkenyldiorganoboranes, prepared readily by hydroboration of terminal alkynes, with bromo- or iodo-alkenes in the presence of a catalytic amount of palladium(0) complex and a base, is known as Suzuki coupling (equation 145)[254]. Stereoselectivity in this reaction is very high and the yields are good. Stereochemistry of both the coupling partners, viz. organoborane and vinyl halide, are retained in the reaction. Since, both *E*—[255] and *Z*-vinylboranes[256] can be prepared stereoselectively from 1-alkynes, this coupling reaction is of immense synthetic value (Table 28)[257]. Vinylboranes can be prepared by *syn* addition of either catecholborane or disiamylborane across terminal alkynes. The presence of an equivalent of a base such as TlOH, Ag_2O or even Na_2CO_3 is a must for this reaction, since the base assists in the formation of organoborates, thereby increasing the acidity of the α-carbon atom[254a,258].



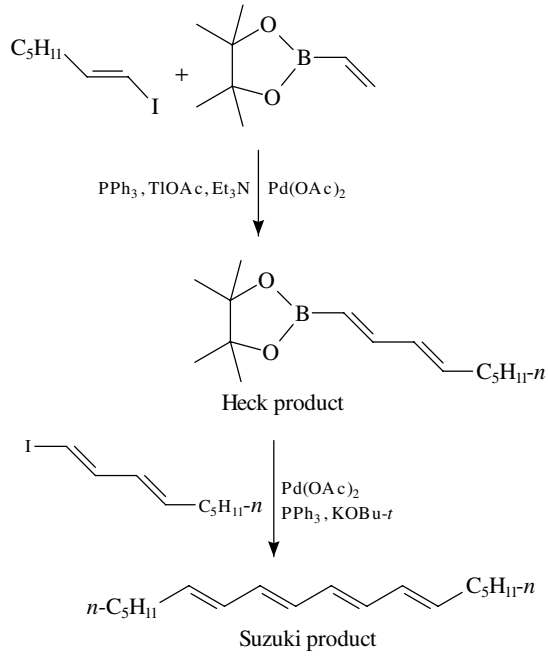
(145)

Stereo- and regioselective synthesis of trienes and tetraenes has been reported by palladium-catalysed coupling of (*E*)- or (*Z*)-1-alkenyl boronates with (*E*)- or (*Z*)-2-bromo-1-phenylthio-1-alkenes followed by treatment with a Grignard reagent in the presence of a nickel catalyst (equation 146)[259].



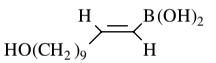
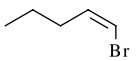
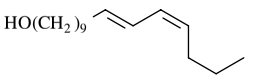
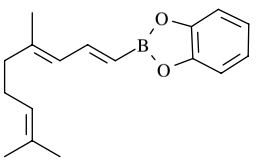
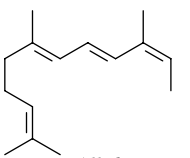
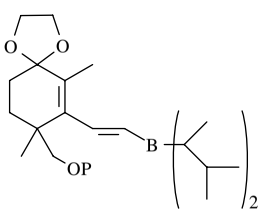
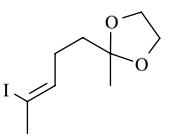
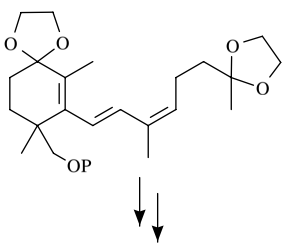
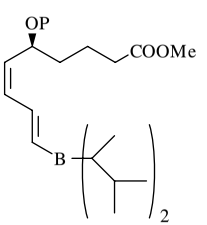
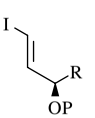
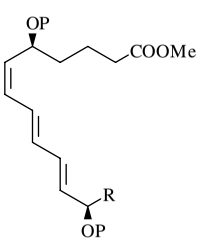
(146)

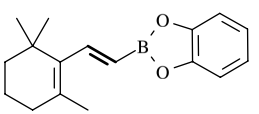
Stewart and Whiting have reported a useful application of sequential Heck and Suzuki coupling reactions of a vinylborane pinacol ester with palladium catalysis to generate a tetraene (equation 147)[260].

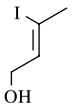


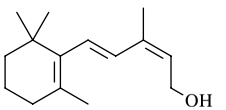
(147)

TABLE 28. Dienes and polyenes through Suzuki coupling

Substrate	Alkenyl halide	Product	Reference
		 Bombykol	257a
		 Allofarnesene	257b
	 P = $PhCH_2$	 Trisporol B	257c
	 P = TBDMS		257d







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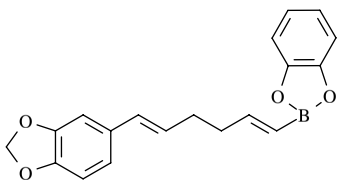

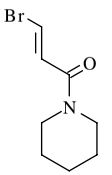

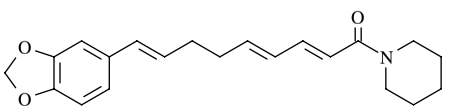

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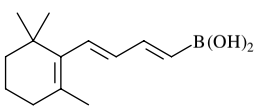

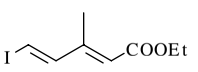

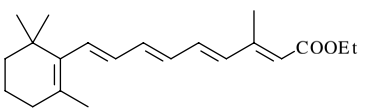

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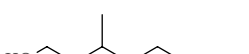

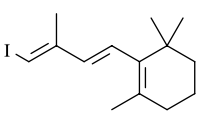

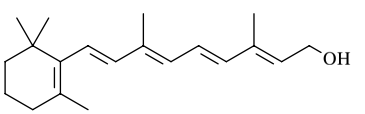

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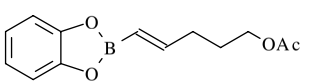
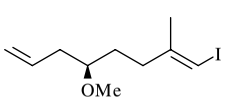
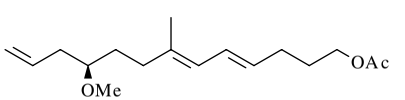




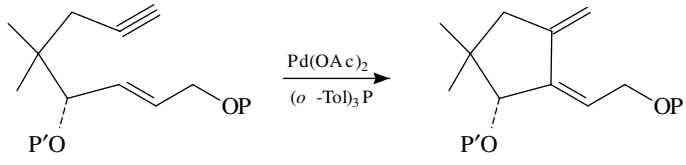


257i

Curacin A intermediate

4. Trost alkene–alkyne cyclizations

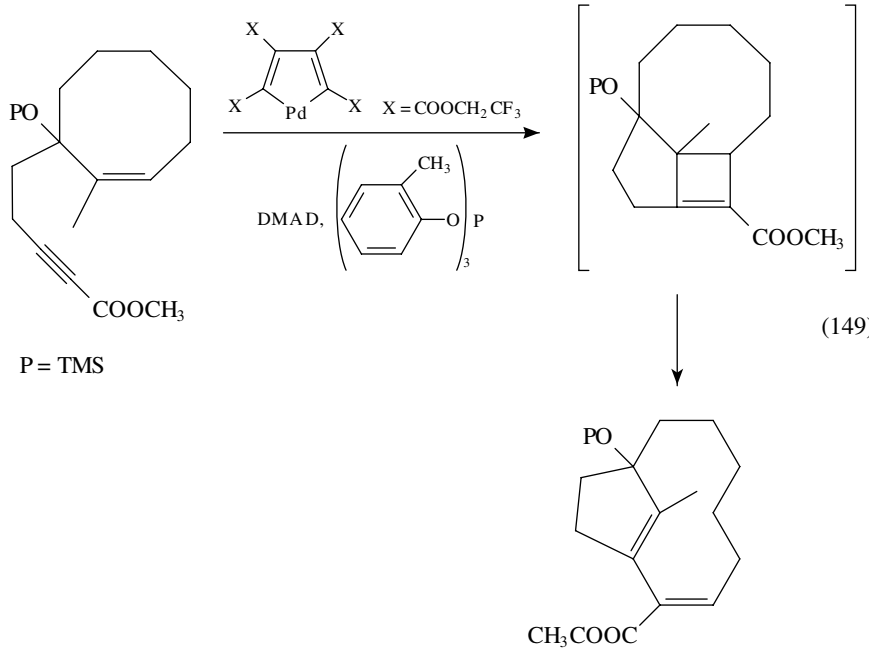
Trost and coworkers extended the synthetic utility of palladium-catalysed intramolecular reactions by finding that suitably positioned alkene–alkyne groups present in an acyclic molecule readily cyclize in the presence of acetic acid to result in cyclic 1,3-dienes[261]. The mechanism of this reaction is markedly different from that of the Heck reaction. The hydridopalladium intermediate, generated by oxidative addition of acetic acid to the Pd(0) catalyst, adds to the carbon–carbon triple bond regio- and stereoselectively to form an organopalladium intermediate. Palladium metal also coordinates with the alkenyl group. The next step is the formation of a carbon–carbon bond to result in the cyclic intermediate. Depending on the substrate, loss of a specific β-proton takes place with the regeneration of catalyst and release of the diene product. Thus, the overall process is a type of Alder-ene reaction (equation 148). Trost utilized the product shown in equation 148 for the synthesis of isolactarane-type sesquiterpenoid sterepolide[261b,262] and merulidial[263].



(148)

P = *t*-BuMe$_2$Si ; P′ = 4-MeoC$_6$H$_4$CH$_2$

Palladocyclopentadiene reagent promotes [2 + 2]-cycloaddition of suitably positioned enynes to form cyclobutenes which undergo symmetry allowed ring opening to form 1,3-dienes with a bridgehead double bond (equation 149)[264].

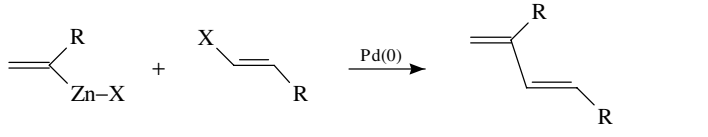


(149)

P = TMS

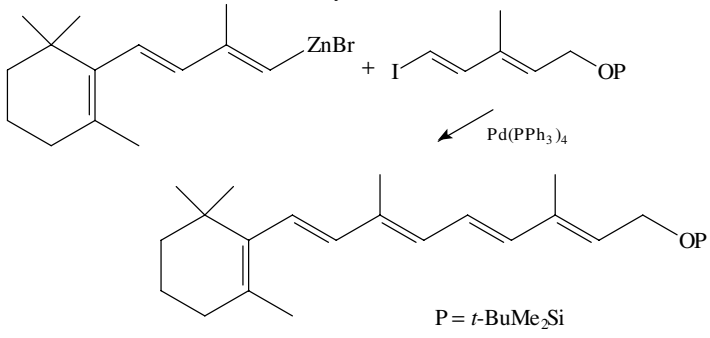
5. Alkenyl zinc intermediates

The alkenylzinc intermediates, prepared by transmetallation of vinyllithium derivatives with zinc halide, couple with alkenyl halides in the presence of a catalytic amount of a palladium reagent, in a process reminiscent of the Heck reaction, leading to dienes stereospecifically (equation 150)[265]. In fact, this type of coupling is among the best known methods for stereospecific generation of dienes. Following this method an efficient synthesis of a vitamin A derivative via C_{14}-alkenyl zinc coupling with C_6-vinyl iodide in the presence of a catalytic palladium(0) species has been described (equation 151)[266]. This method is also an effective way of coupling α-lithio enol ethers with alkenyl halides to furnish 2-alkoxy-1,3-dienes (equation 152)[267].

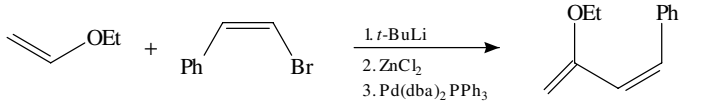


(150)

R = SEt, $SiMe_3$, OEt ; R′ = H, alkyl

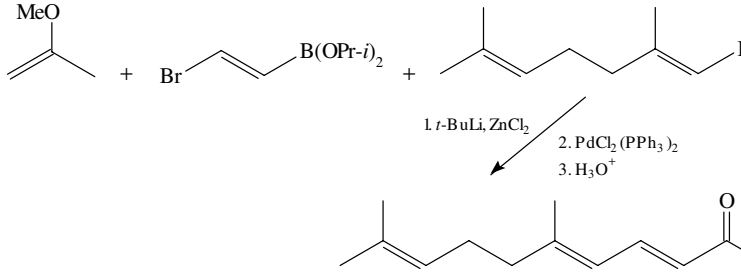


(151)



(152)

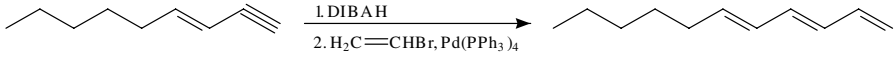
Suzuki and coworkers described a one-pot, stepwise, palladium-catalysed three-component stereospecific cross-coupling of (*E*)-(2-bromoethenyl)diisopropylboron, a vinyl ether and a vinyl iodide. The first coupling is with the organozinc species generated from the vinyl ether and is followed by coupling with vinyl halide to generate (*E*,*E*)-dienone (equation 153)[268].



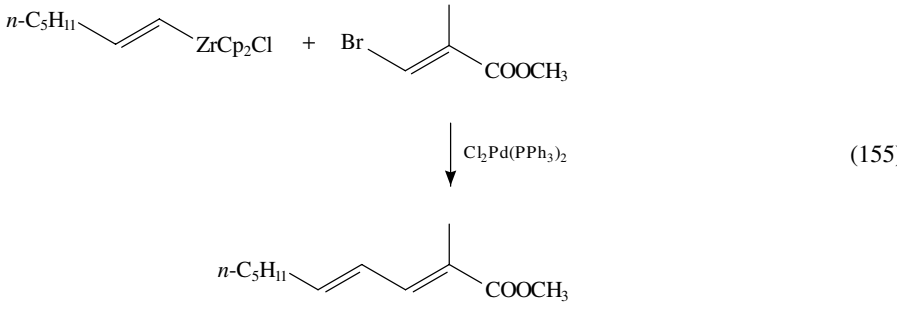
(153)

6. Alkenylalanes and alkenylzirconium intermediates

Similar to the reactions of alkenylboranes, alkenylalanes and alkenylzirconium intermediates undergo facile coupling with vinyl bromides or iodides in the presence of palladium(0) catalyst to generate dienes of high stereochemical purity (equations 154 and 155)[269]. Since alkenylalanes and alkenylzirconium species are prepared from alkynes, this reaction constitutes a method for generation of dienes from alkynes with alkenyl halides. The presence of a stoichiometric amount of zinc chloride in the reaction medium promotes the coupling process. The advantage of the alkenylzirconium method is that many sensitive functional groups such as carbonyl, ester or acetal present on the vinyl halide partner are tolerated.



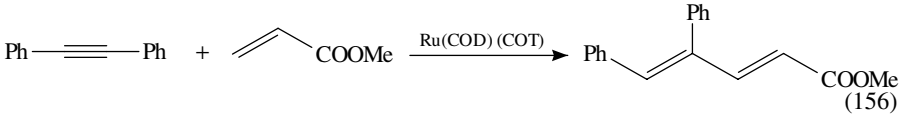
(154)



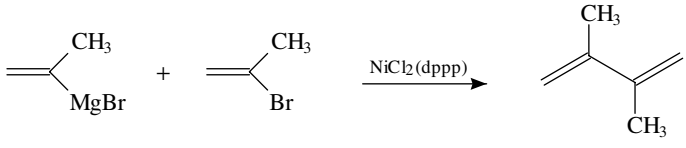
(155)

7. Ruthenium and nickel catalysed coupling reactions

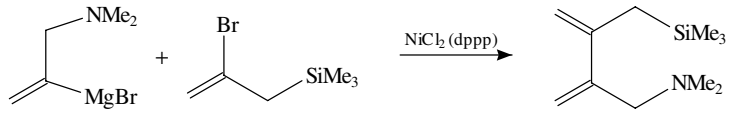
Acetylenic compounds couple with alkenes to furnish stereoselective dienes under ruthenium complex catalysis (equation 156)[270]. Direct coupling of vinyl Grignard reagents with vinyl halides to furnish dienes takes place in the presence of nickel catalysts such as $NiCl_2(PPh_3)_2$ and $NiCl_2$(dppp) (equation 157)[271]. Even though regioselectivity and yields in the reaction are high, it is seldom applied in the synthesis since vinyl Grignard reagents do not tolerate many functional groups. Hosomi and coworkers used this method to prepare 2-dimethylaminomethyl-3-trimethylsilylmethyl-1,3-butadiene, a useful precursor for tandem Diels-Alder reaction (equation 158)[272]. Vinyl Grignard reagent reacts with alkenyl sulphides in the presence of a catalytic amount of $NiCl_2$(dppe) to give dienes in good yields (equation 159)[273].



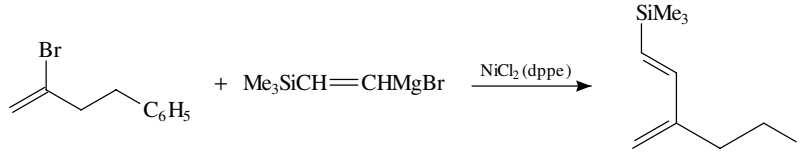
(156)



(157)



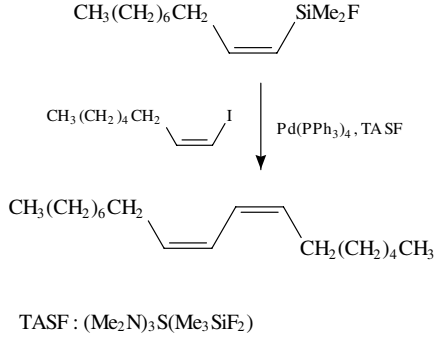
(158)



(159)

8. Alkenylsilanes

Alkenylfluorosilanes readily couple with alkenyl iodides in the presence of a palladium(0) catalyst and TASF to form dienes of high stereospecificity (equation 160)[274]. Since the alkenylsilane preparation and coupling reaction are conducted under neutral conditions, without the involvement of strong reducing agents, this coupling reaction has wide applicability.



(160)

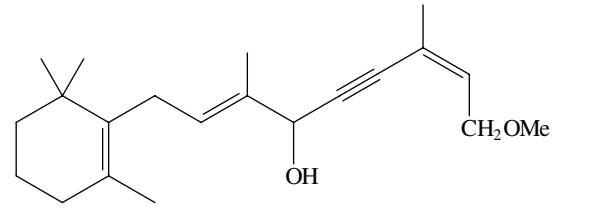
TASF : $(Me_2N)_3S(Me_3SiF_2)$

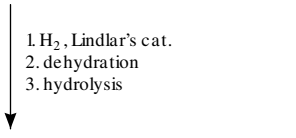
VII. FROM ALKYNES

A. Reduction of Enynes

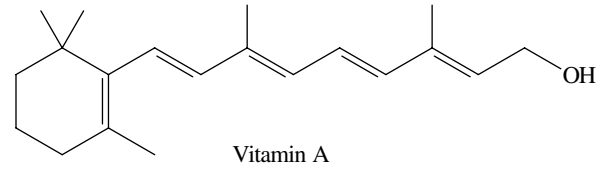
The reduction of conjugated acetylenic compounds to dienes and polyenes is a simple, straight forward method for their generation. A variety of compounds having conjugated or non-conjugated enyne functionality can be generated easily by making use of the acidity of the acetylenic hydrogen. Partial reduction of a carbon–carbon triple bond to a *Z*-double bond can be accomplished by selective hydrogenation[275]. Catalysts prepared from palladium are most commonly used, but additives such as quinoline, pyridine or ethylenediamine, which partially poison the catalyst, and adsorbent materials such as a polymer matrix, $CaCO_3$, $Pb(OAc)_2$, $BaSO_4$ and $SrCO_3$ have a profound effect on selectivity. Lindlar's catalyst (palladium deposited on $CaCO_3$–PbO) in the presence of quinoline is the generally used catalyst for the controlled hydrogenation of enynes to dienes[276]. An interlamellar montmorillonite–diphenylphosphinepalladium(II) complex for the partial hydrogenation of enynes to dienes has been developed as an alternative to the Lindlar catalyst[276c]. The advantage with this semihydrogenation procedure is that the reagents and reaction conditions tolerate a variety of reducible functional groups such as a carbon–carbon double bond, carbonyl, nitrile etc.

Industrial synthesis of vitamin A (Hoffman-La-Roche) goes through partial hydrogenation of an enyne (equation 161)[277]. A number of syntheses of pheromones, where the reduction of an enyne to a diene is the key step, have been devised. A few selected examples are given in Table 29[278]. During the total synthesis of endiandric acids, Nicolaou employed hydrogenation of a polyenyne intermediate with a Lindlar catalyst to generate an intermediate which underwent symmetry-allowed cyclizations to result in the natural product (equation 162)[279].

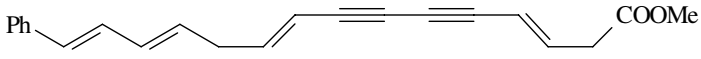


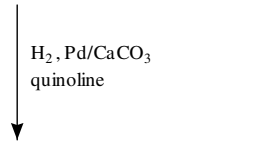


(161)

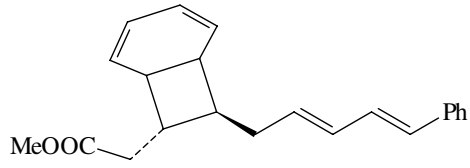


Vitamin A





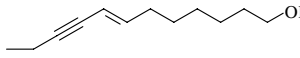
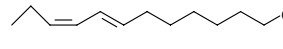
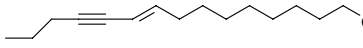
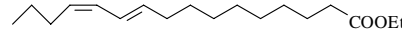
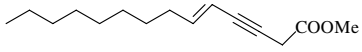
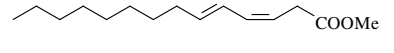
(162)

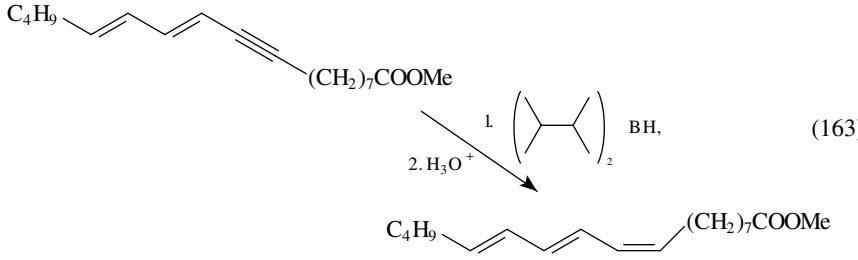


Endiandric acid D methyl ester

A hydroboration–protonolysis procedure for the conversion of conjugated enynes to dienes is far superior to partial hydrogenation over Lindlar's catalyst, in terms of stereoselectivity and yields[280]. Ratovelomanana and Linstrumelle reported the synthesis of methyl α-eleostearate (equation 163) and methyl punicate by employing this strategy[280].

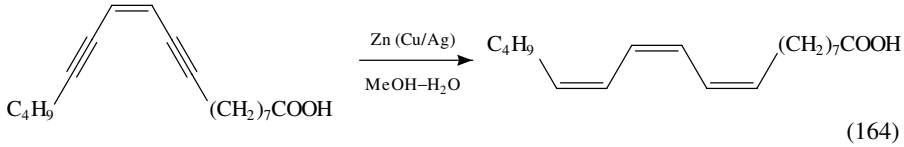
TABLE 29. Dienes through selective hydrogenation of enynes

Eneyne	Diene	Reference
		278a
		278b
		278c

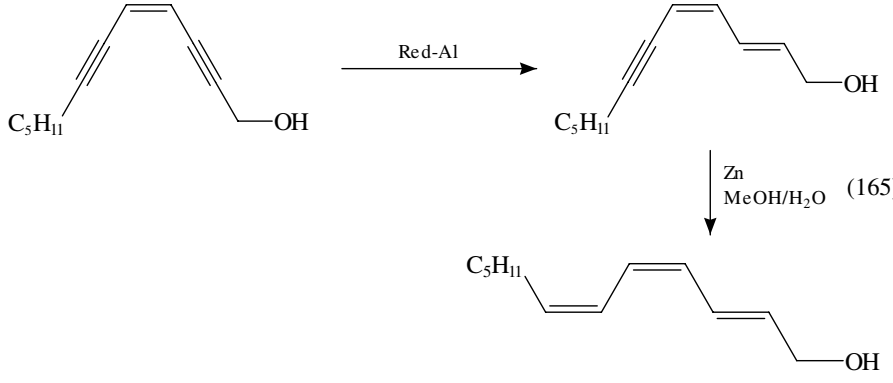


(163)

Carbon–carbon triple bonds in enynes can also be reduced to *E*-double bonds in high isomeric purity with powerful hydride reducing agents such as LAH[281], sodium bis-(ethoxymethoxy)aluminium hydride (Red-Al^R)[282] and *n*-BuLi, DIBAH[282]. Linstrumelle and coworkers reported the synthesis of several trienes and polyenes of defined stereochemistry from enynes by transforming a carbon–carbon triple bond to either a *Z*-double bond using Zn/MeOH–H_2O or an *E*-double bond using Red-Al^R (equations 164 and 165)[283].



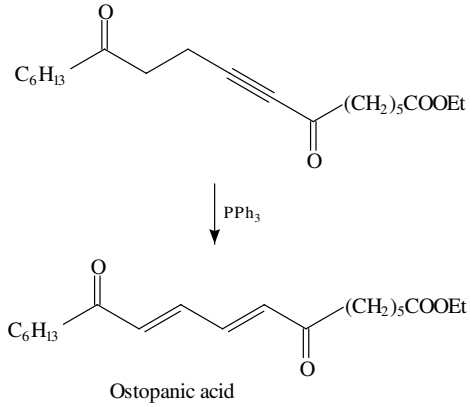
(164)



(165)

B. Isomerization Reactions

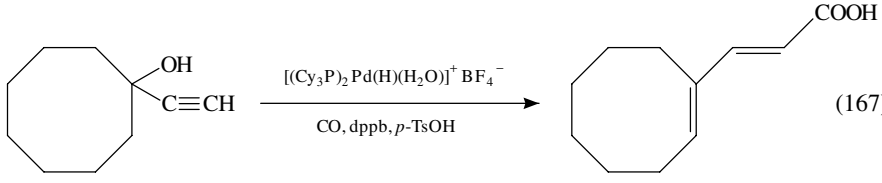
Isomerization of alkynes to dienes is a useful synthetic approach since alkyne derivatives are readily available. Even though alkyne migrations along the chain under basic conditions are well known, isomerizations of isolated alkyne to 1,3-diene do not take place easily. For some alkynones, this reaction takes place readily with triphenylphosphine[284]. Utilizing isomerization of a yne-one as a key reaction, Guo and Lu reported a three-step synthesis of an anti-cancer agent ostopanic acid starting from pent-4-ynal (equation 166)[284a,285].



Ostopanic acid (166)

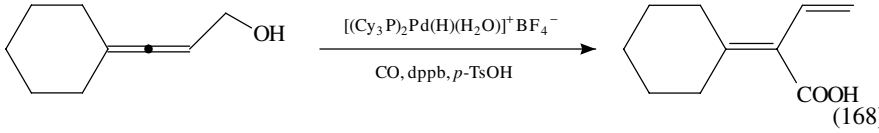
C. Carbonylation and Isomerization via Organometallic Intermediates

Air-stable palladium(0) catalyst, $[(Cy_3P)_2Pd(H)(H_2O)]BF_4$, catalyses carbonylation of propargylic alcohols to generate dienoic acids and esters (equation 167)[286]. Since propargyl alcohols are obtained from carbonyl compounds by acetylide addition reactions, this sequence constitutes a three-carbon homologation. α-Allenic alcohols are converted to α-vinylacrylic acids under similar conditions (equation 168)[287].



(167)

Cy = c-Hex; dppb = 1,4-Bis(diphenylphosphino)butane

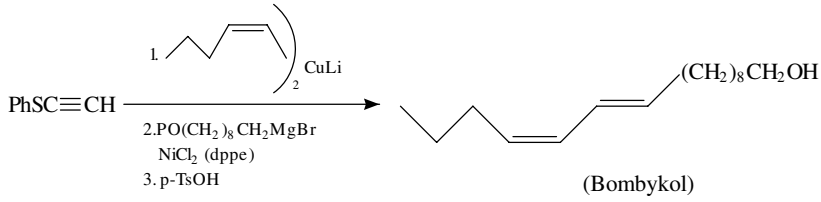


(168)

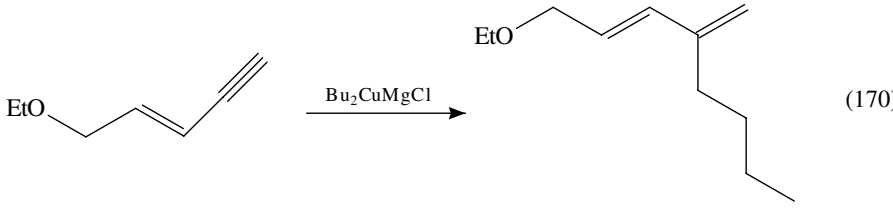
D. Addition of Gilman Reagents

Stereodefined alkenyl cuprates add to alkynes in *syn* fashion to result in 1,3-dienes of predictable stereochemistry[288]. Naso and coworkers used this method for the synthesis

of pheromones having *E*,*Z*- and *Z*,*E*-conjugated diene structures[289]. Thus, *Z*-dialkenyl cuprates were added to phenylthioacetylene to yield *E*,*Z*-alkadienyl sulphide intermediate, which undergoes a cross-coupling reaction with Grignard reagents in the presence of a catalytic amount of a Ni(II) complex, leading to the desired dienes (equation 169)[289]. Alkyl cuprates react with vinylacetylene moiety in a regio- and stereoselective manner to result in alkylated 1,3-dienes (equation 170)[290].



P = $CH_3CH_2OCHCH_3$ (169)



(170)

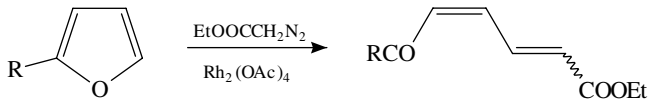
VIII. FROM HETEROCYCLIC COMPOUNDS

A. General Aspects

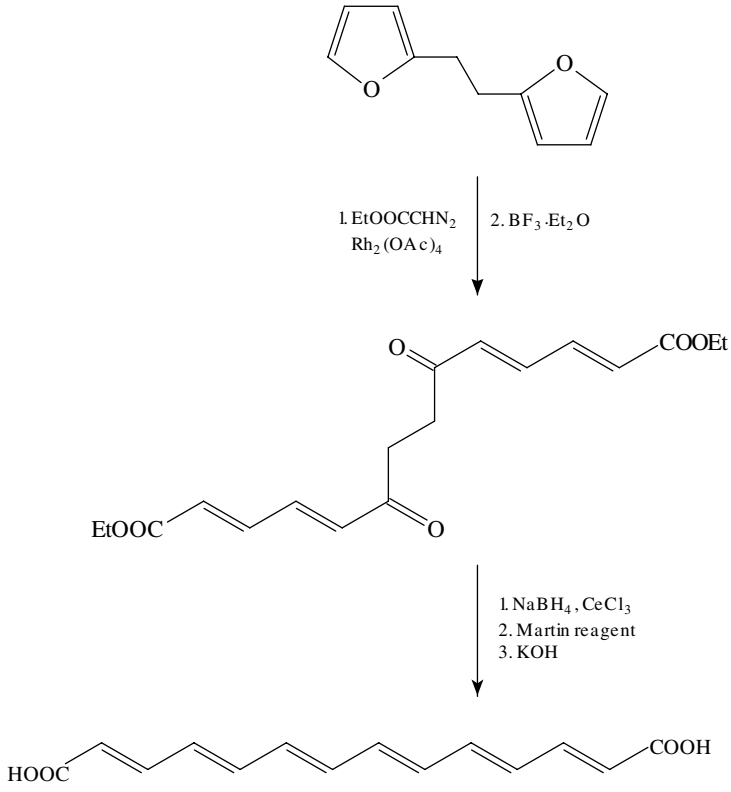
Five- and six-membered oxygen and nitrogen heterocycles, such as furan or pyridine, can be viewed as masked cyclic dienes with predisposed geometry. Appropriate protocols can lead to ring-opening of 5- or 6-membered heterocycles to reveal the diene functionality with well defined stereochemistry. Since substitution reactions can be performed on the heterocycles easily, ring-opening strategy has enormous potential in diene and polyene synthesis[291].

B. From Five-membered Heterocycles

Furan can be viewed as a dienol ether. Wenkert and coworkers found that carbene generated from ethyl diazoacetate using dirhodium tetraacetate add to furan and subsequent *in situ* ring-opening results in 1,4-diacyl-1,3-butadienes (equation 171)[292]. Iodine or BF_3-Et_2O catalysed isomerization of the mixture of diene products results in bifunctional *E*,*E*-dienal ester. Application of this strategy on a bifuran compound resulted in tetraene product which could be elaborated to the hexaene dicarboxylic acid natural product, corticrocin (equation 172)[292]. An intramolecular version of the above strategy was employed for the synthesis of several β-ionone terpenes[293].

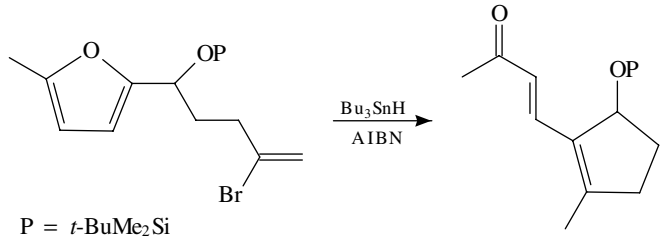


(171)



(172)

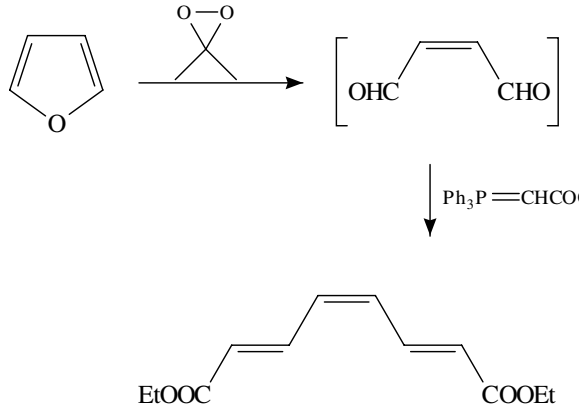
Parsons and coworkers found that intramolecular addition of vinyl radicals, generated *in situ* from the corresponding vinyl bromide and tri-*n*-butyltin hydride in the presence of azobisisobutyronitrile, to the furan ring results in tandem radical addition–fragmentation sequence leading to the formation of five-membered ring compounds having a dienone moiety (equation 173)[294]. Utilizing this strategy, a short synthesis of a prostaglandin model compound was reported[294].



P = *t*-BuMe$_2$Si

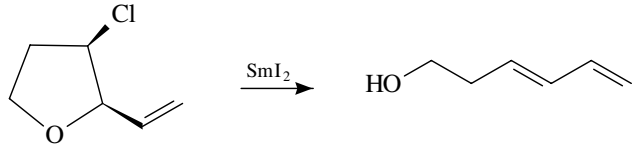
(173)

Furan can be used as a source for malealdehyde. McKervey and coworkers found that oxidation of furan with dimethyldioxirane results in malealdehyde, which can be trapped *in situ* with a variety of Wittig reagents to generate dienes and polyenes (equation 174)[295]. The same sequence with substituted furans gives ketodienealdehydes and ketodieneesters[295].



(174)

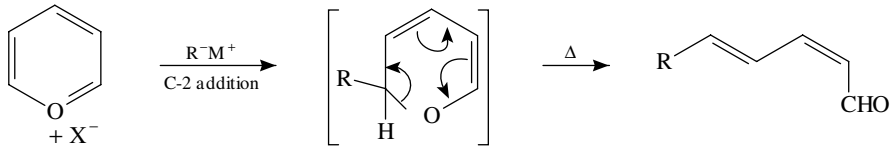
Crombie and Rainbow reported synthesis of terminal dienes of high *E*-selectivity via samarium diiodide mediated scission of 2-vinyl-3-chlorotetrahydrofuran (equation 175) or the corresponding pyran derivatives[296]. Interestingly, both *cis*- and *trans*-2-substituted 3-chlorotetrahydrofurans give the same diene, indicating the involvement of identical intermediates formed by electron transfer from samarium diiodide.



(175)

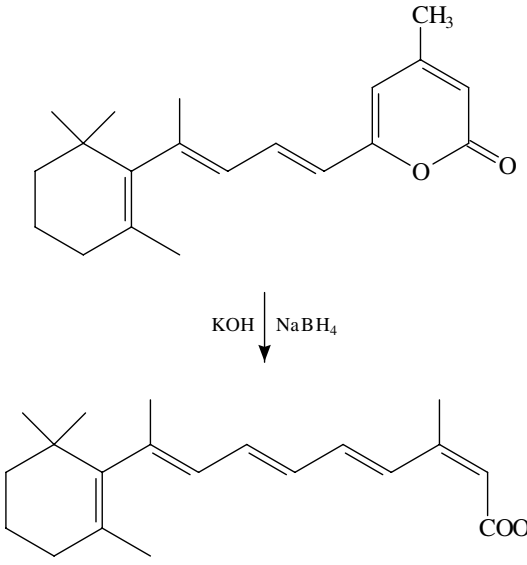
C. From Six-membered Heterocycles

Taylor and coworkers have utilized pyrylium perchlorate[297,298] or pyrylium tetrafluoroborate[299] as a source of five-carbon 2*Z*,4*E*-dienal synthons for diene and polyene synthesis. This method involves C-2 addition of an organometallic reagent to the pyrylium salt followed by electrocyclic ring-opening of the intermediate 2*H*-pyran to give *Z*,*E*-dienal (equation 176) of high stereochemical purity. Taylor applied the above strategy for the synthesis of several diene and triene derivatives which are shown in Table 30[298b,299,300]. Bestmann and coworkers reported an efficient synthesis of 13*Z*-retinoic acid where the 11,13-diene moiety was generated by reductive ring-opening of substituted 2-pyrone (equation 177)[299b,c].



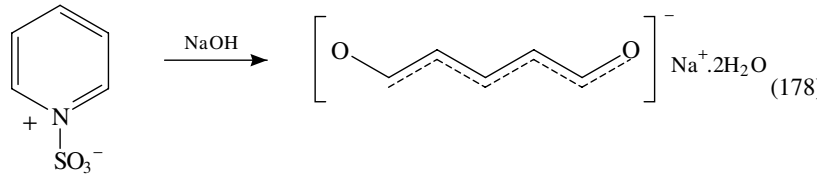
X = ClO_4, BF_4

(176)

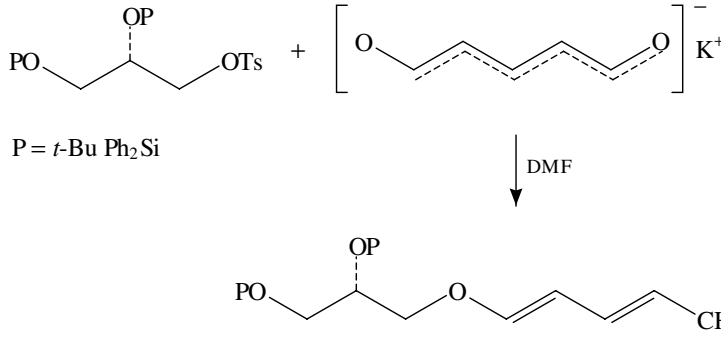


(177)

Treatment of 1-pyridinium sulphonate with sodium or potassium hydroxide generates sodium or potassium salts of 5-hydroxy-2,4-pentadienal (glutaconaldehyde), which are starting materials for a variety of transformations (equation 178)[171b,301]. For example, the reaction of the potassium salt with a carbon electrophile has been used for the preparation of a dienol aldehyde (equation 179)[171b] which was an intermediate in the total synthesis of a mutagen, (S)-3-(dodeca-1,3,5,7,9-pentaenyloxy)propane-1,2-diol.

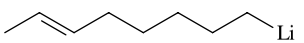
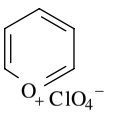
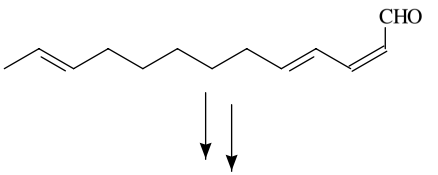
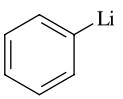
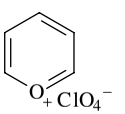
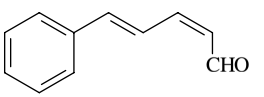
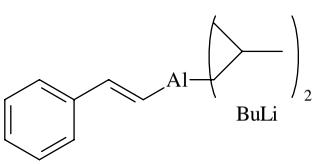
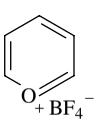
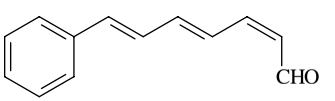


(178)



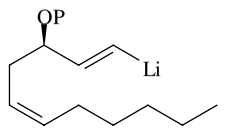
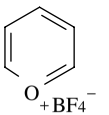
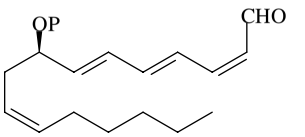
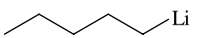
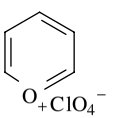
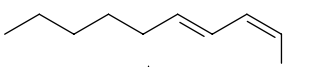
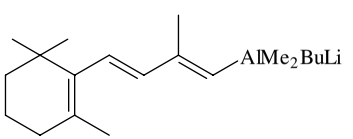
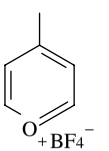
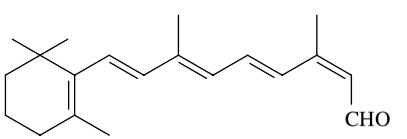
(179)

TABLE 30. Dienes and polyenes from ring-opening of pyrylium salts

Substrate	Reagent	Product	Reference
		 Umbraculumin A	300a
		 Lignarenone A and Lignarenone B	300b
			299a

continued overleaf

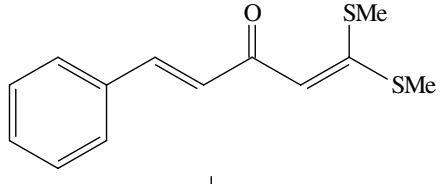
TABLE 30. (*continued*)

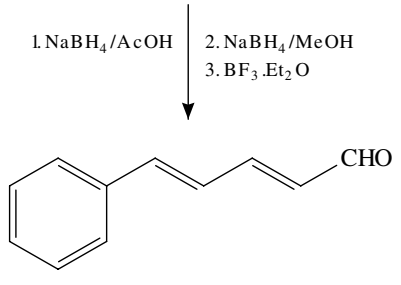
Substrate	Reagent	Product	Reference
 P = TBDMS		  (+)LTB$_4$ methyl ester and (−)(5R)-LTB4 methyl ester	300c
		  (3Z, 5E)-Undeca-1,3,5-triene	298b
		 (13Z-Retinal)	300d

IX. MISCELLANEOUS

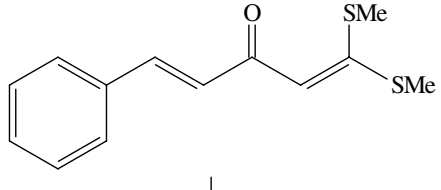
A. Oxoketene Dithioacetals

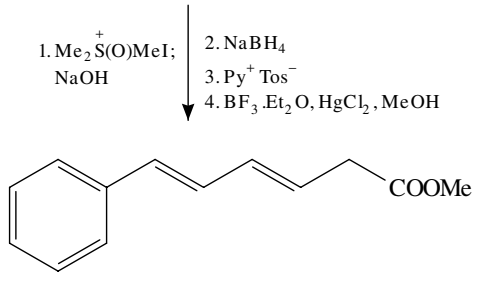
α-Oxoketene dithioacetals are versatile three-carbon synthons in which the carbonyl group can be manipulated either in 1,2-fashion or 1,4-fashion. The ketene dithioacetal portion is a masked ester and the 1,4-reduction product of α-oxoketene dithioacetals, the β-oxodithioacetals, are masked β-ketoaldehydes. Junjappa and Ila have utilized these synthones for the synthesis of diene and polyene aldehydes and esters. For example, sequential 1,4-reduction, 1,2-reduction and hydrolysis of α-oxoketene dithioacetals release the α,β-unsaturated aldehyde. Dienals and polyenals result when this sequence is applied to the substrates having conjugated double bonds (equation 180)[302]. On the other hand, sequential cyclopropanation, 1,2-reduction, dehydration and hydrolysis of the α-oxoketene dithioacetals result in diene esters (equation 181)[303]. Polyene separated oxoketene dithioacetals on 1,2-reduction and hydrolysis yield polyene esters in good yield (equation 182)[304]. This reaction constitutes a method for carbonyl transposition across the polyene chain.



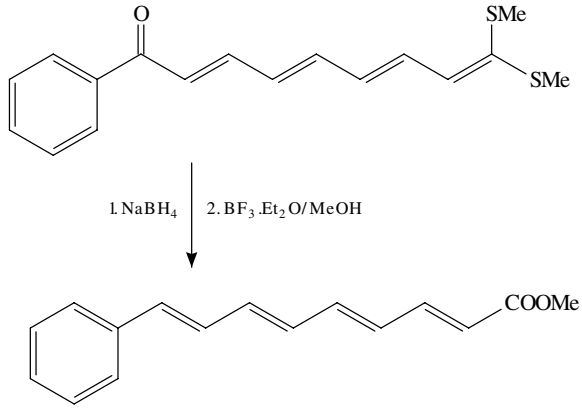


(180)





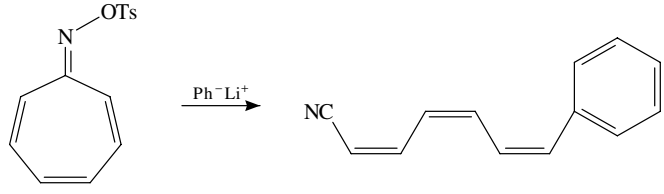
(181)



(182)

B. Trienes from Tropone Oxime Tosylate

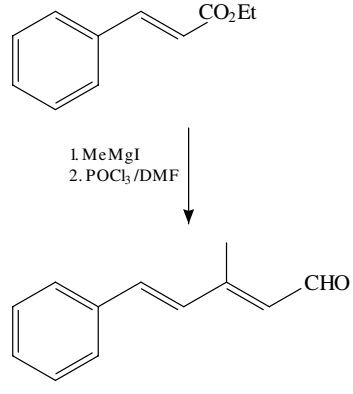
Machiguchi, Nozoe and coworkers have very recently observed that in contrast to chemical reactivity of tropones, the tosylate of tropone oxime undergoes a facile ring-opening to 6-substituted (*Z*,*Z*,*Z*)-1,3,5-hexatriene nitriles on reaction with various nucleophiles[305]. For example, reaction of phenyl lithium results in the corresponding hexatriene carbonitrile (equation 183).



(183)

C. Dienals via Vilsmeier Reaction

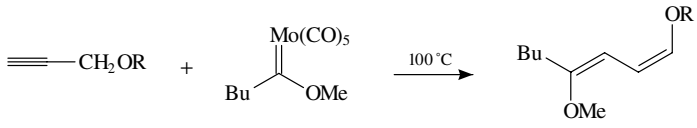
Cinnamic acid esters can be converted to dienals via Grignard addition and Vilsmeier reaction (equation 184)[306].



(184)

D. Carbene Insertion Reactions

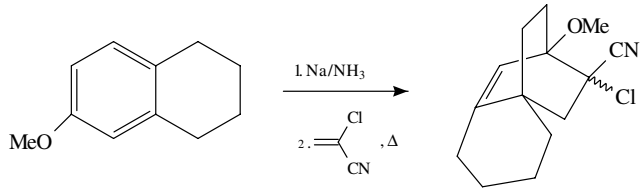
(*Z*,*Z*)-1,4-Dialkoxy-1,3-dienes can be readily prepared from propargyl ethers and molybdenum carbene complexes (equation 185)[307]. High stereoselectivity in this reaction may be due to the formation of stable vinyl hydride complex with the enol ether.



(185)

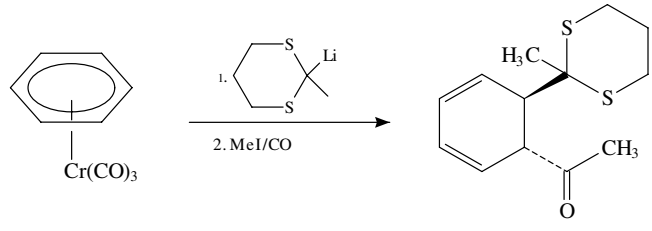
E. From Arenes

Reduction of aromatic compounds to dihydro derivatives by dissolved metals in liquid ammonia (Birch reduction) is one of the fundamental reactions in organic chemistry[308]. When benzene derivatives are subjected to this reduction, cyclohexa-1,4-dienes are formed. The 1,4-dienes obtained from the reduction isomerize to more useful 1,3-dienes under protic conditions. A number of syntheses of natural products have been devised where the Birch reduction of a benzenoid compound to a cyclohex-1,3-diene and converting this intermediate in Diels–Alder fasion to polycyclic products is involved (equation 186)[308f–h].



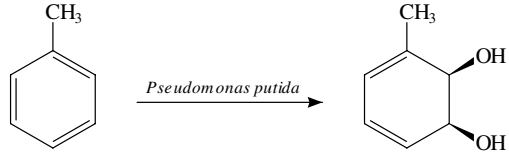
(186)

Arenes can be transformed to *trans*-disubsituted 1,2-dihydroarenes via temporary complexation with the electrophilic $Cr(CO)_3$ group, followed by addition of a nucleophile and an electrophile across the arene double bond (equation 187)[309].



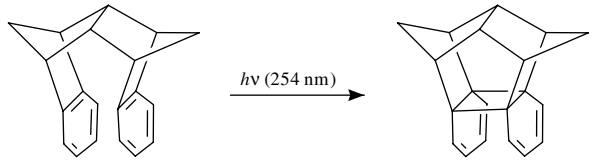
(187)

Benzene and other arenes can be oxidized to *cis*-1,2-cyclohexadienediol enantiospecifically using a mutant of *Pseudomonas putida* through microbial techniques (equation 188)[310].



(188)

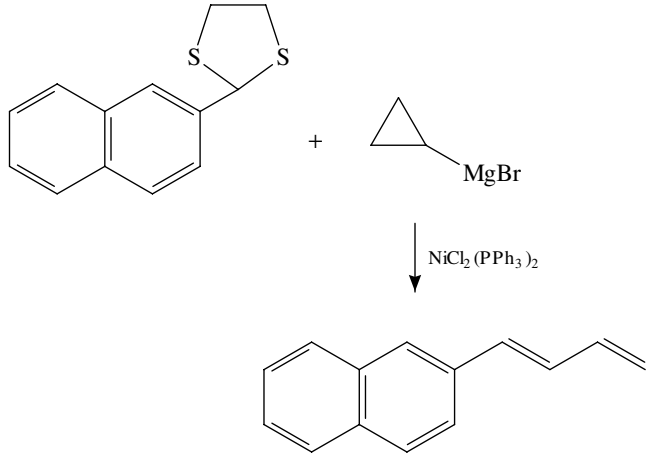
Photochemical 6π-6π cycloaddition of two benzene rings, in principle, produces benzene dimers having two 1,3-dienes units[311]. However, as expected, the dimers are unstable and revert back to benzene rings easily. Prinzbach and coworkers found that two benzene rings, locked in face-to-face relationship, undergo 6π-6π photocycloaddition on irradiation with monochromatic 254-nm light (equation 189)[312]. This reaction was used to generate bisdiene intermediate en route to pagodane.



(189)

F. Cyclopropane Ring-opening

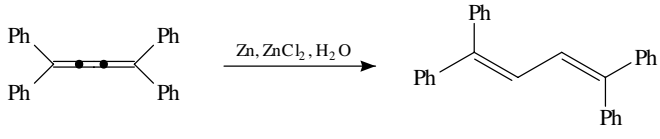
Cyclopropyl organometallic compounds readily undergo ring-opening to give homoallyl organometallic intermediates, which undergo β-elimination to furnish butadienes[313]. Cyclopropylmagnesium bromide reacts with dithioacetals under nickel catalysis to give cyclopropylcarbinyl nickel intermediates, which on ring-opening and spontaneous elimination result in dienes (equation 190)[314].



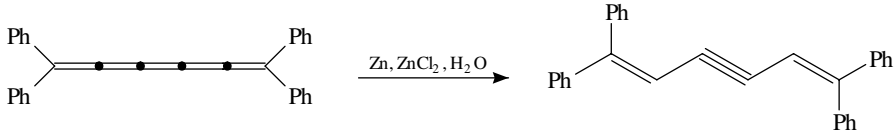
(190)

G. Selective Reduction of Allenes

Aryl group substituted butatrienes and hexapentaenes can be selectively reduced with $Zn–ZnCl_2–H_2O$ to result in aryl-substituted 1,3-butadienes and hexa-1,5-dien-3-ynes, respectively (equations 191 and 192)[315].



(191)



(192)

X. ACKNOWLEDGEMENTS

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CHAPTER **10**

Analysis of dienes and polyenes and their structure determination

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I. INTRODUCTION

In the last fifteen years most efforts aimed at identification and structure determination of dienes and of polyenes were related to studies of bio-originated compounds. The analysis of dienes and polyenes has not been reviewed, so far. The analysis of double bonds containing molecules utilizes the chemical reactivity of the bonds, and hence conjugated double bonds require different approaches than methods used for non-conjugated double bonds. One example is the use of the Diels-Alder reaction which yields derivatives of conjugated dienes whereas isolated double bonds are not affected. Some of the methods

reviewed are very basic and have been in use for many years; others are very specific for the family of compounds studied, as exemplified for carotenoids.

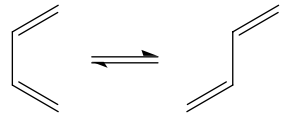
The determination of the structure of synthetic dienes and polyenes is somewhat easier than the identification and structure determination of natural products. Obviously, this stems from the need to separate the latter compounds from very complex mixtures.

The theoretical analysis of the spectra (mostly IR and UV-VIS) of polyenes has been reviewed twice in the last 20 years[1,2]. These reviews concentrate on understanding their biological role and the extension of polyene application. However, both reviews do not cover the structure determination of dienes and polyenes.

One important reason why biologists and biochemists are interested in polyenes is related to the fact that they are light-harvesting antennas and are responsible for triggering the vision signal[1,2]. Moreover, long-chain polyenes appear in vitamins and carotenoids as well as in many antibiotics. Another reason is that the polymeric form, such as polyacetylene, is a natural photo-conductive matter that upon doping becomes conductive, comparable with copper! These properties have ignited the interest of chemists in the synthesis of polyene polymers for 'molecular electronics'. These conjugated functional polymers may be designed to serve as tunable electro-light emitting diodes (LED).

II. SPECTROSCOPIC METHODS

The use of UV-VIS spectra to analyse dienes and polyenes was historically the first method of choice. The spectra of isolated non-conjugated polyenes is actually the superposition of the spectrum of each one of the double bonds. For each double bond the spectrum depends on the various substituents and also on its location in the molecule. It also depends on the stereochemistry, since conjugated double bonds have either *E* or *Z* configuration around each π-bond but also a *cisoid* and *transoid* conformer[3] around the single bond marked as s-*cis* and s-*trans*[4].



s-*cis* s-*trans*

Polyenes can undergo rotation easily about the 'single' bond at room temperature. The s-*trans* conformers are generally more stable because steric interactions in them are minimized.

The s-*cis* conformers tend to be distorted from planarity, and this may influence the UV spectra, as shown by the comparison of butadiene **(1)** and cyclopentadiene **(2)**.

(1) **(2)**

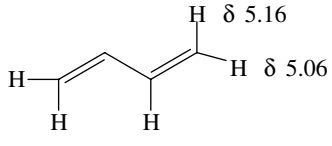
λ 220 nm (ε 20900) λ 238.5 nm (ε 3400)

It is evident that the s-*cis* frozen conformation in the ring of **2** shows a batochromic shift, but a much lower absorption (ε) in comparison with butadiene **(1)**. Woodward and

Fieser and Fieser[5] used an empirical correlation, based on a wide range of compounds, between the diene structure and λ_{max}. This empirical correlation of structure and ultraviolet absorption followed a regular pattern, allowing the calculation of λ_{max} with reasonable accuracy. The early rules were: parent diene 214 nm; for cisoid add 39 nm, extended conjugated diene 30 nm. In the studies of steroids and other cyclic terpenoids these rules were employed to differentiate between homoannular dienes and exocyclic enes (see also Section VII.A)[5]. A more theoretical approach is presented for longer conjugated polyenes, i.e. hexatriene, octatetraene, etc., that have geometrical isomers, i.e. *cis*-polyenes and *trans*-polyenes. For butadiene, all vibrational frequencies have been observed in the IR or Raman spectra[2]. The theoretical analysis of the vibrational properties and the frequencies were reviewed in 1991 by Orlandi and coworkers; their review contains 251 references[2]. However, this review does not offer the analytical tools needed for structural determination. Furthermore, all polyenes examined are conjugated with no branching or ring effects.

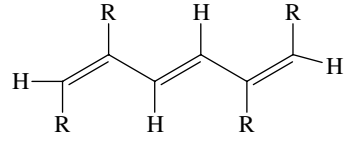
In general, it is noteworthy that one can use the lowering of the energies required to either excite (UV-VIS) or stretch (IR, Raman) the C=C bond with the extension of the polyene system. We have mentioned the batochromic effect (Woodward rule)[5] and will discuss the C=C stretch frequency which correlates with the length of the polyene (e.g. 1640 cm^{-1} for butadiene and 1490 cm^{-1} for the β-carotene homologs, respectively). These correlations can supplement other spectroscopic data to assess the length of the polyene conjugated systems. Of course, the extreme case is cyclic conjugated aromatic systems which are beyond the scope of the present review.

Very powerful tools for the study of dienes and, to some extent, polyenes (in particular annular polyenes) are both ^1H and ^{13}C NMR spectroscopies, which will be discussed in a separate section. As previously mentioned 1,3-butadiene is more stable in the s-*trans* conformation and in the ^1H NMR spectrum both butadiene **(1)** and 2,3,6,7-tetramethyl-2,4,6-octatriene **(3)** display the vinyl proton at a low chemical shift value. In these simple examples the δ value can be predicted theoretically. The ^1H NMR spectrum of a C_{25}-branched isoprenoid was examined as part of the structural determination for biomarkers and is shown in Figure 1[6]. The other spectral and structure assignments are described later in this review.



δ 6.27

(1)



δ 6.62

(3)

R = CH_3

Figure 1 shows a partial ^1H NMR spectrum for H-23, H-5 and H-24 a,b (see the formula of the C_{25} polyene, **4**). These are the hydrogens on the alkenic position and the multiplet between 4.89–5.76 δ (ppm) integrates to four hydrogens, i.e. to a vinyl functionality. Since this is an isoprenoid skeleton it is clear that the position of the double bond must be at C-24. Proton H-23 appears at a lowest field as a heptet due to *cis* coupling with H-24a, *trans* coupling with H-24b and an additional coupling with the vicinal H-22. This indicates the presence of a single H-22 allylic proton, thus supporting the assignment. The double bond between C-5 and C-6 shows the influence of the H-4 allylic hydrogens. These assignments and further discussion on decoupling and ^{13}C NMR spectrum appear in Belt and coworkers[6].

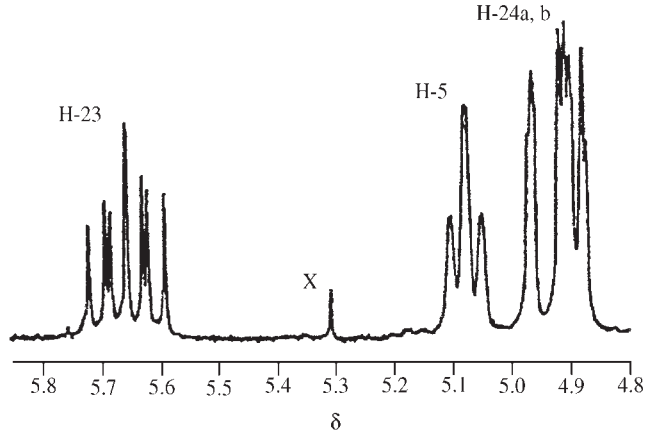
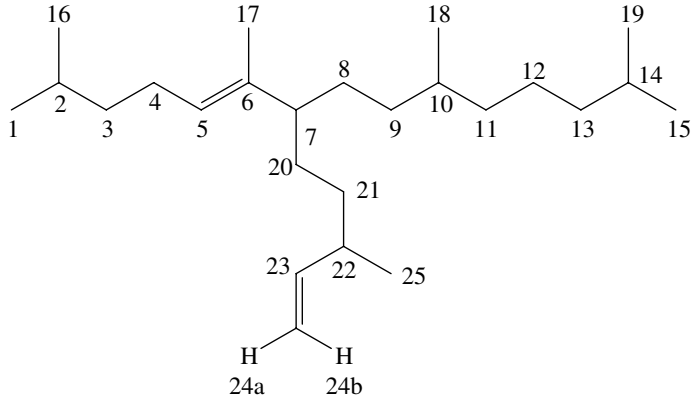


FIGURE 1. The ^{1}H NMR spectrum of the double bonds region (δ 4.8–5.8 ppm) of the high branched C_{25}, compound **4**. The signal X is due to an impurity (see Belt and coworkers[6])

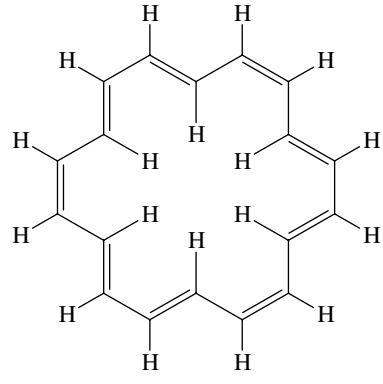


(4)

Although we have stated that we will not include aromatic structures, large π systems of polyenes give rise to long conjugated systems, with very strong shielding and deshielding effects. The annulene family contains systems having the $(4n + 2)$ π-electrons which, according to Hückel, should have a cyclic delocalization but are diatropic. An example is [18] annulene (**5**), where the 12 outer hydrogens absorb at δ 9.28 ppm and the 6 inner hydrogens absorb at δ 2.99 ppm.

In contrast, if the same polyene were to be 'open', no ring current would exist and the NMR spectrum would be very different (see discussion on carotenoids).

Dienes and polyenes show a pronounced molecular ion in the mass spectra and hence the molecular weight of polyenes can be determined by positive ion mass spectra. The easy removal of a π-electron from a diene is usually the reason for the distinct $M^{\bullet+}$. The mass spectral investigation of conjugated polyenes is somewhat similar to that of aromatic structures, due to the high stability of the rearranged ions formed after the



(5)

first electron removal. This phenomenon will be discussed in more detail in the section devoted to carotenoids. For a general discussion on the mass spectrum (MS) of dienes, see Budzikiewicz and coworkers[7]. Since dienes and polyenes are highly sensitive to photodissociation this method was also employed in conjunction with MS[8] for the study of branched dienes.

III. SEPARATION AND CHROMATOGRAPHY OF DIENES AND POLYENES

Chemical separation of conjugated dienes and other polyunsaturated hydrocarbons is based on the availability of π delocalized electrons. The use of a strong dienophile (e.g. tetracyanoethylene, TCNE) will derivatize only conjugated dienes, thus separating the polyunsaturated compounds into two groups. However, such derivatization is not always reversible since a retro-Diels–Alder reaction may require a high temperature. Hence, the retrieved compounds may be the thermostable ones and not those present in the initially analysed mixture.

Even simple dienes and polyenes are difficult to classify in comparison with alkenes. Whereas bromination, oxidation and reaction with tetranitromethane (TNM) can identify the number of double bonds and their location in the molecular structure, conjugated double bonds produce very complex mixtures. Furthermore, many of the tests based on π-complexation can also apply for aromatic moieties. An example is the TNM π-complex which is yellow with benzene and orange with naphthalene and the tests are therefore non-specific.

Basically, the chromatographic separation of dienes and polyenes is similar to that of alkenes. Both gas chromatography (GC) and liquid chromatography (LC or HPLC) can be employed. For low molecular weight, more volatile diene/GC is usually good enough. If a better separation is needed, this can be enhanced by Ag^{+}-π-complexation. HPLC is employed either for more polar derivatives of polyenes or for non-volatile high molecular weight compounds (see special discussion on carotenoids). The use of small particle size silver-nitrate-impregnated silica as stationary phase was adapted for HPLC separation of unsaturated hydrocarbons from petroleums and bitumens[9,10]. The same approach can be used in thin layer chromatography (TLC) to separate the unsaturated components (10% $AgNO_3$/silica gel w/w)[10].

We will discuss in some detail examples where various methods of separation, including chemical derivatization, were complemented by spectroscopic identification. However, even the use of the most advanced analytical methods frequently yields only partial

structure determination, and for more complex compounds comparison with a model compound is the only solution to *total* structure determination.

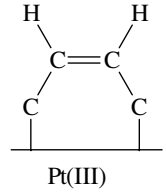
Higher molecular weight dienes and polyenes which are solid and can be crystallized make it possible to study their structure by X-ray diffraction. This, of course, will give information only about the crystalline form (see discussion on steroids and antifungal molecules, Section VII).

IV. THERMAL DESORPTION AND ELECTRON ENERGY LOSS SPECTROSCOPY

Structure determination of unsaturated compounds can be supplemented by thermal desorption (TD) and electron energy loss (EEL) spectroscopies. The two methods use the chemisorption of *cis* and *trans* enes or dienes to the Pt(111) surface over a range of temperatures[11]. The experimental equipment and procedures described[12] show these methods to be employed for dienes such as 1,3-butadiene. At very low temperature the diene is adsorbed on Pt(111) and the thermal desorption is followed by increasing the temperature.

Figure 2 shows a comparison of C_4 hydrocarbon desorption spectra of Pt(111) monitoring temperature and *m*/*z* of 2, 54, 56, 58 using a mass spectrometer. The TD spectrum for a monolayer of 1,3-butadiene is compared with 1-butene, *cis*-2-butene and *trans*-2-butene. Monitoring of the hydrogen thermal desorption shows that for the 1,3-diene no hydrocarbon desorption is recorded, but rather a destructive dehydrogenation of the diene. In the monoenes, up to 300 K one can see the release of *m*/*z* 56 ($C_4H_8^+$) followed at higher temperature by the release of hydrogen, whereas in the diene (Figure 2c) only H_2^+ (*m*/*z* 2) is monitored.

The electron energy loss spectra (EEL) in Figure 3 shows the IR vibrational difference of *cis* and *trans* alkenes up to 170 K, arising from different geometry of the two σ bonds between the metal and the double bond. At 300 K this difference is erased and both form C_4H_6, by loss of hydrogen[11]. The bond formed by the diene (1,3-butadiene) is shown to have the same vibrational properties. Hence, the authors conclude that the end product adsorbed is:



Pt(III)

V. MASS SPECTROMETRY

Simple dialkenes of general formula C_nH_{2n-2} produce a fragmentation pattern which depends upon the relative location of the two double bonds (Scheme 1). The nonconjugated dienes fragment corresponding to the respective allylic fission[13]. The nonconjugated dienes fragmentation pattern is dominated by β-cleavage and the formation of a $C_3H_6^+$ ion if rearrangement is possible (Scheme 1)[6]. The allylic fission[13] is not preferred in conjugated systems, hence the formation of the diene-ion which can be stabilized by cyclization. However, if one examines conjugated dienes and polyenes such as terpenes, the most abundant ion is the $[M - 1]^+$ base peak formed by loss of a single hydrogen atom. Apart from this ion the other abundant ions are the *m*/*z* 53 and *m*/*z* 39, formed by

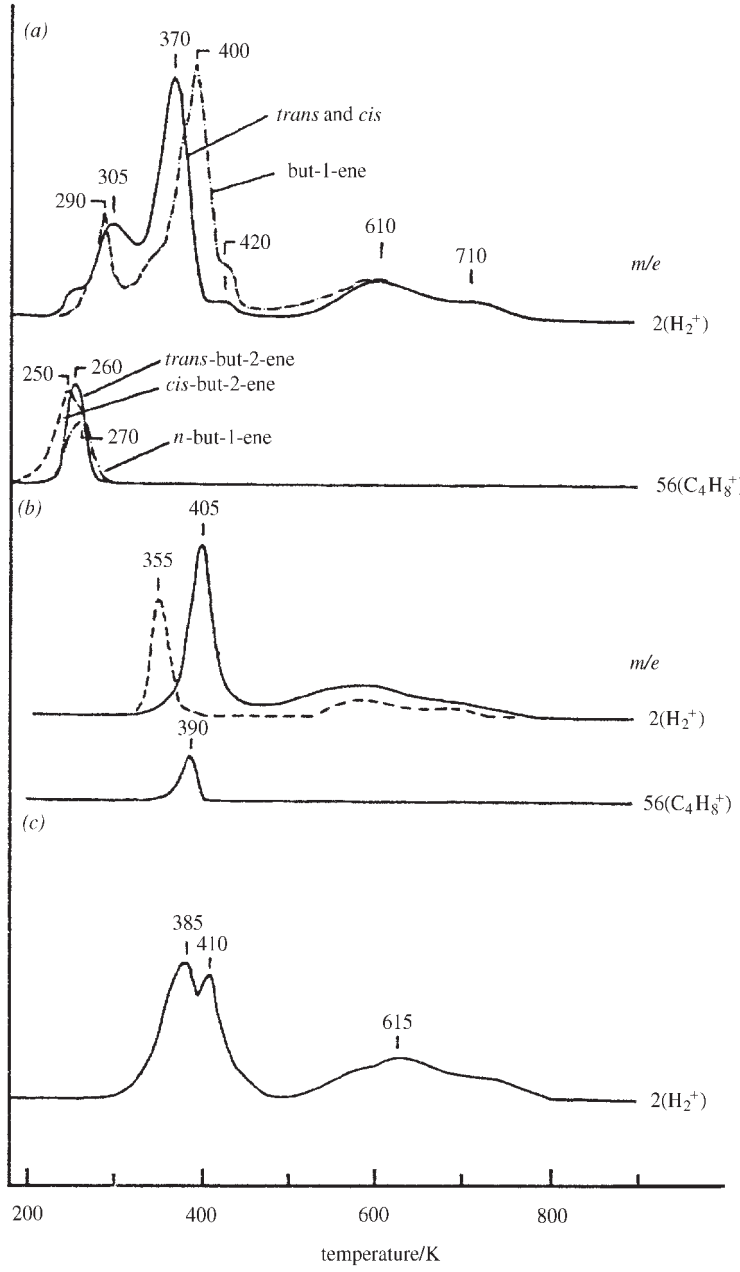


FIGURE 2. Thermal desorption spectra for monoenes and a diene C_4 hydrocarbon, chemisorbed on Pt(III). (a) *cis*-but-2-ene and *trans*-but-2-ene, (b) but-2-yne and (c) 1,3-butadiene. $\theta = 1$ (full line) $\beta = 3\text{KS}^{-1}$ for all. The monitoring of m/z 2, 54, 56, 58 was done by MS (see Avery and Sheppard[11] and references cited therein)

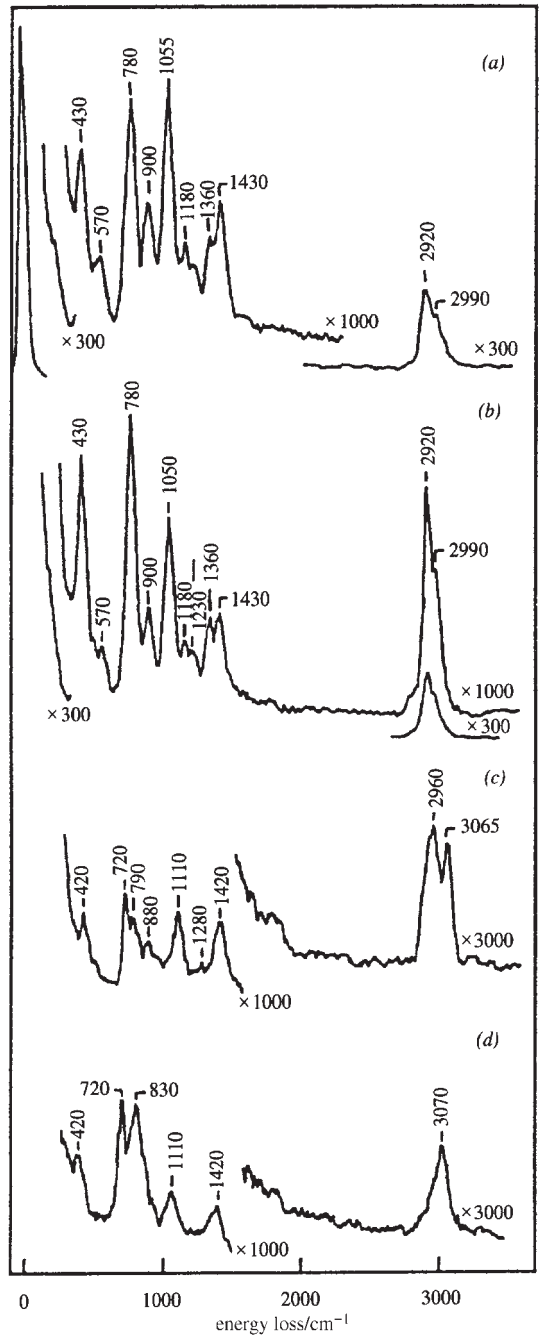
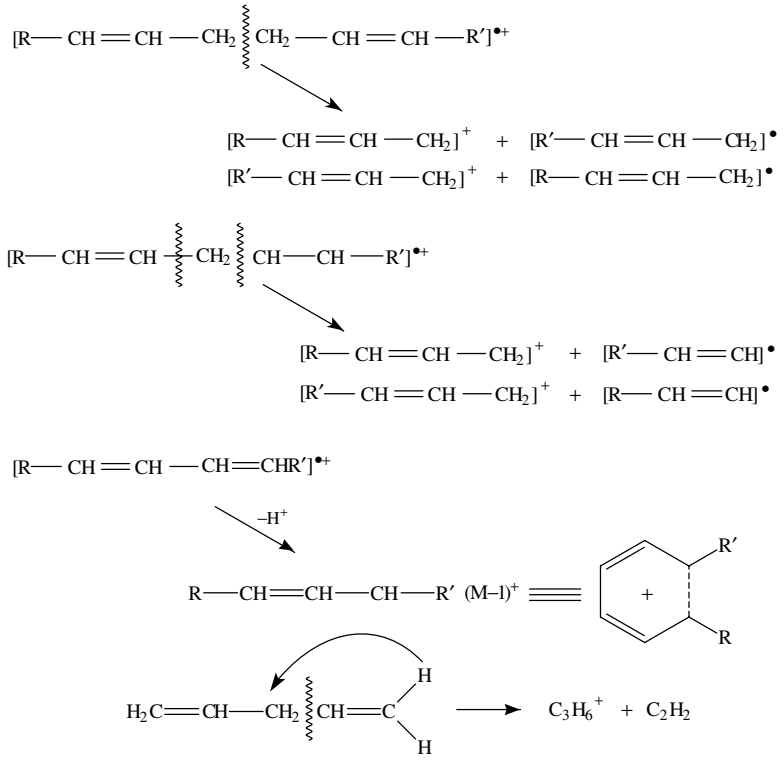
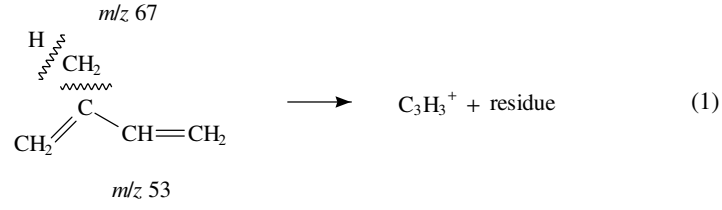


FIGURE 3. Electron energy loss spectra from 1,3-butadiene, chemisorbed on Pt(III) at (a) 170 K, (b) 300 K, (c) 385 K and (d) 450 K[11]



SCHEME 1

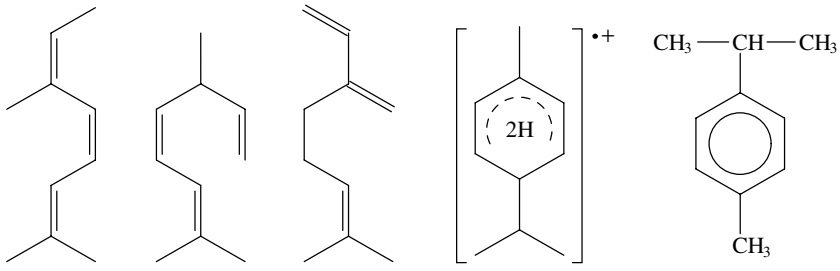
the cleavage shown in equation 1.



(1)

The next conjugated triene of the isoprenoid structure is the *allo*-ocimene **(6)**. *β*-Ocimene **(7)** and myrcene **(8)** also have a triene moiety but only two of their double bonds are conjugated. Comparison of these three isomeric trienes gives insight into the manner in which the relative positions of the double bonds control the fragmentation (Figure 4). The obvious mass spectral differences show that conjugation yields a higher abundance of the M^+ (136) and the base peak of compound **6** is derived by the loss of a methyl group (*m/z* 121). These two ions are much less abundant for **7** and **8**, both showing *m/z* 93 as the most abundent signal whilst **8** shows also *m/z* 69[7].

Cyclic dienes of the terpene family are also very interesting. The MS of the $C_{10}H_{16}$ compounds are discussed extensively in Budzikiewicz and coworkers.[7]. All of them transform



(6) **(7)** **(8)** **(9)** *m/z* 136 **(10)** *m/z* 134

into the ion **9**, having a structure which is very similar to the ion formed from the aromatic cumene **(10)** but differing by 2 hydrogens (*m/z* 136 vs 134), see also compounds **11–14**.

The similarity of the MS spectra of isoterpinolene **(11)**, terpinolene **(12)**, α-terpinene **(13)** and the *allo*-ocimene **(7)** is striking. Whereas the hydrogen rearrangements suggested to explain this similarity might be speculative, they offer a reasonable explanation for the almost identical MS of the open and closed diene structures with that of the triene **(7)** spectrum.

The rupture of an allylic bond, followed by an energetically favoured hydrogen migration, leads to the linear, ionized conjugated triene **(14)**. The molecular ion of triene **14** is comparable to the compound **7** molecular ion[7].

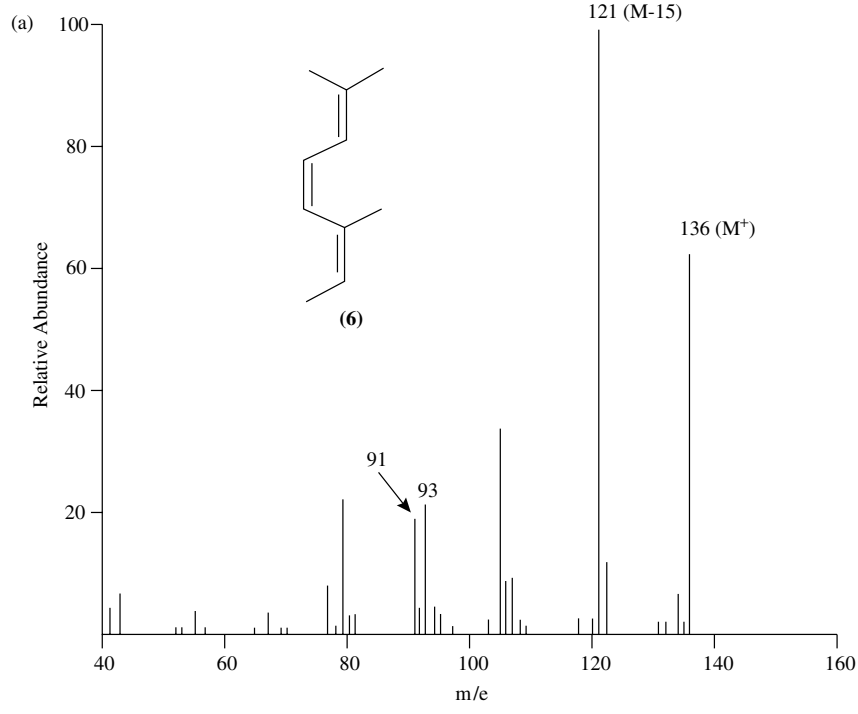


FIGURE 4. Mass spectra of (a) *allo*-ocimene **(6)**, (b) β-ocimene **(7)** and (c) myrcene **(8)**[7]

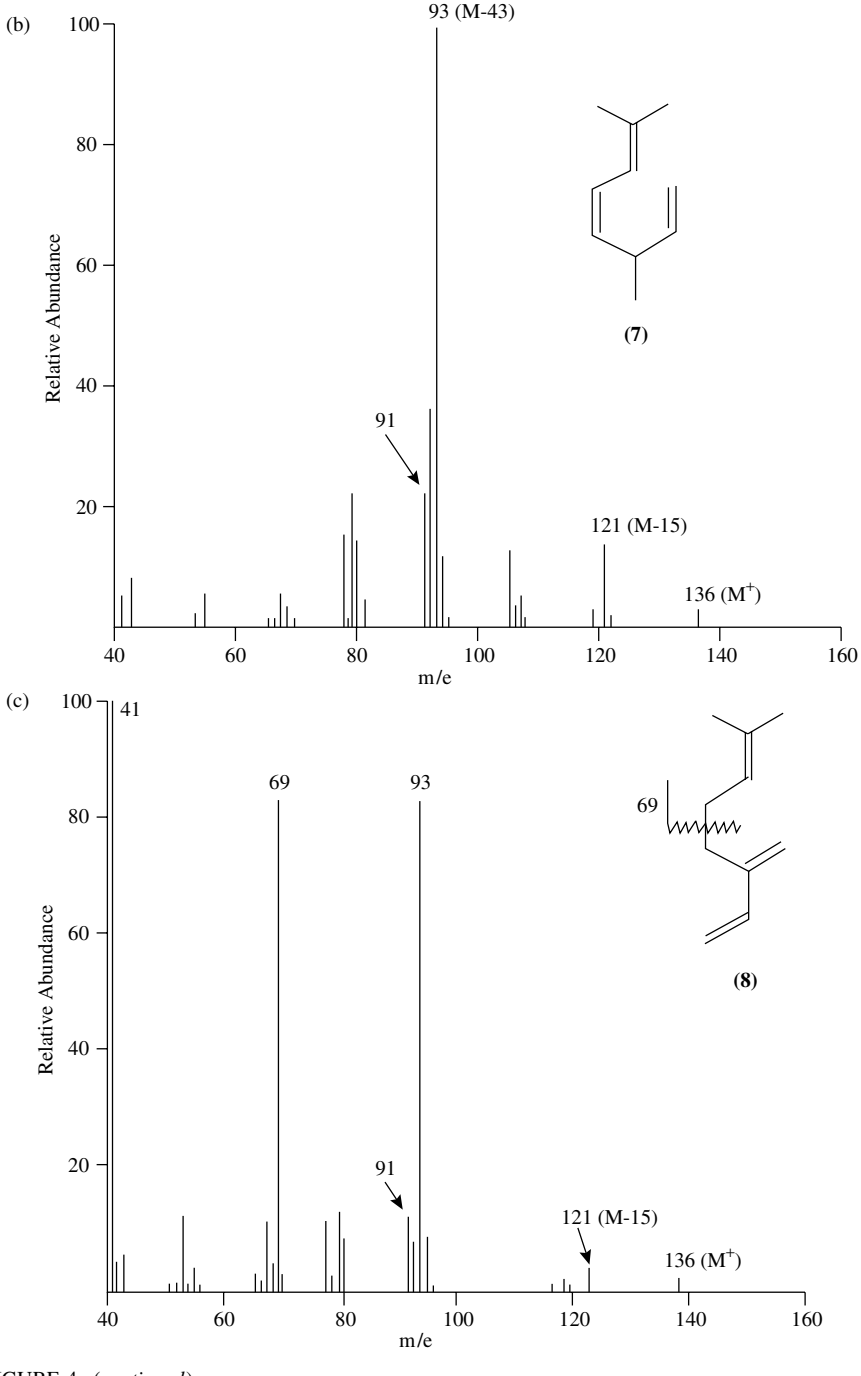
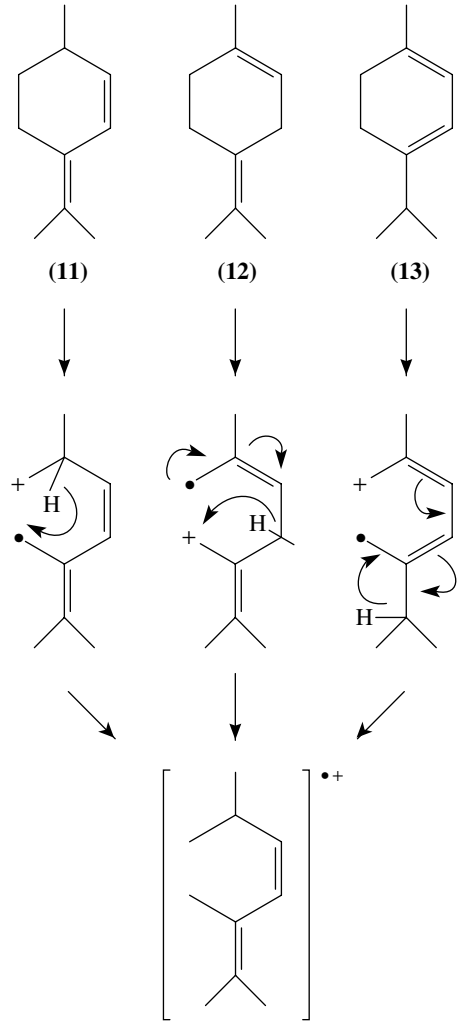


FIGURE 4. (*continued*)



(11) **(12)** **(13)**

(14)

Higher terpenes with diene and polyene moieties have also been investigated by mass spectrometry. However, we should be aware of the possibility that the molecular ion, such as that for $C_{30}H_{50}$ (C_nH_{2n-10}) at *m/z* 410, may indicate, e.g., 6 unsaturated bonds or 5 rings and only one ene unit. A comparison of the MS of squalene and an unknown compound 'X' with an *m/z* 410 molecular ion is shown in Figure 5. The large ionized fragments down to *m/z* 299 may indicate similarity of the spectra, but the base peak for compound 'X' at *m/z* 191 indicates a hopene structure[14]. The use of this *m/z* 191 fragment for the identification of the hopanes and hopenes was reviewed extensively by Aizenshtat[15].

Squalene is a unique natural product of a $C_{30}H_{50}$ structure with 6 non-conjugated double bonds. Hence, its MS shows a fragmentation pattern typical of non-conjugated

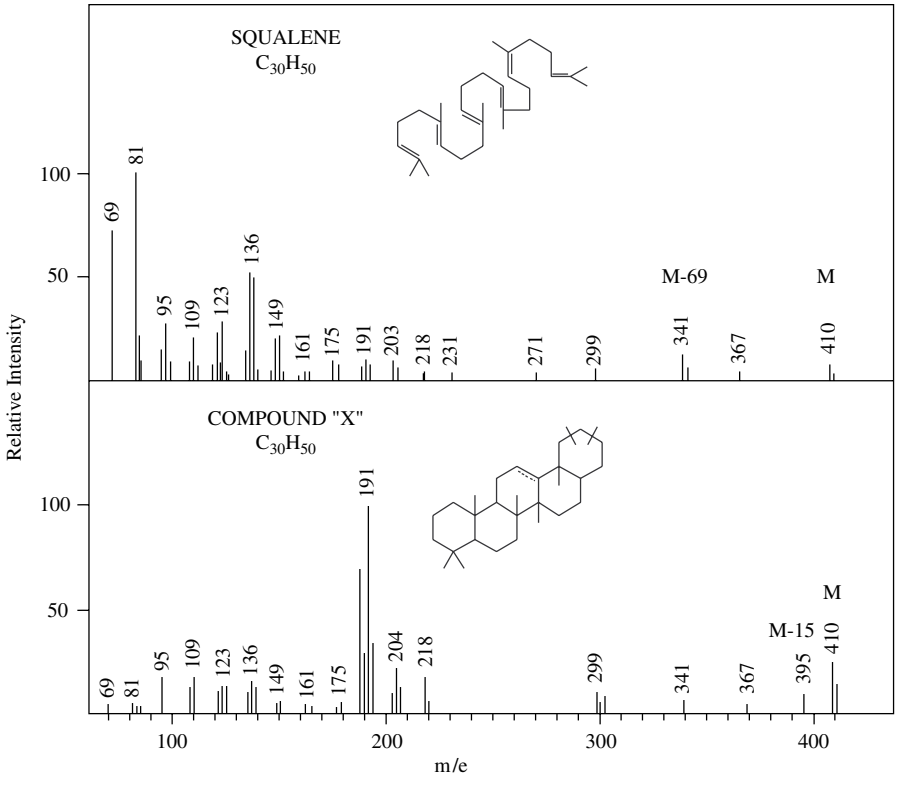


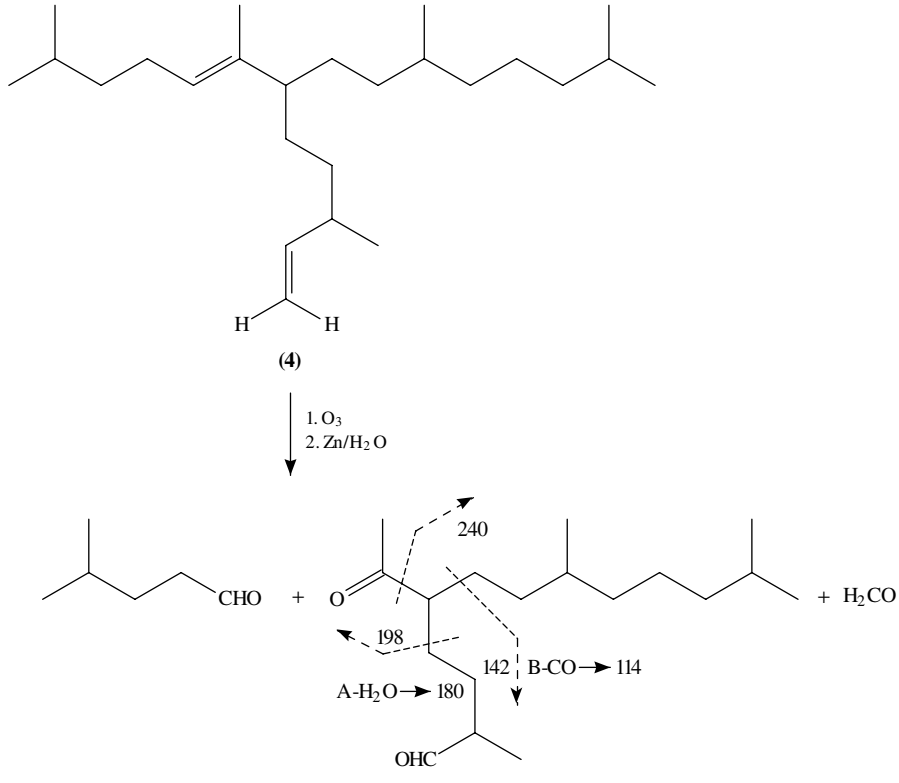
FIGURE 5. Mass spectra of two $C_{30}H_{50}$ isomers. Squalene and hopene (compound X) are isolated from a sedimentary organic matter[14,15]

various polyenes and the base peak at *m/z* 81 and the abundant next peak at *m/z* 136 resemble the spectra of the terpenes discussed previously.

Polyunsaturated (dienes and trienes) lipids found in sediments have been proven to be valuable tools in the determination of palaeo-water temperatures[6,16–18]. These C_{20}, C_{25} and C_{30} highly branched isoprenoids were investigated analytically by all the tools suggested in this review. We will select one diene to demonstrate the use of the MS, oxidation (bis-epoxidation) MS and ^{1}H NMR techniques previously discussed. This diene, 2,6,10,14-tetramethyl-7-(3-methylpent-4-enyl)pentadec-5-ene **(4)**, shows the fragmentation pattern given in Scheme 2.

Compound **4** was epoxidized to give **15** (Scheme 3) and the MS fragmentation of **15** is given by the broken-line *m/z* (relative abundance). To ensure the location of the double bonds, the epoxidation and the MS of **15** was compared with the products of the ozonolysis identified by GC and MS (as marked by the broken lines)[6]. The use of the various derivatization products via oxidation, combined with other spectroscopic methods, is discussed in Section III.

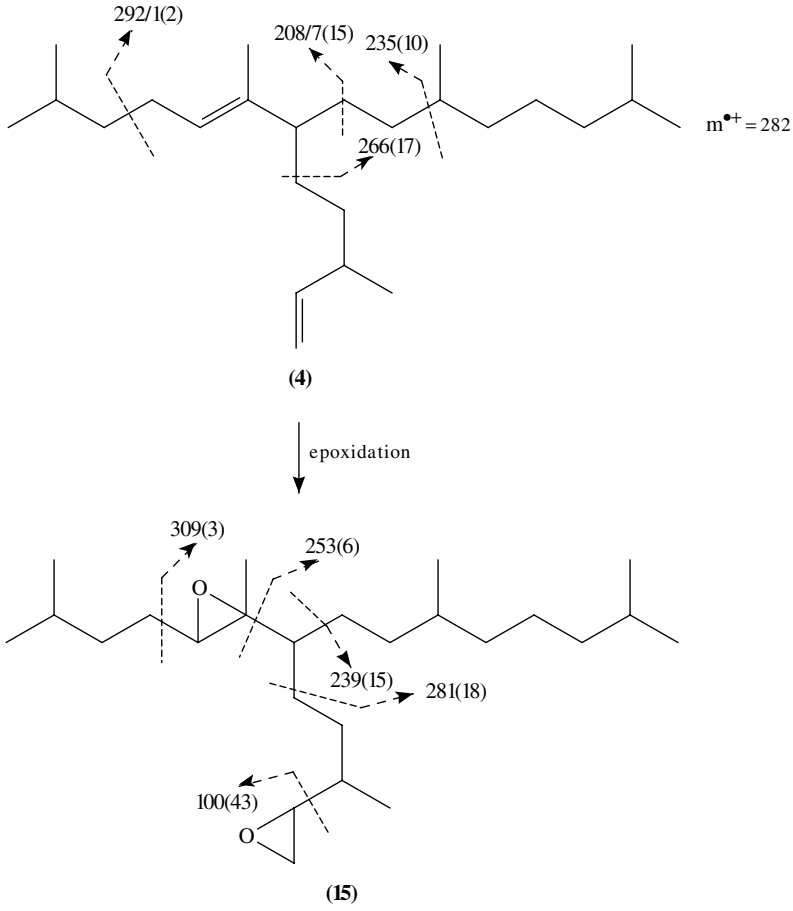
The MS studies of carotenoids have been reviewed previously[19–21]. Most carotenes show a molecular ion. Some carotenes with cyclic end moieties fragment to yield the tropylium ion (*m/z* 91) and some yield the *m/z* 105 xylene fragment. Specific deuteriation



SCHEME 2

of the carotenoid structure helps in the MS assignments and facilities the structure determination. We should bear in mind that some of the carotenoids, e.g. *Xanthomonas*, have oxygen functional groups such as ketones, ethers and phenols and hence they show a different MS fragmentation patterns[22]. The halogenated substituent of *Xanthomonas* polyenes was identified first by MS and the bromine isotopic pattern was characterized[23]. Many ionization methods have been attempted for the studies of carotenoids. Among these, electron impact (EI) was the simplest and only the field desorption technique yielded useful results up to 1990[24].

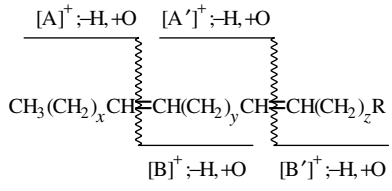
Chemical and other physical methods of ionization were also employed for the structural determination of dienes and polyenes. Such is the case for the recent investigation of aliphatic dienes and trienes by chemical ionization with nitric oxide (NO^+)[25]. It has been known since 1975 that olefins can be chemically ionized by NO^+ [CI(NO)][26]. Two distinct processes may apparently occur: (i) electrophilic addition of NO^+ to the ene leading to $[M + NO]^+$ ion and (ii) an oxidative cleavage (possibly catalysed by the surface) $R{-}CH{=}CH{-}R' \longrightarrow [RCO]^+$ and/or $[R'CO]^+$. Budzikiewicz and coworkers[25] do not have the answer as to which of the two processes dominate, but they have shown experimentally with a series of acetoxyalkadiene that both pathways (i) and (ii) depend on the reaction conditions. For alkadienes and a C_{10}-triene carboxylic acid the position of the double bond can be easily determined if it is in a terminal position C_1. However, if the double bonds are located somewhere in the middle of the carbon chain the ionization



SCHEME 3

by NO^+ yields an abundance of ions which make the determination of the location of the position quite difficult. Measurement of the chemical ionization (NO^+) spectra of the corresponding epoxides or collision activation studies can yield helpful data[25].

Scheme 4, which is discussed in detail elsewhere[25], is an example. If $y = 0$ we have a conjugated system; however, for $y = 1$ the β-cleavage leads to a m/z 83 for $x = 1$ $[CH_3CH_2CH{=}CH{-}C{\equiv}O]^+$. This fragment is not always detectable.



SCHEME 4

TABLE 1. Relative abundances[a] for PDPI/MS of hexadienes

Photoionization energy (eV)	Compound	Fragment (*m/z*)								
		CH_3 (15)	C_2H_3 (27)	C_2H_5 (29)	C_3H_3 (39)	C_3H_5 (41)	C_4H_7 (55)	C_5H_5 (65)	C_5H_6 (66)	C_5H_7 (67)
10.49	Hexa-1,3-diene	27	6	1	30	19	—[b]	12	100	12[c]
	Hexa-1,4-diene	24	48	24	100	41	20	11	89	—[d]
	Hexa-1,5-diene	—[b]	—[b]	—[b]	100	77	—[b]	—[b]	—[b]	—[b]
	Hexa-2,4-diene	18	6	2	24	23	1	12	100	8[c]
9.68	Hexa-1,3-diene	2	2	1	9	14	1	10	100	12
	Hexa-1,4-diene	2	3	11	38	55	28	16	100	4c
	Hexa-1,5-diene	—[b]	—[b]	—[b]	32	100	—[b]	—[b]	—[b]	—[b]
	Hexa-2,4-diene	4	3	1	12	22	2	14	100	19

[a]Relative to the most intense photo-dissociation peak; ionic fragmentation of the parent molecule is not included.
[b]No peak observed; species is typically in less than 1–5% abundance.
[c]Corrected for photo-ionization background.
[d]All signals observed are from photo-ionization background.

In Section I the sensitivity of conjugated systems to possible photo-dissociation (PD) was mentioned. If this PD is conducted in the ionization chamber of a mass spectrometer, a PDPI/MS (photo-dissociation, photo-ionization/mass spectrometry) can be measured[7]. The examination of the PDPI/MS spectra of hexa-1,3-, 1,4-, 1,5- and 2,4-dienes using 9.68 and 10.49 eV photo-ionization (PI) is summarized in Table 1.

The fragments formed CH_3 (*m/z* 15) up to C_5H_7 (*m/z* 67), are recorded by the MS and are semi-quantified. Since the photo-ionization leads first to β-cleavage, the 1,3-diene leads to $CH_3^{\bullet}$ and $C_5H_7^{\bullet}$; however, the ionization of the methyl radical is recorded only at 10.49 eV. Table 1 does not record the ionic parent molecule and fragmentation. It is seen that the data can be used to locate the double bonds of the diene. Whereas the β-cleavage is the dominant PDPI/MS, rearrangement of fragments may also occur[27].

VI. CHEMICAL DERIVATIZATIONS

To support the various spectroscopic methods for structure determination of dienes and polyenes we will mention some typical chemical reactions yielding derivatives that aid in the location of the double bonds, assign the *cis* or *trans* geometry and indicate whether these double bonds are conjugated. It is not our intention to review the chemical versatility of dienes and polyenes but rather to show some cases where the variation helps in the analysis.

Most methods used for analysis of alkenes, such as bromination and hydrogenation, can be employed to determine the number of double bonds in polyenes. These methods were also employed to classify various petroleums ('bromine number'). However, these classical methods are employed less in analysis of conjugated dienes and polyenes mostly because the products produce a less informative mixture than in the alkene case.

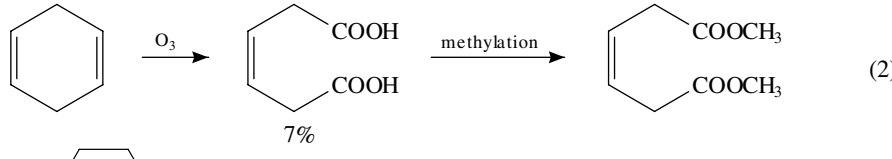
Neumann and Khenkin[28] review most of the various oxidation methods of dienes and polyenes and their mechanisms. They obviously emphasize the difference between non-conjugated and conjugated dienes and polyenes in selected oxidation reactions.

Conjugated dienes and polyenes lead to unique cases of conjugated oxidations, such as the formation of endoperoxide by singlet oxygen attack on the *endo*-diene, e.g. α-terpinene[29].

For analysis of dienes and polyenes via oxidations one has to distinguish between the formation of an oxidized product of the target molecule (epoxide, peroxide, ozonide etc.) and the oxidative fragmentation of the molecule as in the case of ozonolysis[30]. Both

approaches have been extensively reviewed, but mostly for mono-enes or for cases of independent/non-conjugated dienes and polyenes. Examination of the use of oxidative ozonolysis of natural rubber (polyene) and synthetic polyene polymers shows possible structure determination by GC analysis of the methyl esters of the acids formed (FAME method)[30,31].

The use of both 'ozonation' and 'ozonolysis' is reviewed[32]. 'Ozonation' leads to ozonide and 'ozonolysis' leads to oxidized fragments, showing the use of both oxidative ($AgNO_3$) or reductive [$(CH_3)_2S$ or Ph_3P] methods to produce the FAME (fatty acids methyl esters) that by subsequent GC analysis enabled determination of the position of the double bonds in the original molecule (equations 2–4).



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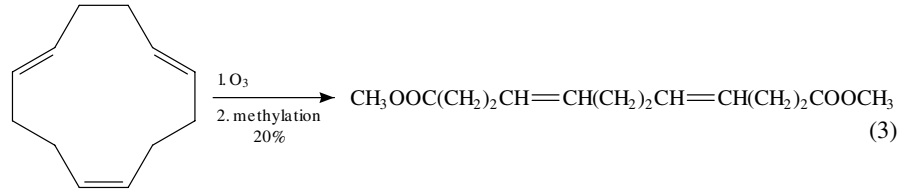

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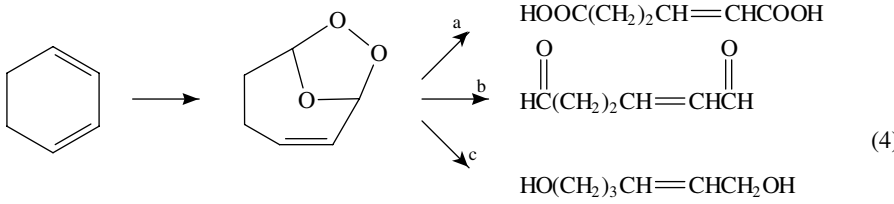


(4)

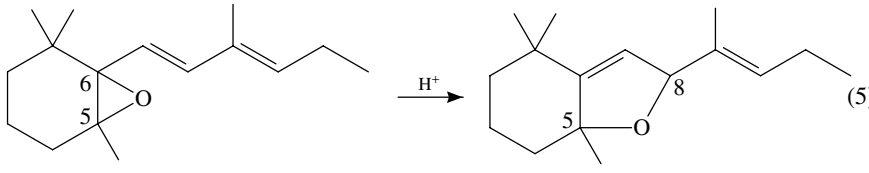
a = Ag_2O
b = $Ba(OH)_2$/Acetone
c = $NaBH_4$

The selectivity of the ozone reaction facilitates differentiation between conjugated bonds and isolated double bonds. Conjugated dienes form mono ozonide, which was claimed to inhibit reaction at the second double bond[33]. Hence, the yield of ozonolysis of one bond is much higher in 1,3-cyclohexadiene than in 1,4-cyclohexadiene and the same was found for other conjugated dienes[33]. Since the end products of the ozonolysis depend on the secondary treatment by the oxidation agents (Ag_2O, H_2O_2, SeO_2 etc.) or reducing agents [$(CH_3)_2S$, $NaBH_4$, H_2/Pd-$CaCO_3$-PbO etc.], the chromatographic or spectroscopic identification must take into consideration the type of product.

A very important point to remember when using ozonolysis for structural investigation of polyenes is that the transoid bond is attacked preferentially[34]. Hence, the advantage of the ozonolysis in polymeric matter is obvious: the fragments formed are easier to analyse and they are also indicative of the double-bond positions (see Schemes 1 and 2).

In principle, all of the methods for selective oxidations of di- and polyenes[28] can be employed for analytical derivatization. However, the complexity of products obtained rules out some of these. Despite this, epoxidation of selected double bonds is used for comparison of spectra (see previous discussion on MS). Epoxidation of isolated non-conjugated

double bonds is carried out mostly by peracids[32]. In recent works it is reported that metal oxides can catalyze hydrogen peroxide oxidation to form epoxides[35]. The bulk of the available information relates to epoxidation of non-conjugated double bonds. Some examples of the use of *tert*-butylhydroperoxide (TBHP) show that epoxidation increases with the increased nucleophilicity of the double bond and some spatial consideration must also control the regioselectivity. Conjugated dienes react slower and stepwise[36]. In carotenoids an 'epoxide' test was developed. The naturally occurring 5,6-epoxide **(16)** isomerizes under acidic catalysis to the 5,8-ether **(17)** leading to hypsochromic shift in the visible spectrum of the carotenoid[50] (equation 5). This is a very interesting rearrangement that may indicate why epoxidation of conjugated polyenes yields a complex mixture. Therefore, it is recommended to use the epoxidation mostly in cases of non-conjugated dienes and polyenes.

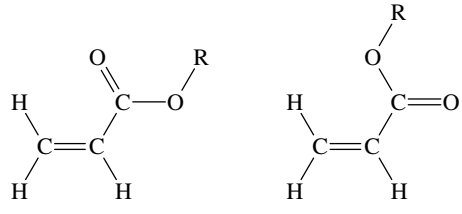


(5)

(16) **(17)**

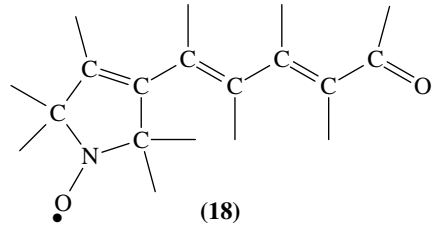
In general, one can use a variety of oxidation techniques to form derivatives of dienes and higher polyenes for their analysis; however, the information obtained with conjugated systems is muddled by the complexity of products. Also, it is obvious that since the oxidized derivatives contain different functionalities, e.g. epoxides, alcohols, acids etc., the analytical techniques employed should also be variable (see also Scheme 2).

Whereas the classical reactions of dienes and polyenes are described in textbooks and in the present volume, some unique derivatives were suggested for structure elucidation. Such is the case with the synthesis of conjugated polyene carbonyl derivatives of the nitroxide spin-label 2,2,5,5-tetramethyl-1-oxypyrroline[37]. In particular, the exact conformation of an oxygen-containing functional group, such as that shown below, cannot be assigned by NMR. Conformational analyses have been carried out with the aim of understanding *cis–trans* isomerization of the retinal[38] and other biochemically interesting aldehydes, acids and esters with long conjugated unsaturated systems. These analyses included dipole moment measurements[39], IR and microwave spectroscopy[40], NMR[41] and theoretical calculations. These techniques were found to possess insufficient sensitivity to assign precise molecular structures, in solution. In particular, even advanced ^{1}H and ^{13}C NMR methods cannot assign the protons of the s-*cis* and s-*trans*, and hence the exact conformation of the oxygen-containing functional group forms below.



s-*cis* s-*trans*

An example is the structure of the derivative **18** formed by reacting the labelled oxypyrrolinyl with 2,4-pentadienal.



(18)

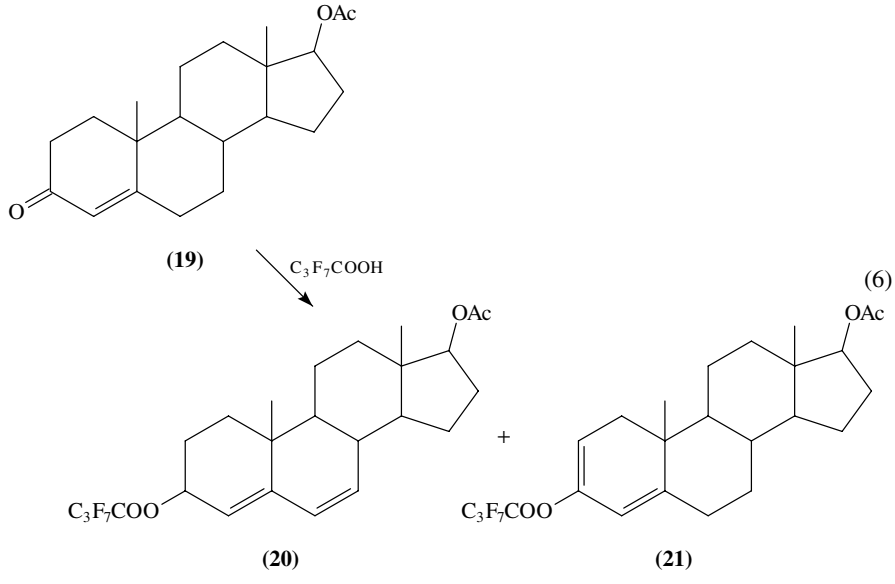
As most of the nitroxyl spin-labelled synthetic derivatives of conjugated polyenes are light yellow crystals, the bond lengths were determined by X-ray crystallography[38]. The spectroscopic method used to measure the conformation is electron nuclear double resonance (ENDOR). It is beyond the scope of the present review to explain the method[38] but the authors of the pertinent paper conclude that ENDOR is an accurate non-crystallographic method to determine polyene structures in solution.

Some derivatization methods mentioned in other sections of this review include chemical ionization by nitric oxide (MS) or epoxidation (MS), formation of π-complexes for NMR (shift agents) etc. Also, the Diels–Alder reaction, which was mentioned several times as a tool for derivatization of conjugated dienes and polyenes, was extensively described and reviewed in the literature.

VII. SELECTED EXAMPLES OF MULTI-PARAMETER ANALYSIS FOR DIENES AND POLYENES: STRUCTURE DETERMINATION

A. Enolic Dienes Derived from Testosterone-17β-acetate

Enolization of α,β-unsaturated ketones, e.g. **19**, under strong acid conditions leads to a mixture of homoannular and heteroannular $\Delta^{2,4}$- and $\Delta^{4,6}$-dienes (e.g. **20** and **21**; see equation 6)[42].



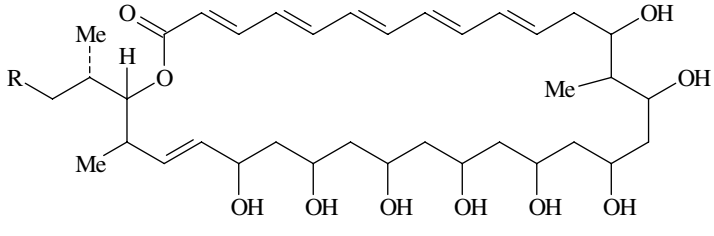
(19) **(20)** **(21)** (6)

The heteroannular diene is thermodynamically more stable and the UV spectra of the two dienes differ, as suggested by Woodward and Fieser's rules[5].

The heptafluorobutyrate derivative was selected for gas chromatographic separation, using electron capture detector (ECD), in order to enable the detection of ultramicro quantities[43]. The interest in the analysis of natural and synthetic hormones in very small concentrations enhanced the development of the GC method, in comparison with the UV study.[44]

B. Antiviral and Antifungal Mycoticin (A and B) Partial Structure Determination

The natural products Mycoticin A (**22**, R = H) and B (**22**, R = Me) belong to the skipped-polyol-polyene class of antibiotics. Our analytical interest here is to use this very complex molecular structure to demonstrate some of the tools employed, mainly for the elucidation of the polyene part of the molecule. This family of 'polyene macrolide class' was discovered in 1950[45] with the finding of Nystatin **(23)**, which is produced by the *Streptomyces* bacteria. The exact structure was elucidated only in 1970 by Chong and Rickards[46] and, in 1971, Nystatin A_1 **(23)** and A_2 (not shown in this review) were separated.



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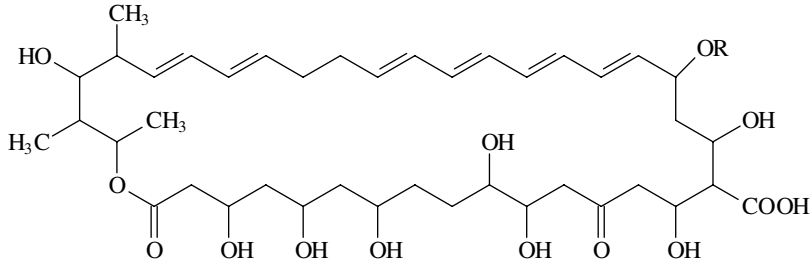
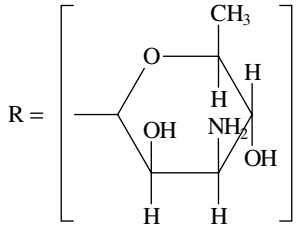


(23)



Mystatin is a light-yellow optically active solid (d.p. > 160 °C) with UV λ_{max} 290, 307, 322 nm. Many of the polyene mycolides (e.g. Amphotericin B) are yellow solids with a similar conjugated transoid (5 to 7 double bonds) system, claimed to be derived, by structure similarity, from α-prinarate $CH_3CH_2(CH{=}CH)_4(CH_2)_7COOCH_3$. Some 200 members of this family were isolated and the structures of 40 of them were elucidated. Up to 1987 the only claim for full stereochemical elucidation by various techniques was for Amphotericin B[47]. Despite the fact that most of these compounds are solids, not all of them could be determined structurally by X-ray crystallographic methods and this includes the structures of Mycoticin A, B and derivatives[47]. Hence, other chemical and spectrocopical methods had to be employed. For spectroscopic measurements the free OH-groups were formylated, and the tetraformyl derivative exhibited well-resolved signals in the ^{1}H NMR and ^{13}C NMR spectra[48]. For this derivative use of the 2D COSY NMR and NOE techniques enabled a better assignment of non-equivalent hydrogens. The polyene part showed the all-*trans* stereochemistry. Ozonolysis of the tetraacetonide derivative **(24)** followed by $NaBH_4$ reduction provided three, readily separable products **25–27** (see Scheme 5)[48] whereas the polyene conjugated system is totally oxidized to small water-soluble acids.

VIII. ANALYSIS OF CAROTENOIDS AS AN EXAMPLE OF POLYENE STUDIES

This section is based on a review written in 1985 by Liaaen-Jensen and Andrewes[49] and a book on Natural Products by Ikan[50]. Both reviews cover some 200 references and discuss the various isolation and identification methods at length. It is therefore redundant to repeat the information presented in them.

Nevertheless, during inspection of the above-mentioned reviews and many of the works cited therein, many excellent analytical methods which can be applied to other polyene molecules were found.

Since the recognition of the carotenoid family of pigments, approximately 500–600 naturally occurring members of the various families were recognized. The C_{40} skeleton of 8 isoprenoid units (tetraterpenoid) allows endless combinations with various positions carrying substituted groups such as alcohols, ketones, acids and others. The characteristic property which makes the carotenoids natural pigments is the long polyene conjugated systems. Carotenoids are found in almost all photosynthesizing biota from quite primitive bacteria to fruits and high plants. Because of their natural source many food manufacturers use carotenoids as food colors, hence the commercial interest.

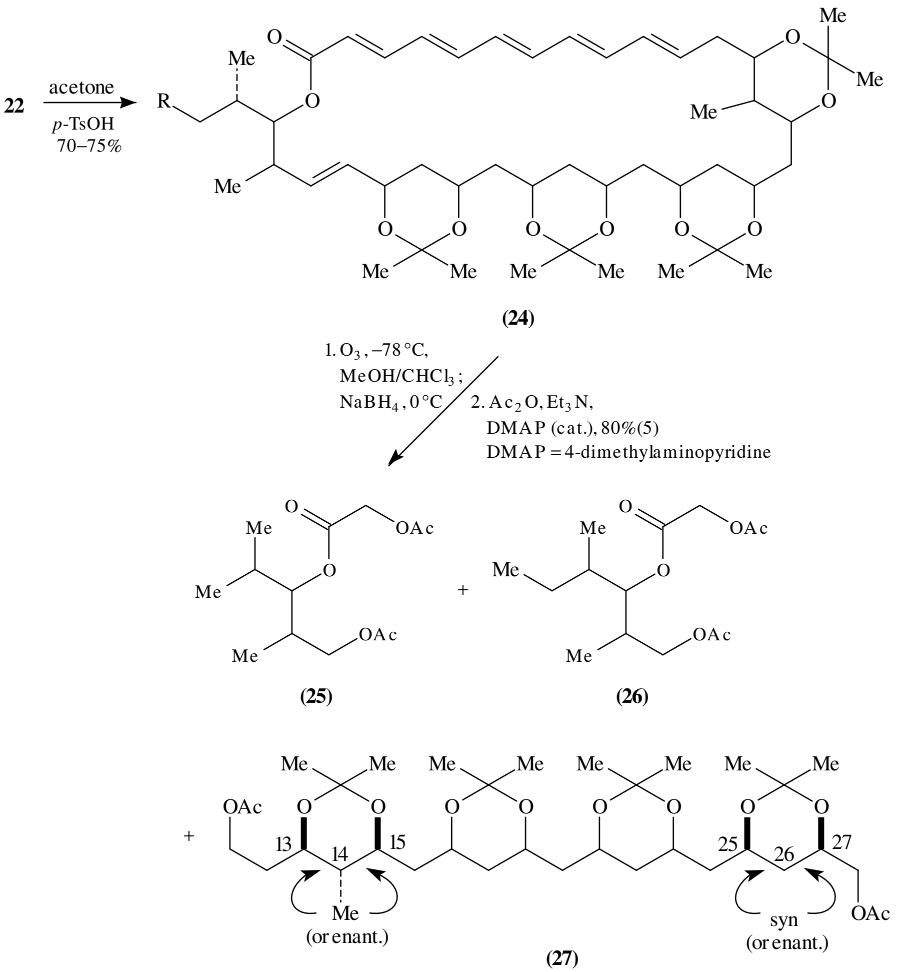
Ikan's book on laboratory techniques[50] concentrates on the origin and isolation procedures of carotenoids. The spectra given (IR, UV-VIS and NMR, MS) help also to classify the various carotenoids. The longest open conjugated system (no rings) is found in lycopene, **28**, which contains 11 conjugated and 2 non-conjugated double bonds, has an all-*trans* geometry and possesses a very intensive red colour (λ_{max}^{EtOH} 443, 472, 504 nm). This 536-dalton molecular weight ($C_{40}H_{56}$) polyene is analysed well by MS with most abundant fragments appearing at *m/z* 145, 119, 105, 93, 91, 86, 69 (base peak), 41 as shown below. The ^{1}H NMR and ^{13}C NMR assignments for the hydrogens and carbons double bond are as follows:

^{13}C NMR (in $CDCl_3$) in ppm

C-1 131.64; C-2 124.12; C-3 26.83; C-4 40.30; C-5 139.30; C-6 125.94; C-7 124.87; C-8 135.54; C-9 136.15; C-10 131.64; C-11 125.21; C-12 137.46; C-13 136.54; C-14 132.71; C-15 130.17; C-16 25.66; C-17 17.70; C-18 16.97; C-19 12.90; C-20 12.81.

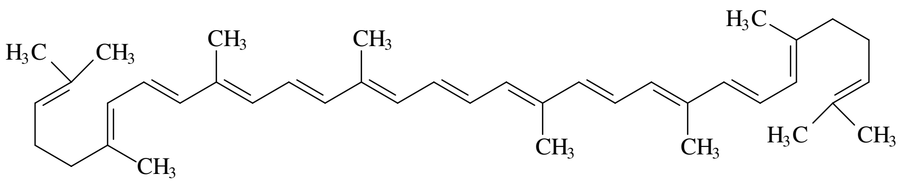
^{1}H NMR (in $CDCl_3$) in ppm

H-2 δ5.11; H-3/H-4 2.11; H-6 5.95; H-7 6.49; H-8 6.25; H-10 6.19; H-11 6.64; H-12 6.35; H-14 6.23; H-15 6.63.



(24) **(25)** **(26)** **(27)**

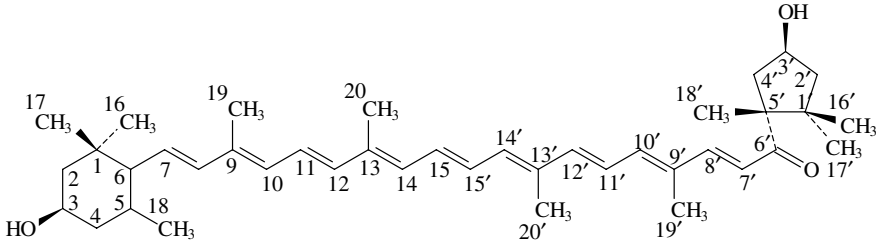
SCHEME 5



(28)

Mass spectrum
m/z 536 (21.7%, M), 145 (38%), 119 (34%), 105 (47%), 93 (36%), 91 (47%), 81 (36%), 69 (100%), 41 (57%).
λ_{max}^{EtOH} 443, 472, ($\varepsilon = 3.10^5$) 504 nm.

For comparison the ^{1}H and ^{13}C NMR spectra, the mass spectral fragments and the UV-VIS spectrum of Capsantin, **29** (the red colour of paprika), are as follows:



(29)

^{1}H NMR (in $CDCl_3$) in ppm

0.840[s,3H, Me (16′)], 1.075[s, 6H, Me(16), Me(17)], 1.207[s, 3H, Me(17′)], 1.367[s, 3H, Me(18′)], 1.736[s, 3H, Me(18)], 1.957[s, 3H, Me(19′)], 1.974[s, 6H, Me(19), Me(20)], 1.989[s, 3H, Me(20′)], 2.39[ddd, J = 17.6, *ca* 1.5, 1H, Hα–C(4)], 2.96[dd, J = 15.5, 9, 1H, Hα–C(4′)], *ca* 4.00[br, m, 1H, Hα–C (3)], 4.52[m, 1H, Hα–C(3′)], 6.13[s, 2H, H-C(7), H-C(8)], 6.16[d, J = 11.6, 1H, H-C(10)], 6.26[d, J = 11; 1H, H-C(14)], 6.35[d, J = 11, *ca* 1H, H-C(14′)], 6.36[d, J = 15, 1H, H-C(12)], 6.45[d, J = 15, 1H, H-C(7′)], 6.52[d, J = 15, 1H, H-C(12′)], 6.55[d, J = 11, 1H, H-C(10′)], *ca* 6.6–6.8[m, 4H, H-C(11), H-C(11′), H-C(15); H-C(15′)], 7.33[d, J = 15, 1H, H-C(8′)].

^{13}C NMR (in $CDCl_3$) in ppm

12.75[C(19)], 12.79[C(20)], 12.84[C(19′)], 12.90[C(20′)], 21.39[C(18′)], 21.63[C(18)], 25.16[C(17′)], 25.95[C(16′)], 28.80[C(16)], 30.32[C(17)], 42.69[C(4)], 44.01[C(1′)], 45.49[C(4′)], 48.61[C(2)], 51.06[C(2′)], 59.01[C(5′)], 65.41[C(3)], 70.44[C(3′)], 121.04[C (7′)], 124.13[C(11′)], 125.58[C(11)], 125.93[C(7)], 126.30[C(5)], 129.74[C(15′)]; 131.27[C(10)], 131.68[C(15′)], 132.39[C(14)], 133.69[C(9′)]; 135.24[C(14′)]; 135.93[C (13′)], 137.46[C(12)], 137.60[C(13)], 137.85[C(6)], 138.51[C(8)], 140.63[C(10′)], 141.97[C(12′)], 146.86[C(8′)], 202.82[C(6′)].

Mass spectrum

m/z 584 (75%, M), 478 (62%), 429 (6%), 145 (51%), 127 (36%), 109 (100%), 106 (31%), 105 (44%), 91 (65%), 83 (56%).

$\lambda_{max}^{benzene}$ 486 ($\varepsilon = 1.2 \times 10^5$), 520 nm.

All polyenes are susceptible to changes under various chemical conditions: oxygen, peroxides, light, acids and elevated temperature, etc. Therefore, one should bear in mind that carotenoid separation must be very carefully planned. Various extractions and liquid chromatographies are offered[51] with special separation by partition between immiscible solvent systems. Another problem caused during separation is a geometrical isomerization usually in the *cis* ⟶ *trans* direction. During the 1950s column chromatography was exclusively used, whereas since then TLC and PTLC (Preparative Thin Layer Chromatography) are employed[51]. HPLC (High Performance LC), both reversed phase and on regular silica (>5 μ), are used with various UV-VIS detectors (see Section III).

The carotenoids exhibit very high ε values of 10^5–3×10^5 and hence very small quantities can be detected. Due to the high molecular weights of carotenoids and other polyenes GC can be employed only with the perhydrogenated compounds[15] due to the high temperatures needed[52].

Although ^{1}H NMR and ^{13}C NMR spectroscopy of dienes and polyenes is discussed elsewhere, these tools of analysis are very nicely demonstrated in the studies of carotenoids.

The advancement of >400 MHz NMR instruments with spin decoupling and Fourier transform software now allows identification of individual olefinic protons of nanogram carotenoids[53]. We have shown two examples (lycopene and capsantin) for which the chemical shifts have been employed in the assignment of relative configuration[49]. As for review of the ^{13}C NMR of carotenoids, Englert in 1981[54] gave information especially on the position of the *cis* double bonds in a polyene chain.

The fragmented ions are stabilized in aromatic structures and therefore their formation may be misleading. However, some carotenoids do have aromatic moieties (e.g. flexirulein and some of the xanthomonadins). Therefore, if we examine the MS of capsanthin (see above) we see the base peak at *m/z* 109 (C_7H_9O or C_8H_{13}) next in abundance to the molecular peak (75%) at *m/z* 584 and the tropylium ion $C_7H_7^+$ (65%) at *m/z* 91. It is interesting that although lycopene has no ring structures it exhibits an *m/z* 91 fragment as a very strong peak. It is therefore very helpful to check for the presence of other functional groups such as OH, CO, etc. by IR spectroscopy.

The carotenoid family have chiral centres which enable the use of circular dichroism. However, the chirality of carotenoids is not sufficiently characteristic so that the chiroptical properties do not serve as a good analytical tool.

Various chemical derivatizations of natural carotenoids may serve to improve separation and lead to better characterization of structure. These methods are discussed in Section VI.

IX. ACKNOWLEDGEMENTS

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The Chemistry of Dienes and Polyenes. Volume 1
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CHAPTER **11**

Intramolecular cyclization of dienes and polyenes

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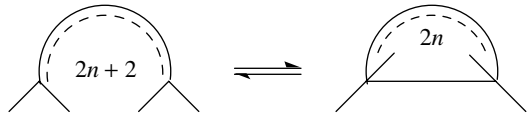
I. INTRODUCTION

This chapter deals with thermal ring-closure reactions of dienes and polyenes resulting in carbocyclic compounds; the formation of heterocycles is mentioned only occasionally. The account is highly selective, concentrating on recent work, since two comprehensive general reviews have appeared[1,2]. Other pertinent reviews are cited at appropriate places in the text.

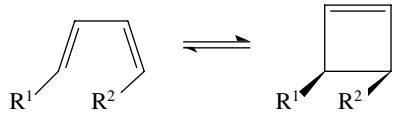
II. ELECTROCYCLIC REACTIONS

The cyclization of fully conjugated polyenes containing $2n + 2$ π-electrons (equation 1) was termed 'electrocyclic' by Woodward and Hoffmann, who showed that the steric course of such reactions was governed by the rules of orbital symmetry[3].



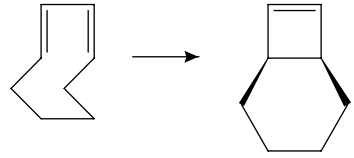
(1)

The thermal ring-closure of butadienes to cyclobutenes proceeds in a conrotatory fashion (equation 2) but this reaction is only observed in special cases because, in general, the equilibrium lies on the side of the open-chain isomer.



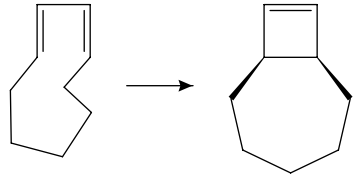
(2)

The strained *cis,trans*-1,3-cyclooctadiene **1** cyclizes quantitatively at 80 °C to the bicyclo[4.2.0]octene **2** (equation 3). The higher homologue **3** exists in equilibrium with the bicyclic isomer **4** above 175 °C (equation 4)[4].



(1) (2)

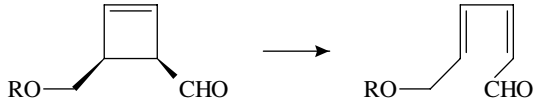
(3)



(3) (4)

(4)

Ring-opening of cyclobutenes to butadienes is very common; a recent example is the formation of the aldehyde **6** in greater than 97% diastereomeric purity from the cyclobutene **5** (R = 4-methoxybenzyl) above −78 °C (equation 5)[5].

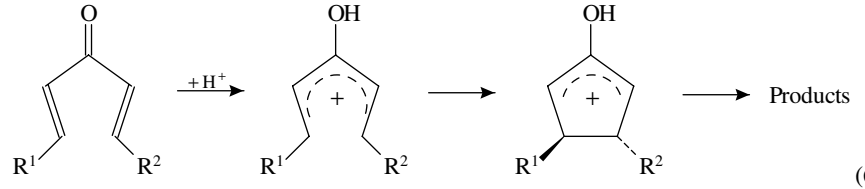


(5) (6)

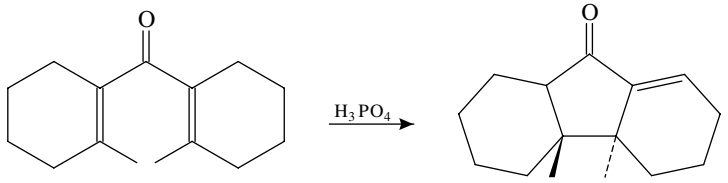
(5)

The acid-catalysed ring-closure of divinyl ketones to cyclopentenones (equation 6), the Nazarov reaction[6–8], represents a conrotatory electrocyclization of 4π-cyclopentadienyl cations. The conrotatory course of the reaction was confirmed for the case of the dicyclohexenyl ketone **7**, which yielded solely the tricyclic ketone **8** on treatment with phosphoric acid (equation 7)[3b]. Cycloalkanocyclopentenones **10** with *cis*-fused rings are obtained from the trimethylsilyl-substituted ketones **9** (n = 1, 2 or 3) and iron(III) chloride and

subsequent aqueous work-up (equation 8). In the cyclization of the cyclopentene derivatives **11**, the silyl moiety exerts a remote stereocontrol: the isomers **12** and **13** are formed in the ratios 54:46, 62:38, 76:24 and 79:21 as the silyl group varies from $SiMe_3$ to $SiMePh_2$, $SiPh_3$ and $Si(Pr\text{-}i)_3$ (equation 9)[9].

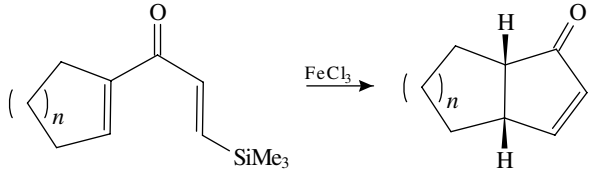


(6)



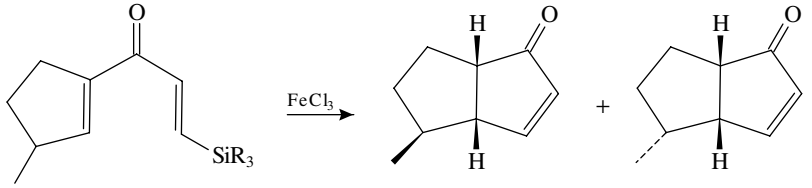
(7)

(7) **(8)**



(8)

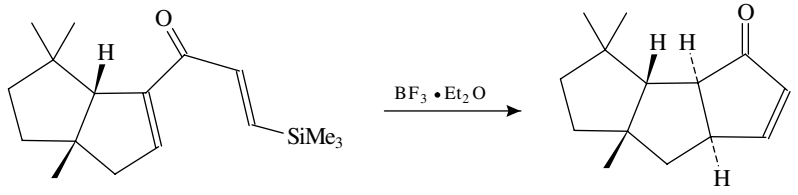
(9) **(10)**



(9)

(11) **(12)** **(13)**

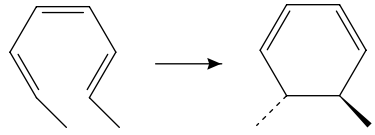
The action of boron trifluoride etherate on the ketone **14** results in the tricyclic ketone **15** in 80% yield (equation 10)[10].



(10)

(14) **(15)**

The thermal disrotatory cyclization of hexatrienes leads to cyclohexadienes (equations 11 and 12)[11–13].



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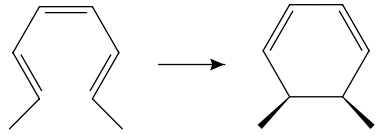
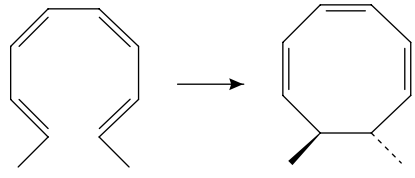


(12)

The predicted conrotatory cyclization of octatetraenes was confirmed for the case of the methyl-substituted compounds, which above 16 °C readily formed the cyclooctatrienes shown in equations 13 and 14)[14]. We conclude this section with an electrocyclic reaction involving ten π-electrons, that is, the formation of azulene **(17)** when the fulvene **16** is heated (equation 15)[15,16].



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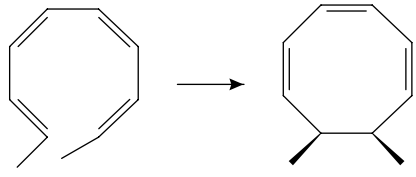

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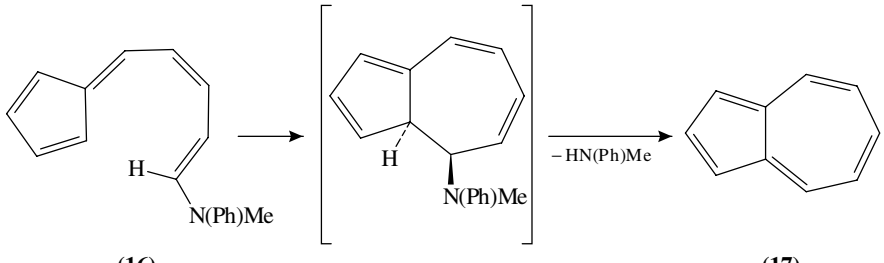
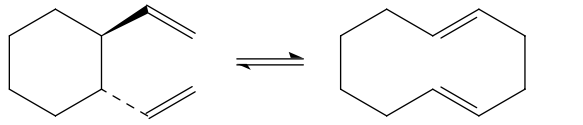


(16) **(17)** (15)

III. A COPE REARRANGEMENT

The 'Cope ring-expansion' of *trans*-1,2-divinylcyclohexane results in 1,5-cyclodecadiene (equation 16); however, the equilibrium favours the monocyclic compound[17]. In the case of the allene **18**, ring-expansion occurs: at 90 °C the methylenecyclodecadiene **19** is formed

in greater than 99% yield (equation 17)[18].



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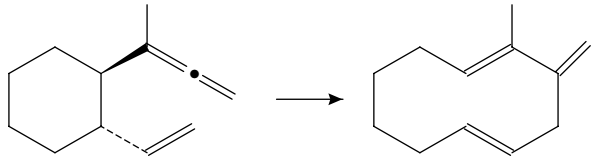
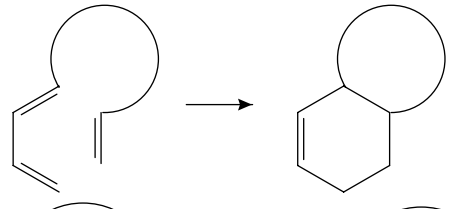


(17)

(18) **(19)**

IV. INTRAMOLECULAR DIELS–ALDER REACTIONS

Several reviews on intramolecular Diels–Alder reactions have appeared[19–23]. The products may be either fused (equation 18) or bridged (equation 19). The vast majority of reported examples of the reaction result in fused products; bridged compounds are rarely observed and only in cases where the diene and dienophile are separated by ten or more carbon atoms, e.g. **20** ⟶ **21** (equation 20)[24]. The decatriene **22** cyclizes at 200 °C to the *trans*-fused octalins **23** and **24** (equation 21)[25,26]. Heating the ester **25** yields a 1:1 mixture of the *cis*- and *trans*-octalins **26** and **27** (equation 22)[27]. The palladacycle



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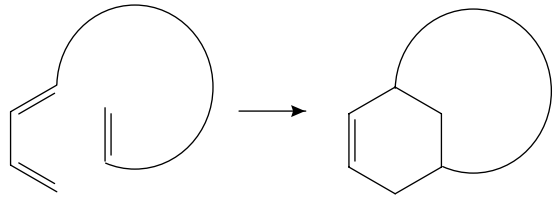

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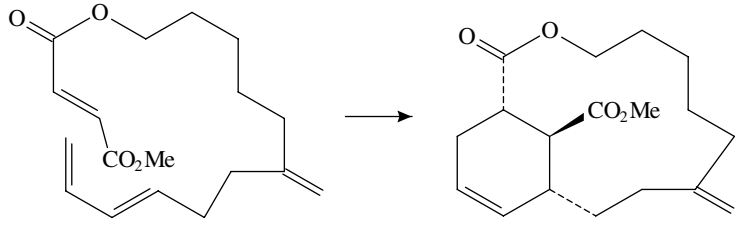
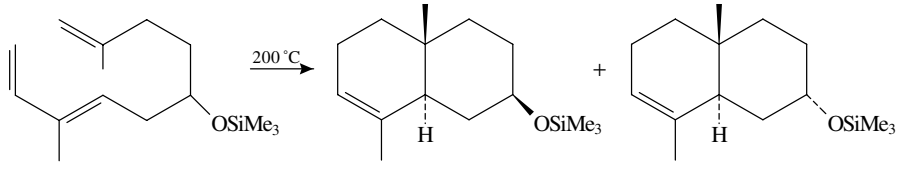


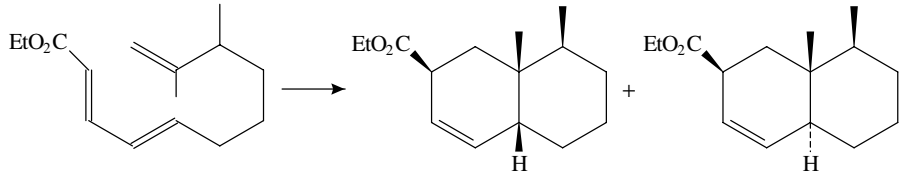
(20)

(20) **(21)**

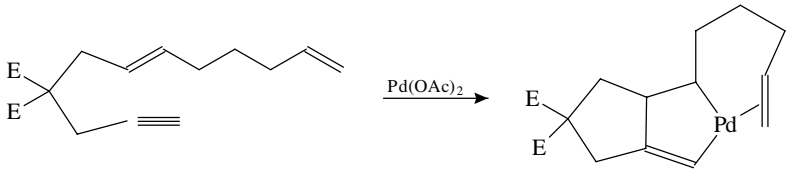
29, produced from the dienyne **28** (E = CO_2Me) and palladium(II) acetate in boiling toluene, decomposes to the triene **30**, which forms the cyclization product **31** in 72% overall yield (equation 23)[28]. Thermal ring-closure of **32** gives the *trans*-fused tricyclic alcohol **33** (equation 24)[29].



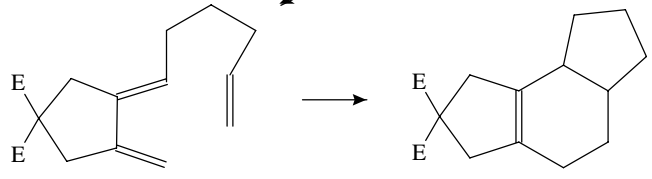
(22) **(23)** **(24)** (21)



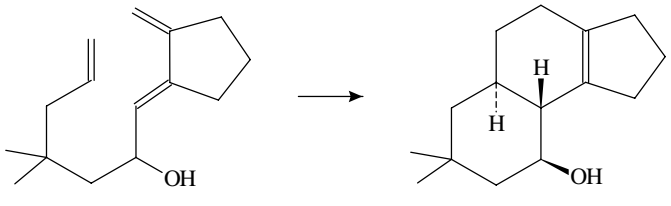
(25) **(26)** **(27)** (22)



(28) **(29)** (23)

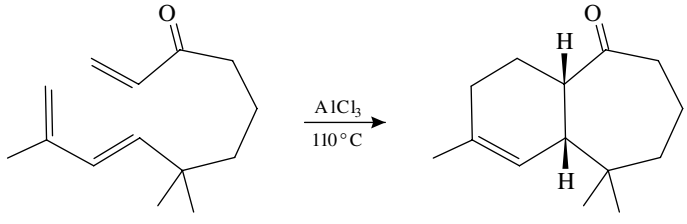


(30) **(31)**



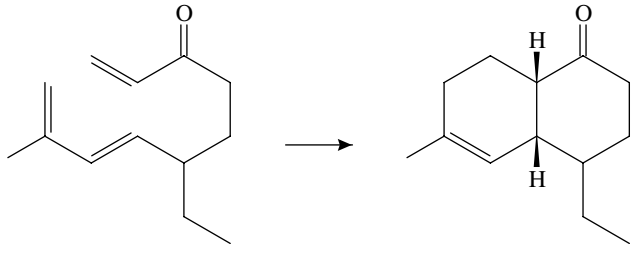
(32) **(33)** (24)

A number of stereospecific intramolecular Diels–Alder reactions of trienones leading to *cis*-fused products have been described. The ketone **34** forms solely compound **35** on treatment with aluminium trichloride at 110 °C (equation 25)[30]. The lower homologue **36** undergoes a spontaneous cyclization to **37** below 20 °C (equation 26)[31] and the isomeric ketones **38** and **40** similarly give **39**[32] and **41**[33], respectively (equations 27 and 28).



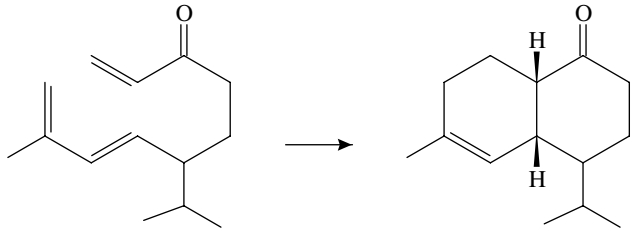
(25)

(34) **(35)**



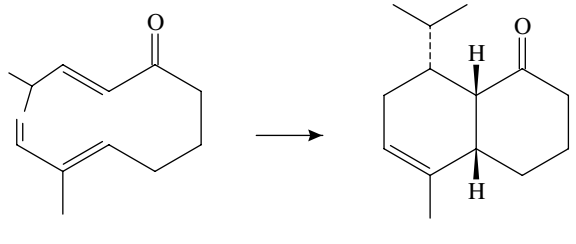
(26)

(36) **(37)**



(27)

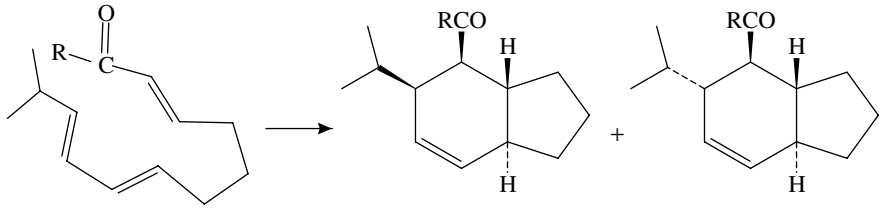
(38) **(39)**



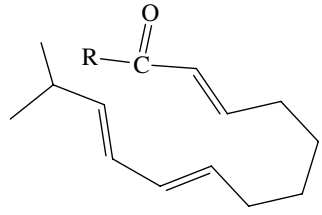
(28)

(40) **(41)**

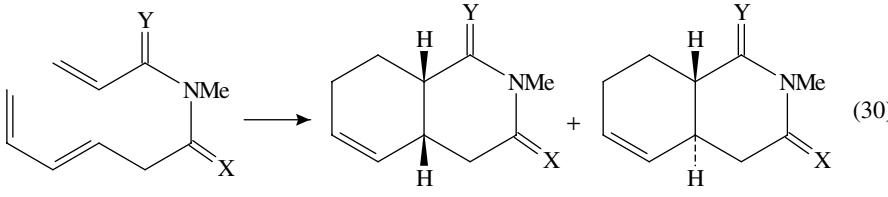
The stereoselectivity of the thermal ring-closure of the dodecatrieneones **42** is determined by the nature of the remote group R. *trans*-Fused products **43** predominate over *cis*-products **44** and their ratio increases as R varies from MeO through Me to H (equation 29). If the reactions are catalysed by diethylaluminium chloride only *trans*-compounds are formed. The homologues **45** behave similarly[34]. In contrast, the 7-azadeca-1,3,9-trienes **46** (X, Y = H_2 or O) yield more of the *cis*- than the *trans*-fused compounds, regardless of the nature of X and Y (equation 30)[35].



(42) **(43)** **(44)** (29)



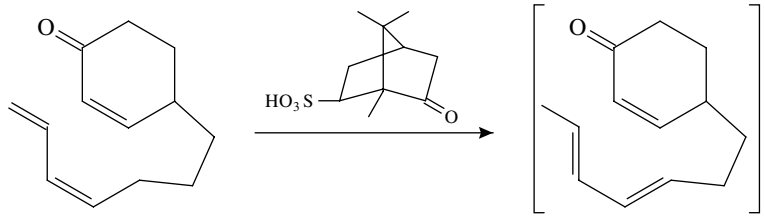
(45)



(46) major minor (30)

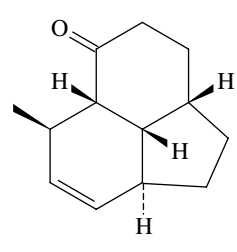
The acid-catalysed intramolecular ring-closure of the heptadienylcyclohexenone **47** yields the tricyclic compound **49** via the rearranged intermediate **48**, the product of a proton shift (equation 31)[36]. Similarly, 1,9,11-dodecatrien-3-one **(50)** gives a mixture containing 94% of **51** and only 6% of the unrearranged product **52** (equation 32)[36]

ortho-Quinodimethanes possessing a suitably positioned double bond undergo intramolecular Diels–Alder reactions spontaneously (equation 33)[37]. The quinodimethanes have been generated by thermolysis of 3-isochromanones (equation 34)[38] by the action of tetrabutylammonium fluoride on *o*-(1-trimethylsilylhept-6-enyl)benzyltrimethylammonium iodide (equation 35)[39] and by heating alkenyl-dihydrobenzo[*c*]thiophen 2,2-dioxides at 240 °C in diethyl phthalate (equation 36)[40]. The tricyclic hydrocarbons **53**

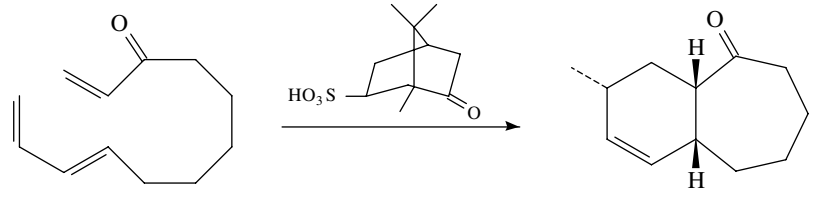


(47) **(48)**

(31)

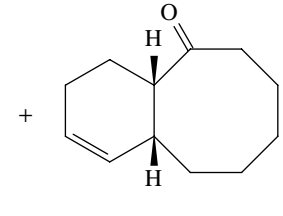


(49)

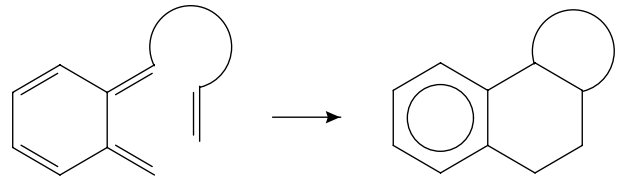


(50) **(51)**

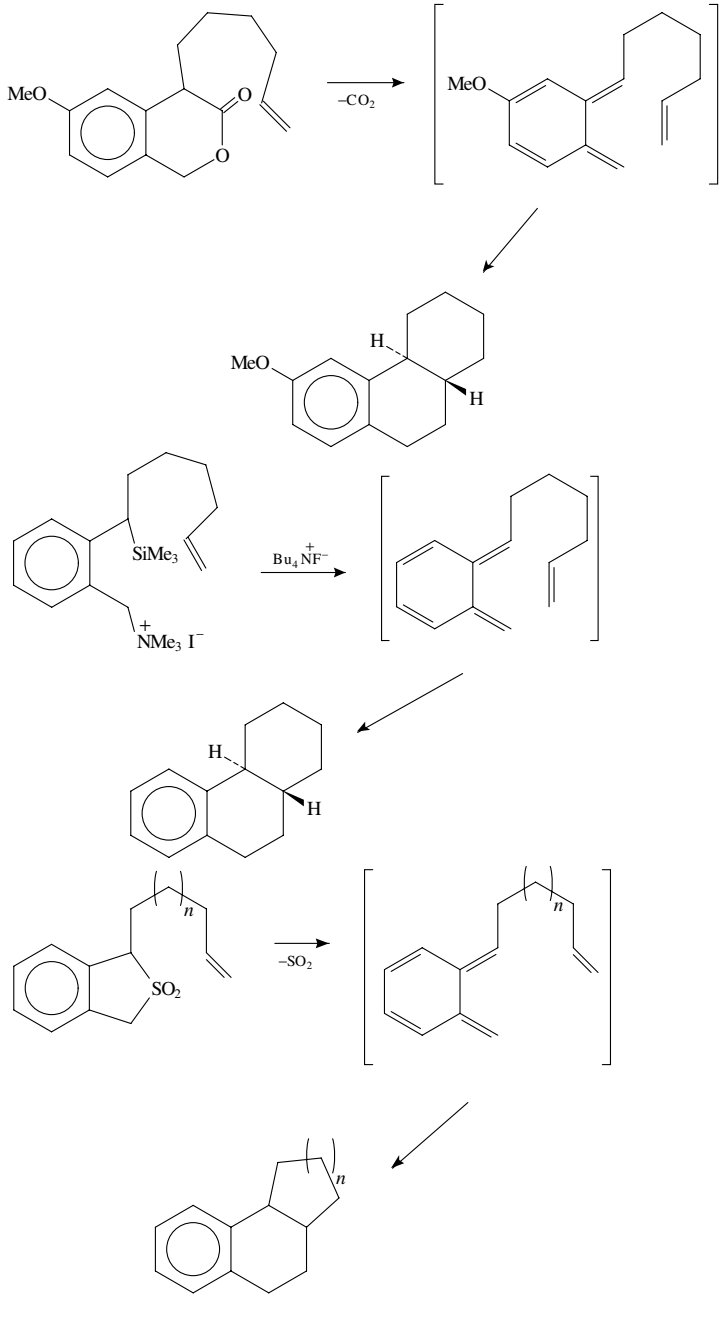
(32)



(52)



(33)



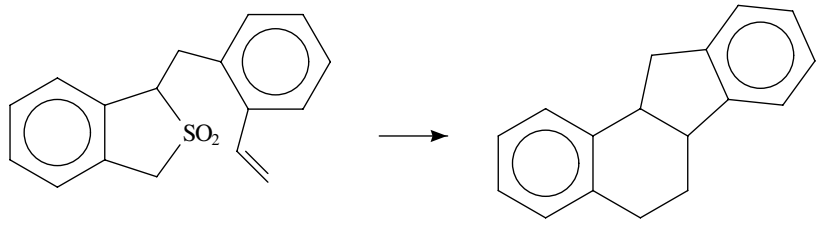
(34)

(35)

(36)

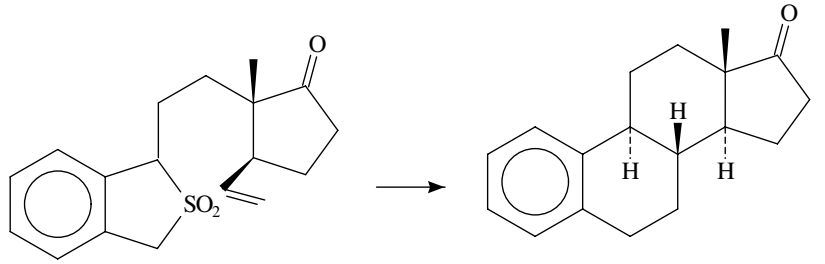
(53)

($n = 1$ or 2) were obtained in 85–89% yields in this way and **54** gave the tetracycle **55** (equation 37)[40]. The products are obtained as mixtures of *cis*- and *trans*-isomers with the latter predominating. The reaction was applied to the total synthesis of estra-1,3,5-(10)-trien-17-one **(56)** (equation 38)[41]. The thermal ring-opening of benzocyclobutenes results in *ortho*-quinodimethanes (equation 39). Thus the dextrorotatory estradiol derivative **58** was prepared in 77% yield by heating **57** (equation 40)[42]. The cyclopentadienylcobaltdicarbonyl-catalysed addition of bis(trimethylsilyl)acetylene to the enediyne **59** generates the benzocyclobutene **60**, which forms the octahydrophenanthrene **61** containing less than 5% of the *cis*-isomer (equation 41)[43].



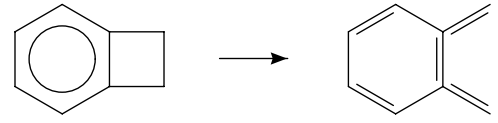
(37)

(54) **(55)**

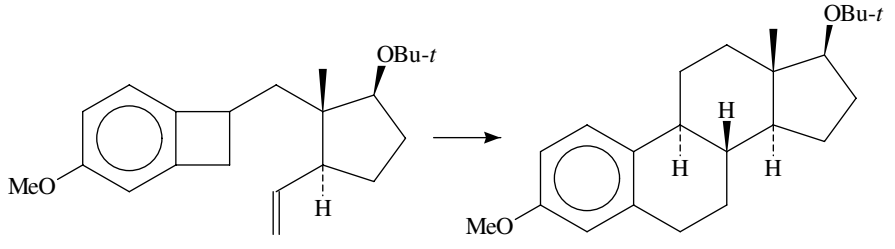


(38)

(56)

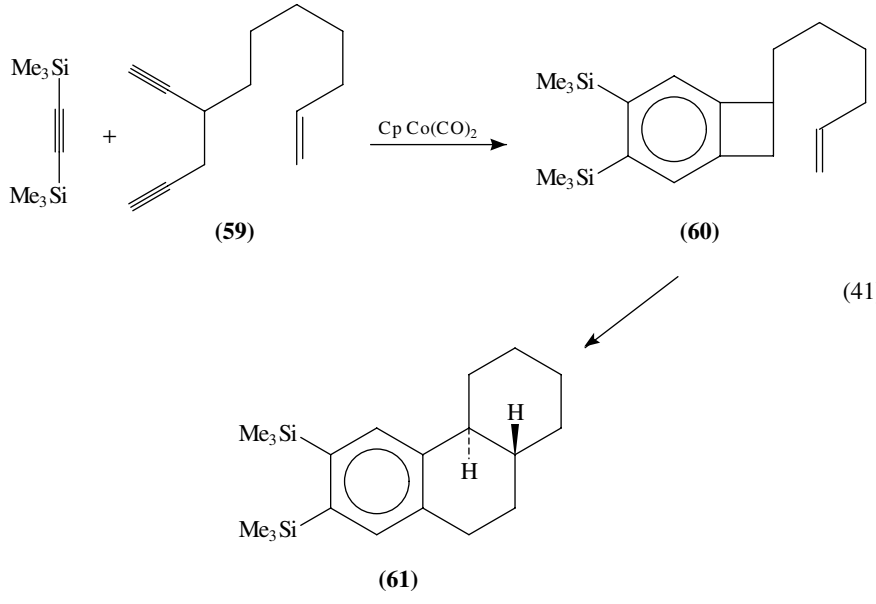


(39)



(57) **(58)**

(40)

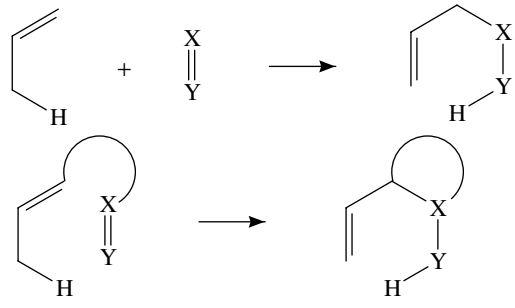


(59) **(60)** (41)

(61)

V. INTRAMOLECULAR ENE REACTIONS

The ene reaction (equation 42) is the 'indirect substituting addition' of an unsaturated compound X = Y to an olefin possessing an allylic hydrogen atom, which is transferred in the process[44,45]. The intramolecular version of the reaction (equation 43) has been applied to the formation of five-, six- and seven-membered rings[46].

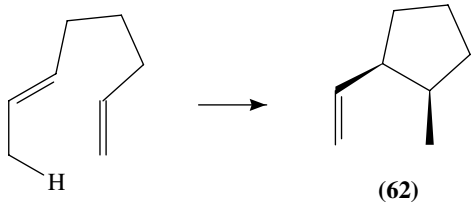


(42)

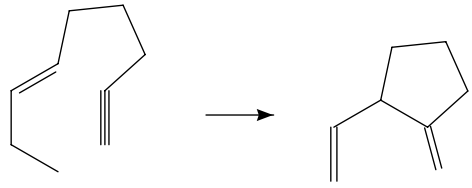
(43)

1,6-Octadiene cyclizes to *cis*-1-methyl-5-vinylcyclopentane **(62)** at 450 °C (equation 44a)[47]. An analogous reaction of the enyne **63** gives 1-methylene-2-vinylcyclopentane (equation 44b)[48]. Heating the 1,7-diene **64** at 490 °C results in a mixture of *cis*- and *trans*-1-isopropenyl-2-methylcyclohexane, **65** and **66**, respectively (equation 45)[49]. The presence of the ester group in **67** facilitates its cyclization: it undergoes ring-closure at 400 °C to give **68** as a mixture of three diastereomers (equation 46)[49]. The [3.3.3]propellane **70** is formed in 76% yield when compound **69** is heated to 250 °C (equation 47)[50]. Thermolysis of the cyclohexene derivative **71** yields a mixture of the spiro-compounds **72** and **73** (equation 48)[51]. Lewis-acid catalysis of intramolecular ene

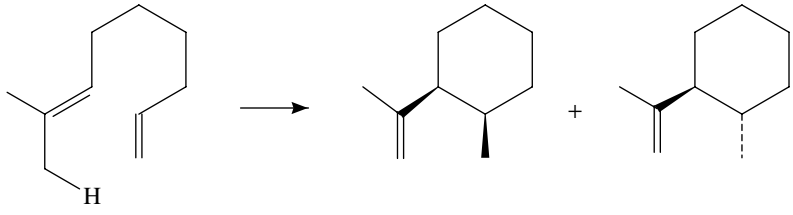
reactions has been observed. The diene **74** undergoes ring-closure to the *trans*-cyclohexane derivative **75** in boiling *o*-dichlorobenzene (equation 49). In the presence of zinc bromide the reaction takes place at room temperature[52]. The chiral analogue **76** cyclizes in the presence of zinc bromide at 25 °C to afford a 96:4 mixture of the ene-products **77** and **78** diastereo- and enantioselectively (equation 50)[53].



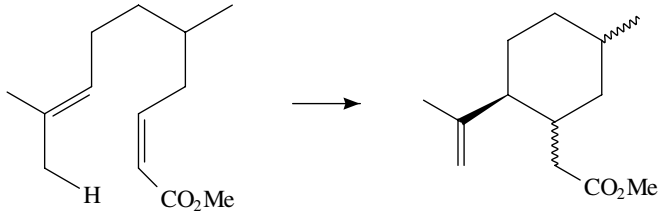
(62) (44a)



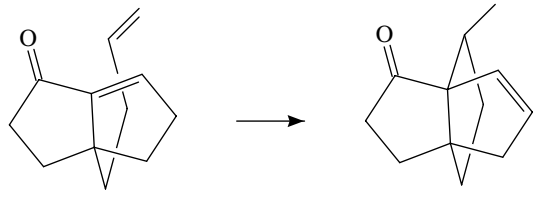
(63) (44b)



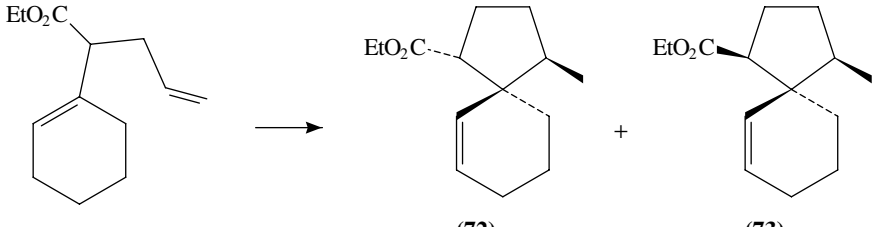
(64) **(65)** **(66)** (45)



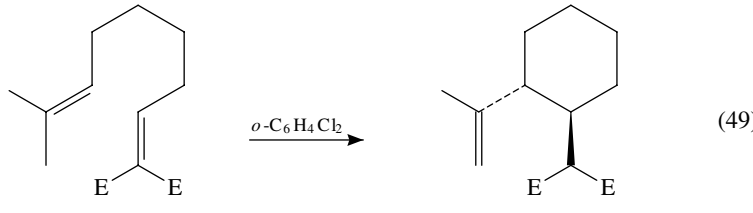
(67) **(68)** (46)



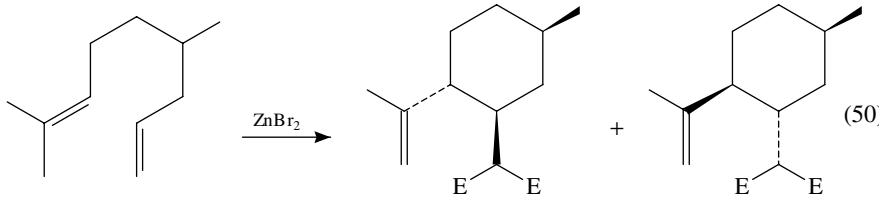
(69) **(70)** (47)



(71) **(72)** **(73)** (48)

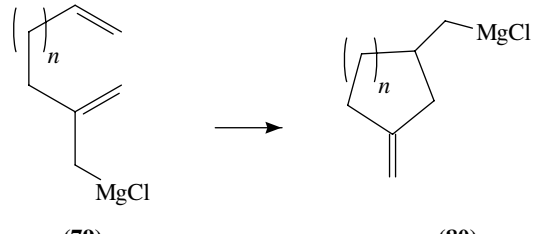


(74) E = CO_2Me **(75)** (49)

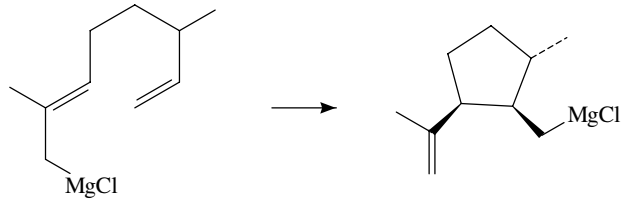


(76) E = CO_2Me **(77)** **(78)** (50)

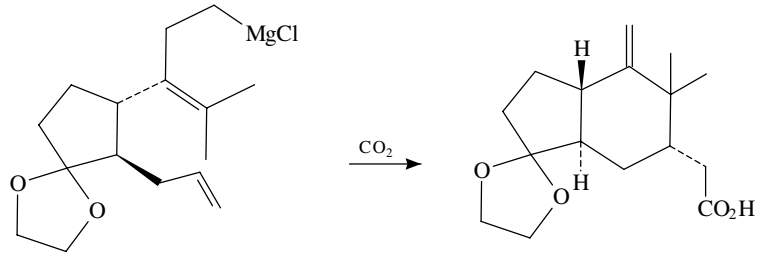
Ene reactions involving transfer of a metal rather than hydrogen are known as 'metallo ene reactions'[54]. In an intramolecular version of the reaction, the Grignard reagents **79** (n = 1, 2 or 3) undergo ring-closure to **80** on heating (equation 51)[55] and 2,6-dimethyl-2,7-octadienylmagnesium chloride **(81)** forms the cyclopentane derivative **82** (equation 52)[56]. The rearranged carboxylic acid **84** is obtained from **83** and carbon dioxide (equation 53)[57]. Similarly, successive treatment of the norbornene derivative **85** with magnesium and carbon dioxide affords the tricyclic acid **86** (equation 54)[58]. The disulphones **87** (R = H or Me) form palladium complexes **88** (L = ligand) by the combined action of bis(dibenzylideneacetone)palladium and triphenylphosphine; the complexes cyclize in acetic acid in a 'palladium ene reaction' to yield derivatives **89** of cyclopentane (equation 55)[59].



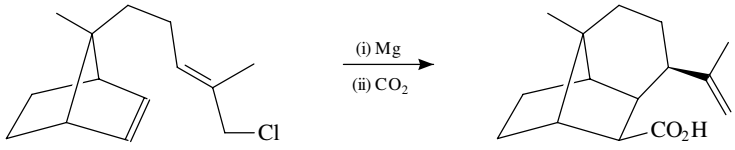
(79) **(80)** (51)



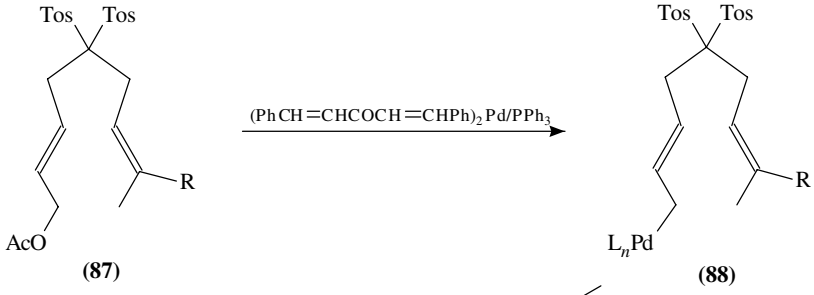
(81) (82) (52)



(83) (84) (53)



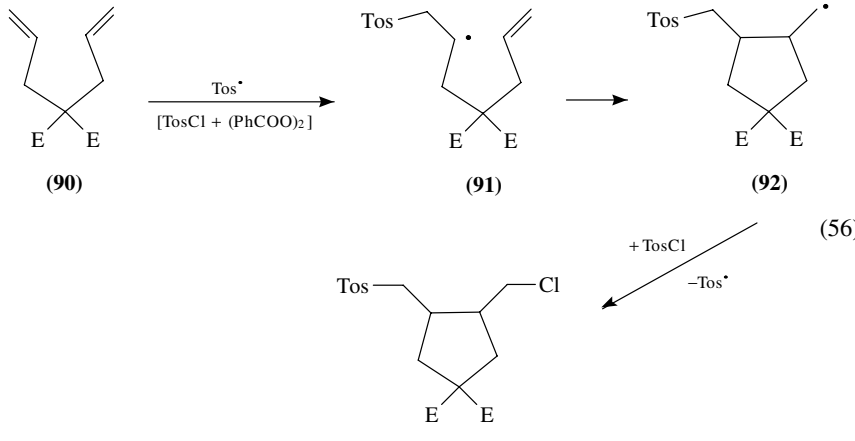
(85) (86) (54)



(87) (88) (89) (55)

VI. FREE-RADICAL CYCLIZATIONS

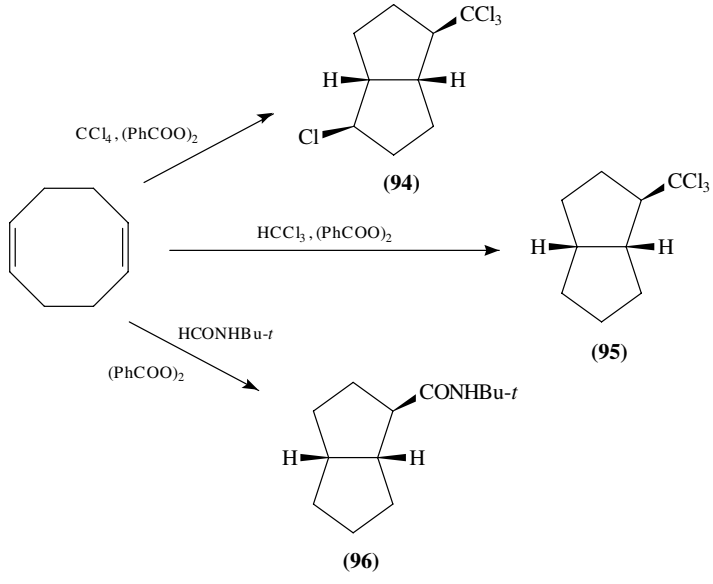
Free-radical chain reactions have been reviewed[60]. The cyclization of dienes by the action of free radicals is illustrated for the case of the 1,6-heptadiene derivative **90** (E = CO_2Me) in equation 56. Treatment with tosyl radicals, produced from tosyl chloride and a catalytic amount of dibenzoyl peroxide, generates the radicals **91**, which cyclize to **92**. The latter reacts with tosyl chloride to form **93** and tosyl radicals are regenerated. The product is obtained in 85% yield as a 6:1 mixture of *cis*- and *trans*-isomers[61].



(56)

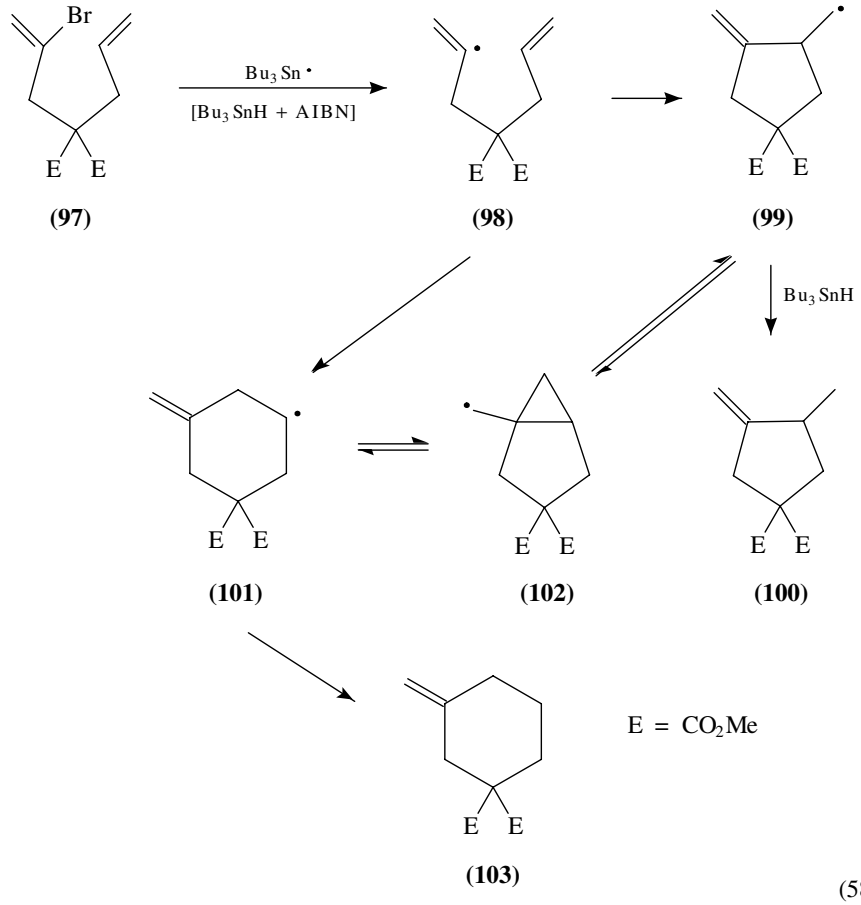
E = CO_2Me

A similar reaction of 1,5-cyclooctadiene with trichloromethyl radicals, produced from carbon tetrachloride and dibenzoyl peroxide, leads to 2-chloro-6-trichloromethylbicyclo-[3.3.0]octane **(94)**, with chloroform and dibenzoyl peroxide the analogue **95** is obtained and *N*-*t*-butylformamide affords compound **96** (equation 57)[62,63].



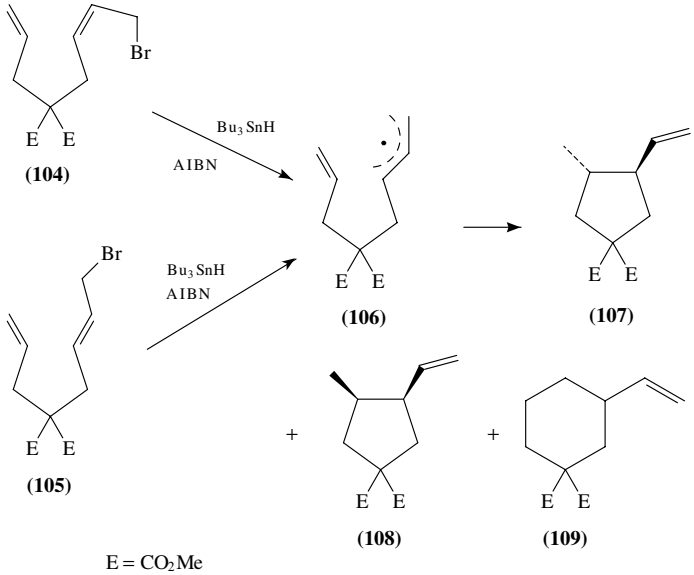
(57)

The diester **97** reacts with tributyltin radicals, produced from tributyltin hydride and AIBN (2,2′-bisazoisobutyronitrile), to form the vinyl radical **98**, which cyclizes to the methylenecyclopentylmethyl radical **99**. Abstraction of hydrogen from tributyltin hydride yields the product **100**. An alternative cyclization of **98** gives the methylenecyclohexyl radical **101** and thence dimethyl 3-methylenecyclohexanedicarboxylate **(103)**. The proportion of the products **100** and **103** depends on the concentration of the reactant **97**: at 0.02 molar concentration the products are formed in the ratio 3:1; at 1.7 molar concentration only **100** is observed. It is suggested that the cyclohexyl radical **101** might also arise from the cyclopentylmethyl radical **99** via the bicyclic radical **102** (equation 58)[64,65]. An analogous cyclization of the allyl radical **106**, generated from the bromides **104** or **105**, affords a 6:3:1 mixture of compounds **107**, **108** and **109** (equation 59)[66].

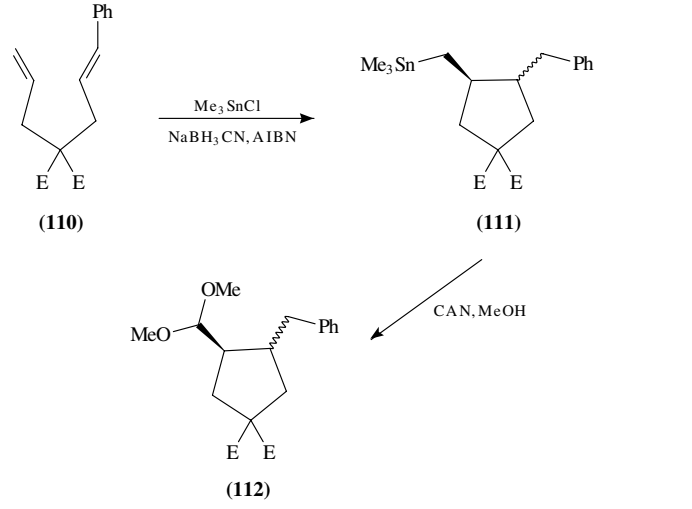


(58)

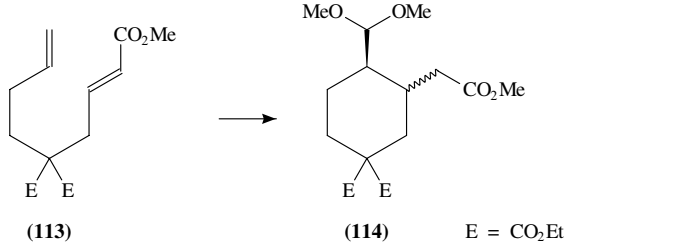
The diester **110** (E = CO_2Et) reacts with a mixture of trimethyltin chloride and sodium cyanoborohydride under AIBN catalysis to give the cyclopentane **111** as a 4:1 mixture of *cis*- and *trans*-isomers. The products are destannylated to the acetals **112** by treatment with methanolic ceric ammonium nitrate (CAN). The 1,7-octadienyl derivative **113** was similarly converted into the cyclohexanes **114** (*cis/trans* = 1:1) (equation 60)[67].


Br
E E
(104)
Bu3SnH
AIBN
(106)
(107)
Br
Bu3SnH
AIBN
(105)
+
+
(108)
(109)
E = CO2Me

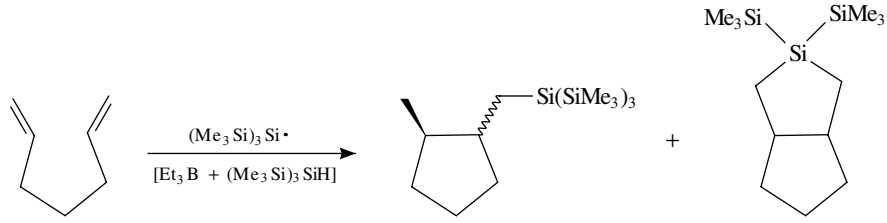
(59)


Ph
E E
(110)
Me3SnCl
NaBH3CN, AIBN
Me3Sn
Ph
(111)
CAN, MeOH
OMe
MeO
Ph
(112)

(60)


CO2Me
E E
(113)
MeO
OMe
CO2Me
(114)
E = CO2Et

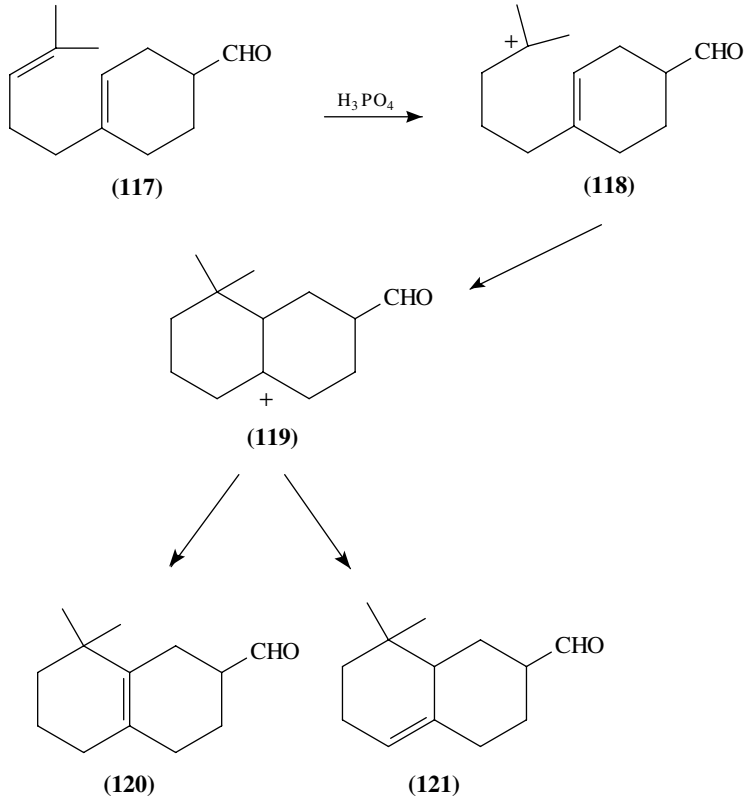
The action of a catalytic amount of triethylborane on tris(trimethylsilyl)silane induces the formation of tris(trimethylsilyl)silyl radicals, which promote the ring-closure of 1,6-heptadiene to a mixture of the *cis*- and *trans*-cyclopentane derivatives **115**, together with a small amount of the silicon heterocycle **116** (equation 61)[68].



(115) **(116)** (61)

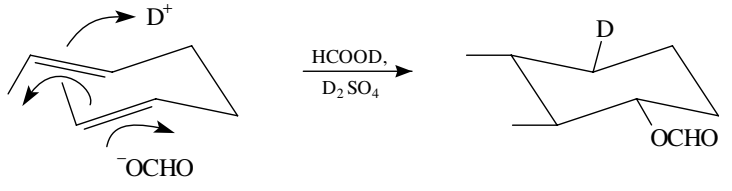
VII. CATIONIC CYCLIZATIONS[69–71]

The dienaldehyde **117** cyclizes to a mixture of the octalins **120** and **121** on treatment with concentrated orthophosphoric acid. It was suggested that the reaction is initiated by formation of the cation **118**, which undergoes ring-closure to the bicyclic cation **119**. Proton loss in two alternative ways leads to the products (equation 62)[72].



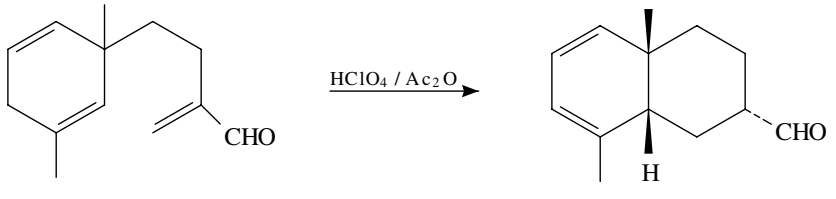
(117) **(118)** **(119)** **(120)** **(121)** (62)

Treatment of *trans,trans*-2,6-octadiene (**122**) with deuteriated formic acid HCO_2D in the presence of deuteriosulphuric acid gave the cyclized formate ester **123**. A concerted mechanism (equation 63) was proposed for this reaction[73]. The stereospecific ring-closure of the 1,4-cyclohexadiene derivative **124** in acetic anhydride/perchloric acid affords the octalin **125**, which was isolated as the diacetate **126** (equation 64)[74].



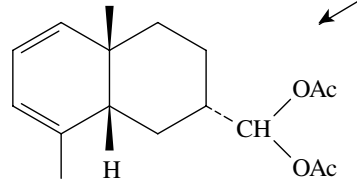
(63)

(122) **(123)**



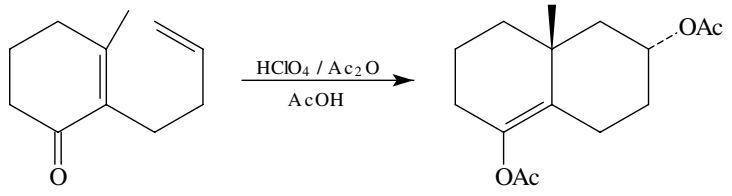
(124) **(125)**

(64)



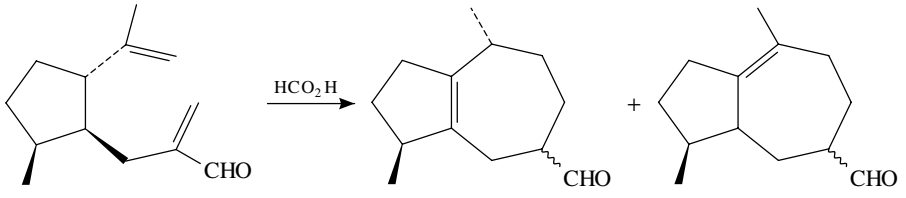
(126)

Another example of the formation of an octalin is the conversion of the cyclohexenone **127** into the enol acetate **128** by the action of acetic anhydride and perchloric acid in the presence of acetic acid (equation 65)[75]. The acid-induced ring-closure of the cyclopentane derivative **129** gives a 85% yield of a mixture of the octahydroazulenes **130** and **131** (equation 66)[76].



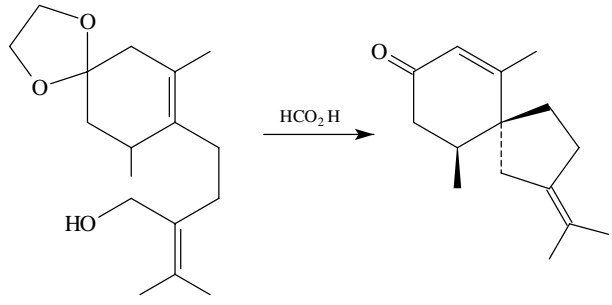
(65)

(127) **(128)**



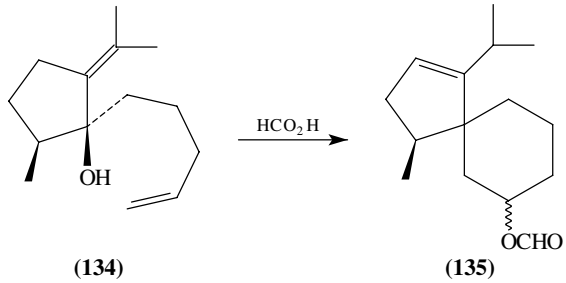
(129) **(130)** **(131)** (66)

The formation of a number of spiro compounds by cationic cyclization has been reported. Formic acid transforms the ketal **132** into **133** in 40% yield (equation 67)[77] and the alcohol **134** into the formate **135** (35%) (equation 68)[78]. The alcohols **136** and **138** yield the spiro compounds **137** (45–50%) (equation 69)[79] and **139** (25%) (equation 70)[80], respectively. Pallescensin A **(141)** is produced in 84% yield by the twofold cyclization of the furan derivative **140**, induced by boron trifluoride (equation 71)[81].



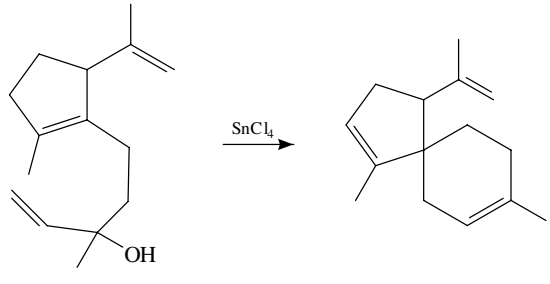
(67)

(132) **(133)**



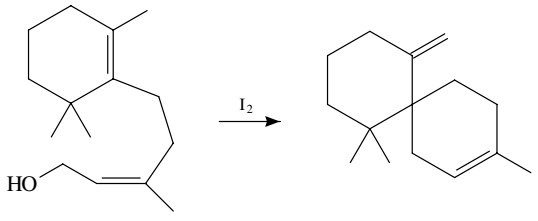
(68)

(134) **(135)**



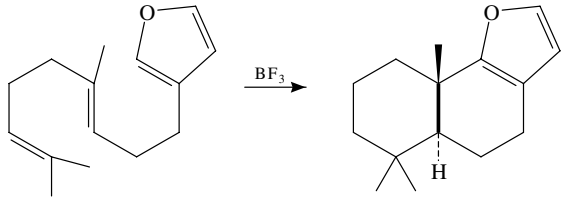
(69)

(136) **(137)**



(70)

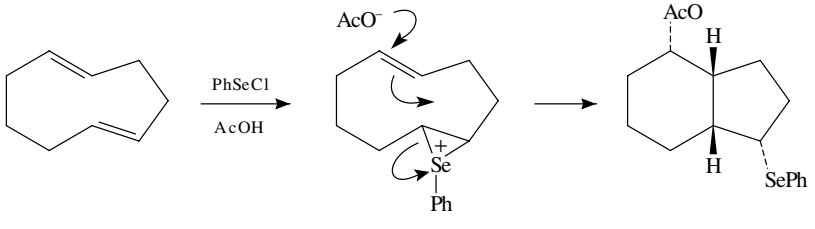
(138) **(139)**



(71)

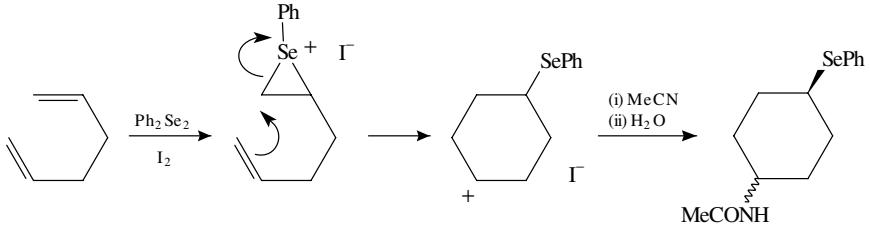
(140) **(141)**

Treatment of cyclonona-1,5-diene **(142)** with benzeneselenyl chloride in acetic acid yields solely the bicyclic product **144** via the episelenonium ion **143** (equation 72)[82]. The reaction of 1,5-hexadiene with benzeneselenyl iodide, generated from diphenyl diselenide and iodine in acetonitrile, likewise results in addition-cyclization. The substituted cyclohexane **145** is obtained as a mixture of *cis*- and *trans*-isomers (equation 73)[83]. Thallium(III) compounds effect the ring-closure of dienols. Thus geraniol **(146)** yields a mixture of the cyclic ethers **147–149** (equation 74)[84] and nerol **(150)** gives **151**, **152** and a mixture of four diastereomers having the gross structure **153** (equation 75)[85]. Treatment of *o*-geranylphenol **(154)** with thallium trifluoroacetate, followed by hydrolysis, affords the tricyclic benzopyrans **155** and **156** (equation 76)[86].



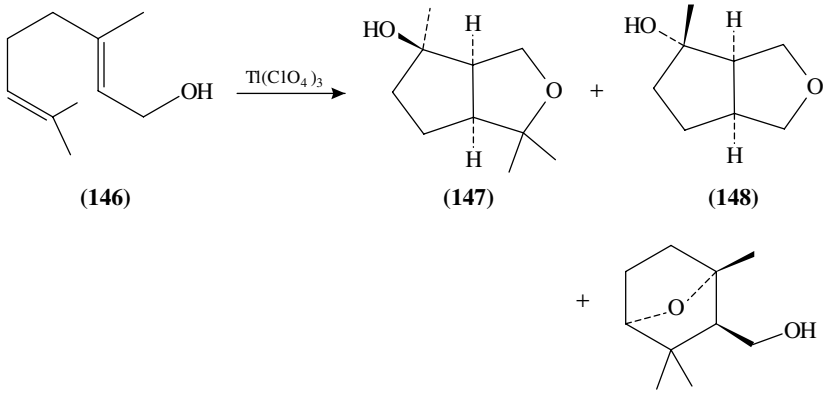
(72)

(142) **(143)** **(144)**

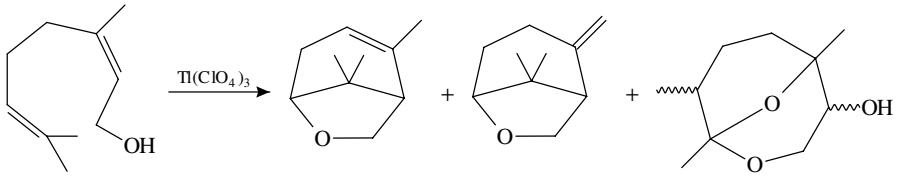


(145)

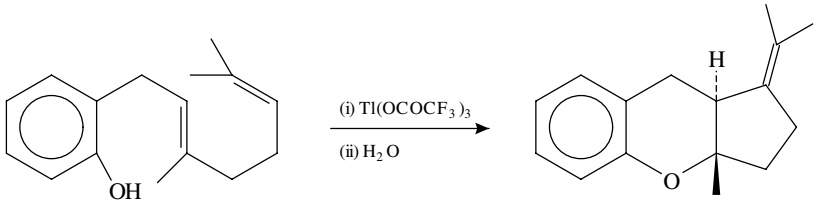
(73)



(146) **(147)** **(148)** **(149)** (74)

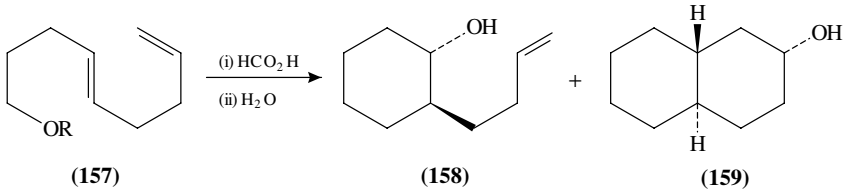


(150) **(151)** **(152)** **(153)** (75)

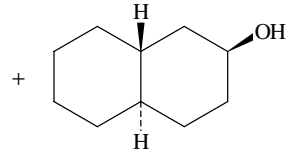


(154) **(155)** **(156)** (76)

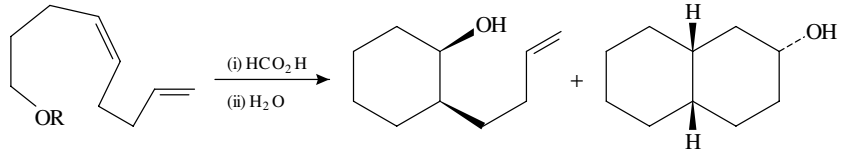
Ionization of *p*-nitrobenzenesulphonate esters of dienols generates carbocations which undergo cyclization. Thus *trans*-5,9-decadienyl *p*-nitrobenzenesulphonate **(157)** (R = $O_2SC_6H_4NO_2$-*p*) reacts with formic acid, followed by hydrolysis, to yield the butenylcyclohexanol **158**, together with the decalinols **159** and **160** (equation 77)[87]. The *cis*-ester **161** affords the *cis*-products **162–164** (equation 78)[88]. The steric course of these reactions is consistent with a concerted mechanism (equation 79).



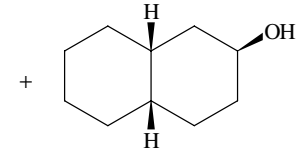
(157) **(158)** **(159)**



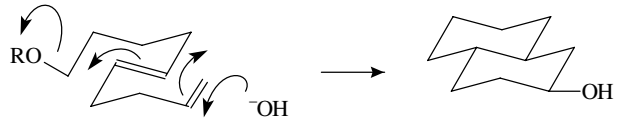
(160) (77)



(161) **(162)** **(163)**

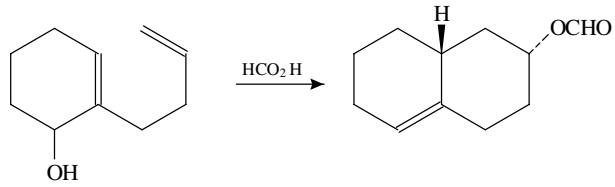


R = $O_2SC_6H_4NO_2$-*p* **(164)** (78)

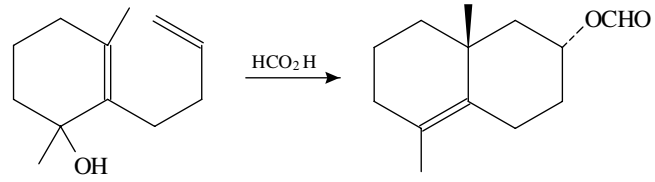


(79)

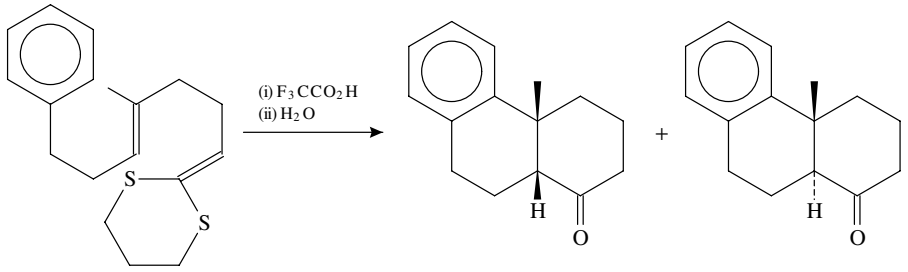
The octalinyl ester **166** is produced in excellent yield when the butenylcyclohexenol **165** is treated with formic acid at room temperature (equation 80)[89]. The dimethyl analogue **167** reacts similarly to give **168** (equation 81)[90]. The trifluoroacetic acid-catalysed ring-closure of the ketene thioacetal **169** to give a 1:2 mixture of the *cis*- and *trans*-ketones **170** and **171** (equation 82) has been reported[91].



(165) **(166)** (80)

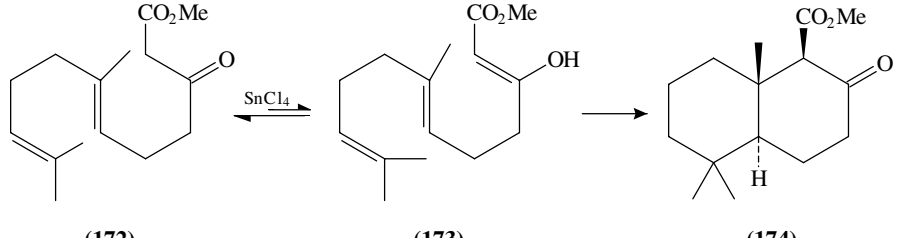


(167) (168) (81)

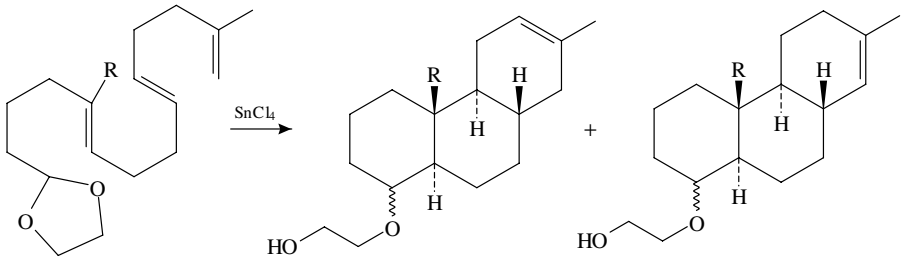


(169) (170) (171) (82)

The formation of the decalinone **174** in 68% yield in the reaction of the dienone **172** with tin(IV) chloride (equation 83) is thought to proceed by way of the enol **173**[92]. The triene **175** (R = H) cyclizes quantitatively to a mixture of the isomeric dodecahydrophenanthrenes **176** and **177** when treated with tin(IV) chloride at 0 °C (equation 84)[93]; the homologue **175** (R = Me) reacts analogously[94].

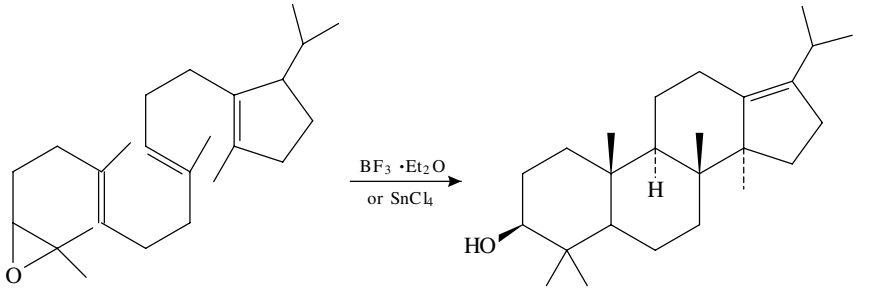


(172) (173) (174) (83)

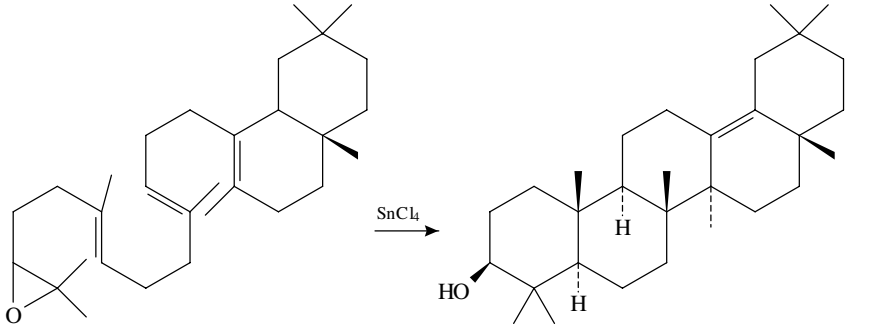


(175) (176) (177) (84)

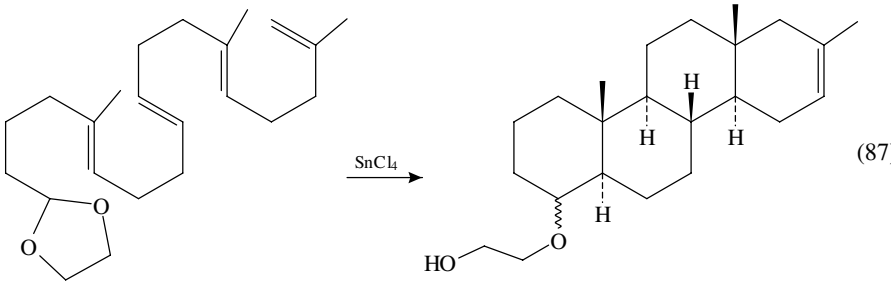
The tetracyclic alcohol **179** is produced by the action of boron trifluoride etherate or tin(IV) chloride on the oxirane **178** (equation 85)[95]. A similar cyclization of the oxirane **180** yields DL-δ-amyrin **(181)** (equation 86)[96]. In the $SnCl_4$-catalysed ring-closure of the tetraene **182** to the all-*trans*-tetracycle **183** (equation 87) seven asymmetric centres are created, yet only two of sixty-four possible racemates are formed[97]. It has been proposed that multiple ring-closures of this kind form the basis of the biosynthesis of steroids and tetra- and pentacyclic triterpenoids, the 'Stork–Eschenmoser hypothesis'[98,99]. Such biomimetic polyene cyclizations, e.g. the formation of lanosterol from squalene (equation 88), have been reviewed[69,70].



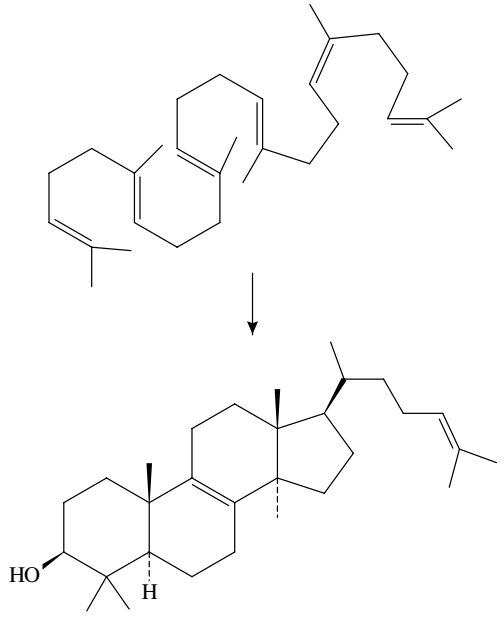
(178) **(179)** (85)



(180) **(181)** (86)

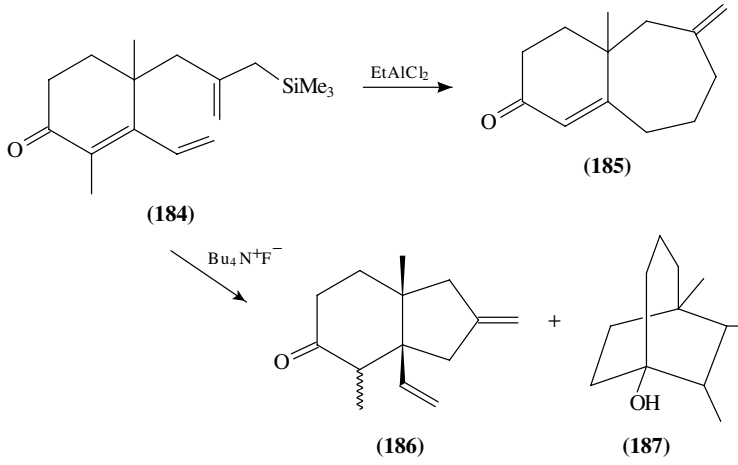


(182) **(183)** (87)

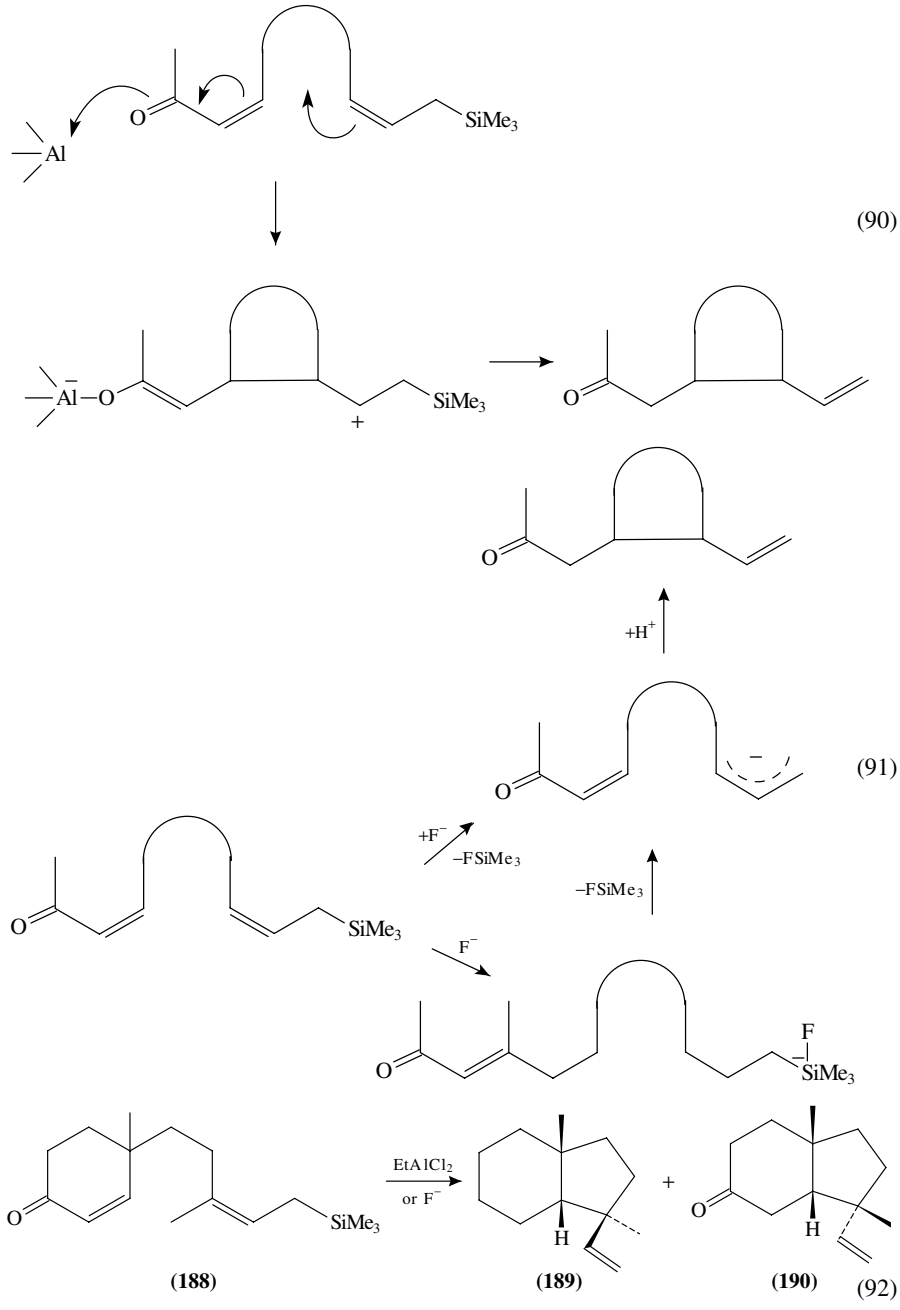


(88)

Cyclization reactions of vinyl- and alkynylsilanes have been reviewed[100]. The course of the reaction of the cyclohexenone derivative **184** depends on the catalyst employed: ethylaluminium dichloride gives solely the product **185** of 1,6-addition, whereas tetrabutylammonium fluoride yields a mixture containing 69% of the '1,4-adduct' **186** and 31% of the bridged compound **187** (equation 89)[101]. Intramolecular addition reactions of allylic silanes[102] may also be catalysed by Lewis acids (equation 90) or fluoride ions, and in this case an allyl anion or a pentavalent silicon intermediate may be involved (equation 91). Such reactions are exemplified by the formation of a 1:5 mixture of the diastereomers **189** and **190** when the cyclohexenone derivative **188** is treated with ethylaluminium dichloride (equation 92). In the presence of fluoride anion the ratio of the isomers is reversed[103].

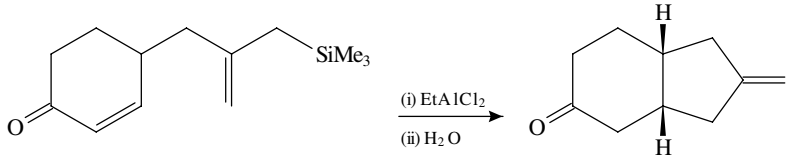


(89)



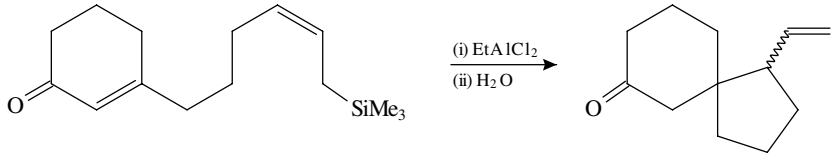
Cyclization of the allylic trimethylsilane **191** with ethylaluminium dichloride, followed by hydrolysis, gives solely the *cis*-fused product **192** (equation 93)[104]. Under similar

conditions, the cyclohexenone **193** yields the spiro compound **194** as a mixture of diastereomers (equation 94)[104].



(93)

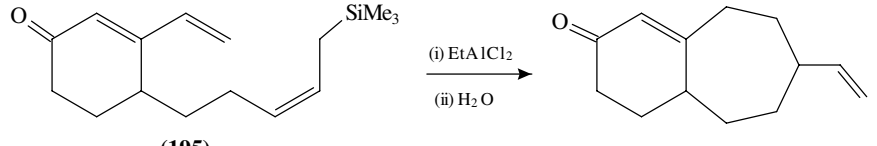
(191) **(192)**



(94)

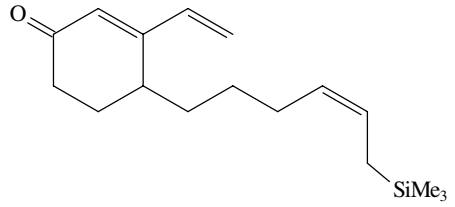
(193) **(194)**

A seven-membered ring is formed in the cyclization of **195** (equation 95)[105]. The homologue **196** affords the fused cyclooctane **197**, together with the *cis*- and *trans*-decalinones **198** (equation 96)[106]. Six-, seven- and eight-membered rings are produced in Lewis acid-catalysed reactions of various cyclohexenones with side-chains terminating in allylic trimethylsilyl groups (equations 97–99)[107].



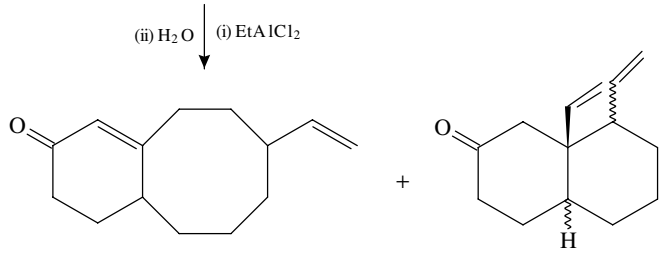
(195)

(95)

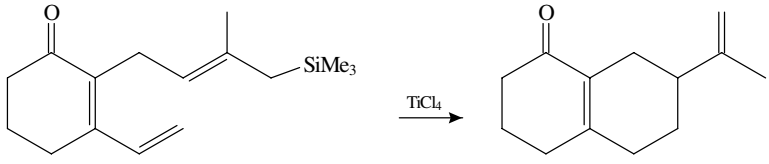


(196)

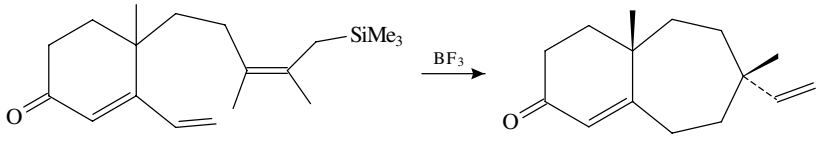
(96)



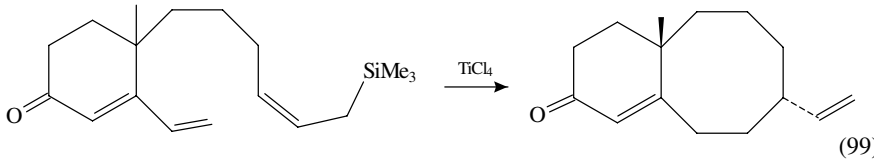
(197) **(198)**



(97)



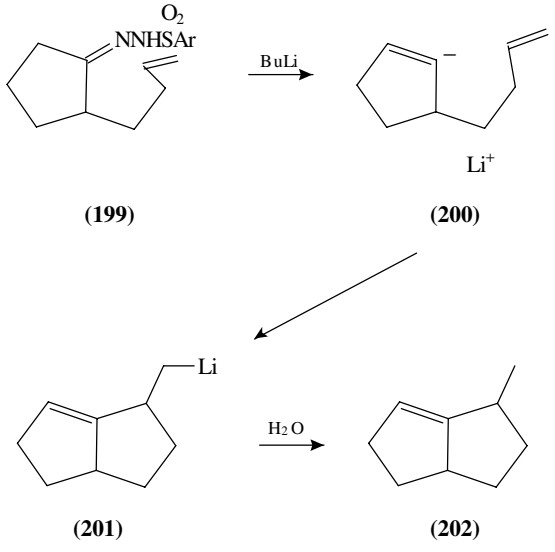
(98)



(99)

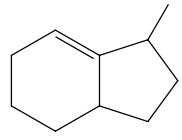
VIII. ANIONIC CYCLIZATIONS

Treatment of the 2,4,6-triisopropylbenzenesulphonylhydrazone **199** of 2-(3-butenyl)cyclopentanone with butyllithium generates the lithium compound **200**, which cyclizes spontaneously to **201**. Aqueous work-up gives the bicyclic hydrocarbon **202** in good yield (equation 100). The six-membered ring analogue **203** is formed in very poor yield by this method. Ring-closure of the acyclic lithium derivative **204** gives 65% of *cis*-2,4-dimethylmethylenecyclopentane **(205)** (equation 101)[108].

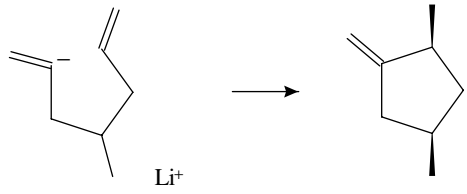


(100)

Ar = 2, 4, 6-*i*-$Pr_3C_6H_2$

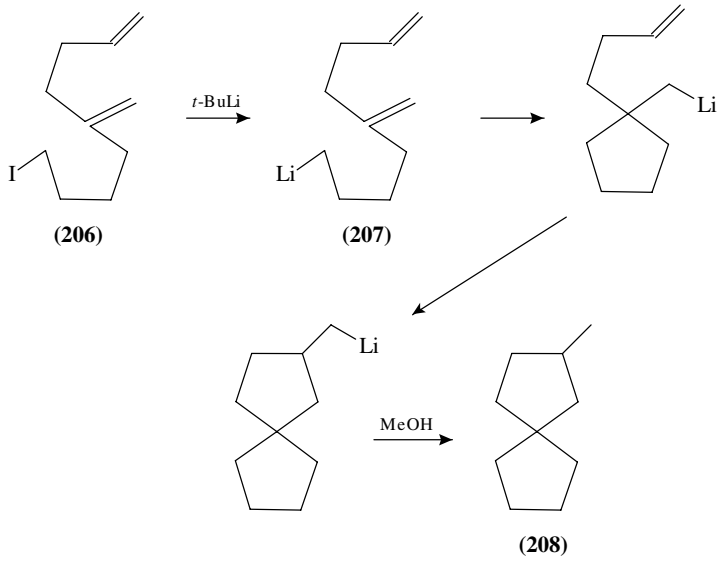


(203)

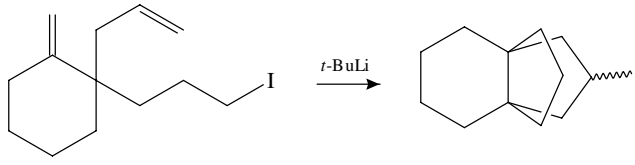


(204) **(205)** (101)

The action of *t*-butyllithium on 5-methylene-8-nonenyl iodide **(206)** leads to the lithium compound **207**, which undergoes a 'tandem cyclization' to yield eventually 84% of 2-methylspiro[4.4]nonane **(208)** (equation 102). An analogous reaction of the iodide **209** (equation 103) results in the [4.3.3]propellane **210** (81%) as a mixture of *endo*- and *exo*-isomers[109].

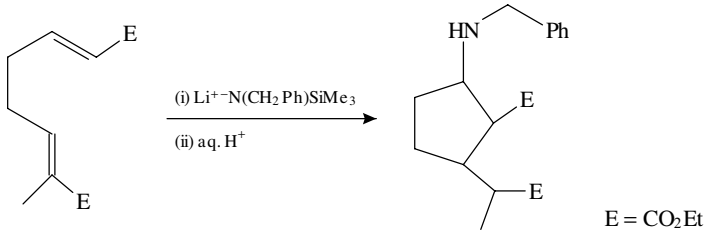


(206) **(207)** **(208)** (102)

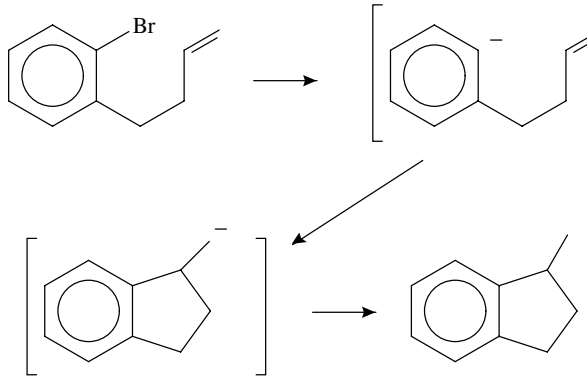


(209) **(210)** (103)

Treatment of the diester **211** (E = CO_2Et) with lithium *N*-benzyltrimethylsilylamide, followed by aqueous acid, yields the cyclopentane derivative **212**, the product of an intramolecular Michael addition (equation 104)[110]. 1-Methylindane is produced in moderate yield by the electrochemical reduction of *o*-bromo-(3-butenyl)benzene (equation 105)[111].

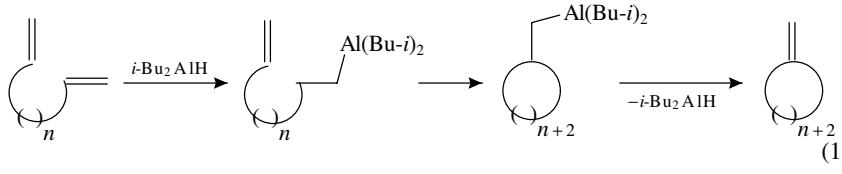


(211) **(212)** (104)

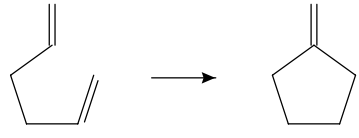


(105)

Diisobutylaluminium hydride catalyses the ring-closure of various dienes. It is proposed that the process involves addition of the aluminium hydride to a terminal double bond, followed by ring-closure and, finally, elimination of the catalyst (equation 106). Thus 1,5-hexadiene gives methylenecyclopentane **(213)** (equation 107), 1,6-heptadiene gives methylenecyclohexane **(214)** (equation 108), 4-vinylcyclohexene gives bicyclo[3.2.1]oct-2-ene **(215)** (equation 109) and the spiro compound **217** is obtained from 5-methylene-1,8-nonadiene **(216)** (equation 110)[112].

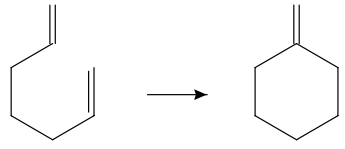


(106)



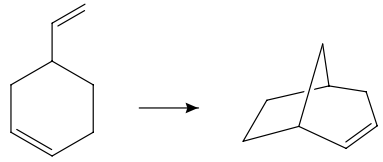
(107)

(213)



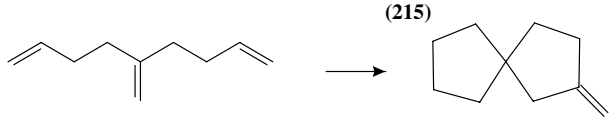
(108)

(214)



(109)

(215)

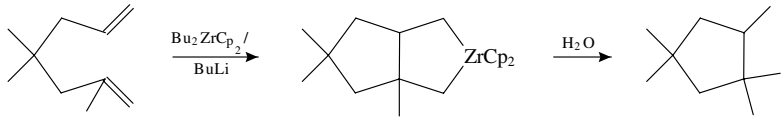


(110)

(216) **(217)**

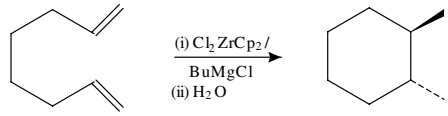
IX. METAL-CATALYSED CYCLIZATIONS

Zirconocene, $ZrCp_2$, generated in situ from zirconocene derivatives, mediates diverse ring-closures[113]. Thus treatment of 2,4,4-trimethyl-1,6-heptadiene with butyllithium and Bu_2ZrCp_2 yields the zirconium complex **218**, which gives 1,1,3,3,5-pentamethylcyclopentane on aqueous work-up (equation 111)[114]. The reaction of 1,7-octadiene with butylmagnesium chloride and a catalytic amount of zirconocene dichloride, followed by water, gives *trans*-1,2-dimethylcyclohexane **(219)** in excellent yield (equation 113)[115]; similarly, the diene ether **220** affords the cyclopentane derivative **221** (equation 113)[116].



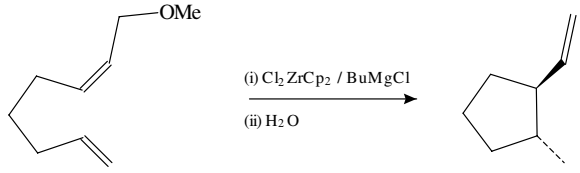
(218)

(111)



(112)

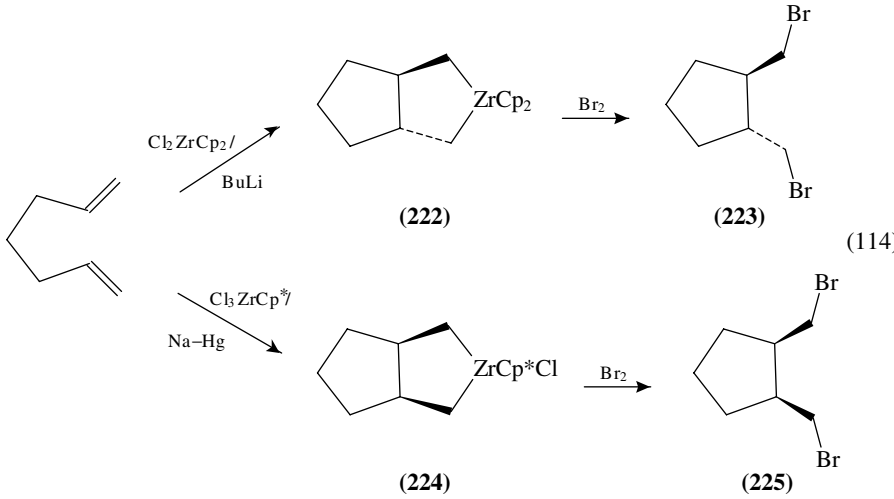
(219)



(113)

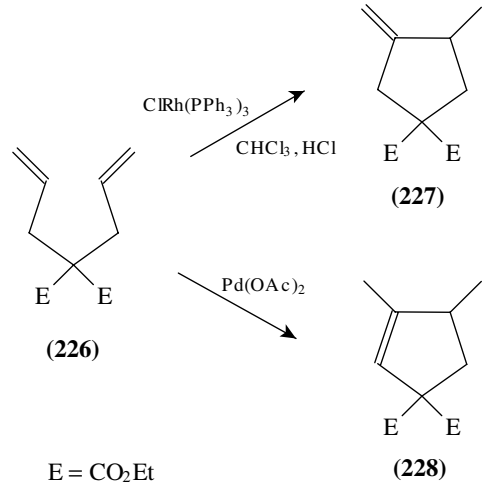
(220) **(221)**

1,6-Heptadiene and zirconocene, generated from zirconocene dichloride and butyllithium, form an intermediate, presumably the metallocycle **222**, which is transformed into *trans*-1,2-di(bromomethyl)cyclopentane **(223)** by the action of bromine at −78 °C. In contrast, a similar reaction of 1,6-heptadene with Cp^*ZrCl (Cp^* = pentamethylcyclopentadienyl) (from Cp^*ZrCl_3 and sodium amalgam) gives solely the *cis*-isomer **225** via the complex **224** (equation 114)[117].



(114)

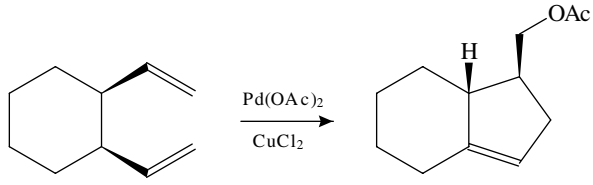
The diester **226** undergoes ring-closure to the methylenecyclopentane derivative **227** in the presence of a catalytic amount of chlorotris(triphenylphosphine)rhodium in boiling chloroform saturated with hydrogen chloride. In contrast, if the reaction is catalysed by palladium(II) acetate, the isomeric cyclopentene **228** is produced (equation 115)[118].



(115)

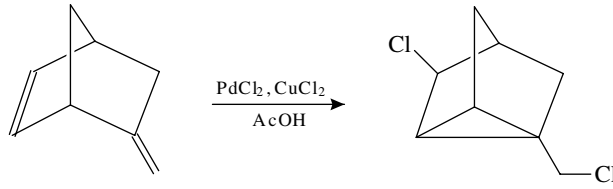
Dienes are oxidized by palladium(II) salts; if copper(II) chloride is added, the reactions become catalytic with respect to the palladium salt. Thus *cis*-divinylcyclohexane reacts

with palladium(II) acetate to give the bicyclic acetate **229** stereospecifically (equation 116), 5-methylenenorbornene and palladium(II) chloride/copper(II) chloride in acetic acid afford compound **230** (equation 117) and 5-vinylnorbornene **231** is transformed into a mixture of *endo*- and *exo*-**232** (equation 118)[119].



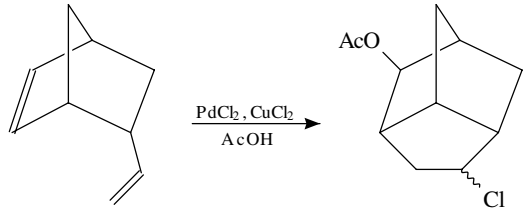
(116)

(229)



(117)

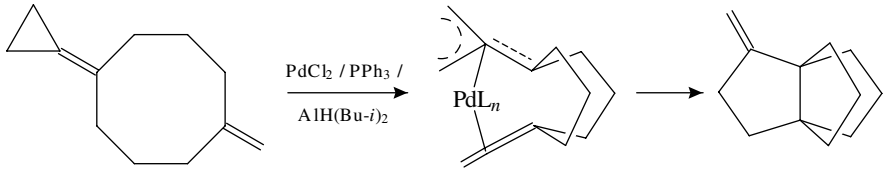
(230)



(118)

(231) **(232)**

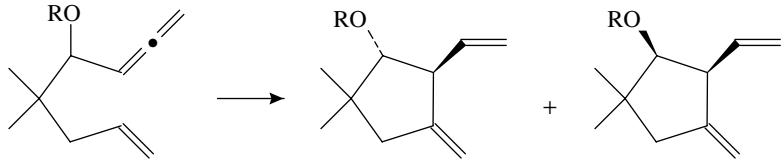
'Tandem cyclization' of 1-cyclopropylidene-5-methylenecyclooctane **(233)** with palladium(II) chloride/triphenylphosphine in the presence of diisobutylaluminium hydride leads to the [3.3.3]propellane **235** in 74% yield by way of the proposed intermediate **234** (L = ligand) (equation 119)[120].



(223) **(234)** **(235)** (119)

A nickel-chromium catalyst prepared from chromous chloride and (*p*-diphenylphosphinopolystyrene)nickel dichloride mediates the ring-closure of the ene-allene **236** (R = H) to a mixture of 3.4 parts of **237** and 1 part of **238** (equation 120)[121]. An analogous reaction of the *t*-butyldimethylsilyl ether of **236** yields solely the (*E*)-isomer **237** (R = *t*-BuMe$_2$Si). Cyclization of the ene-allene **239** affords the perhydroindane **240** in 72%

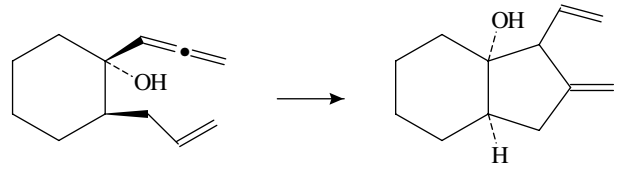
yield (equation 121)[121].



(120)

(236) **(237)** **(238)**

R = H, *t*-BuMe$_2$Si

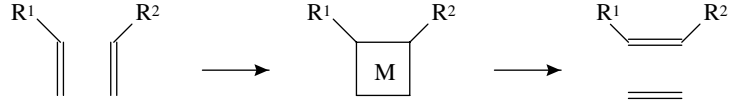


(121)

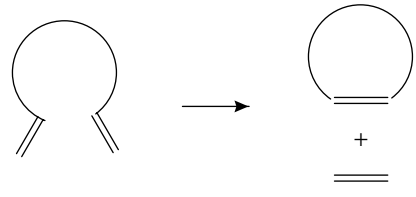
(239) **(240)**

X. RING-CLOSING METATHESES

The metal-catalysed olefin metathesis (equation 122) when applied to dienes results in ring-closure and expulsion of an olefin (equation 123). Thus the molybdenum carbene complex **241** promotes the decomposition of the 1,6-heptadiene derivative **242** to a mixture of the cyclopentene **243** and ethylene (equation 124)[122]. An analogous reaction of the alcohol **244** gives **245** (equation 125), and 4-benzyloxy-1,7-decadiene **(246)** affords the cyclohexene **247** and 1-butene (equation 126). These transformations, which occur in benzene at room temperature, proceed in excellent yields[122].

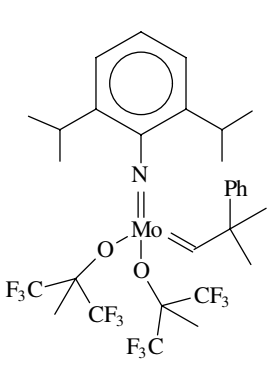


(122)

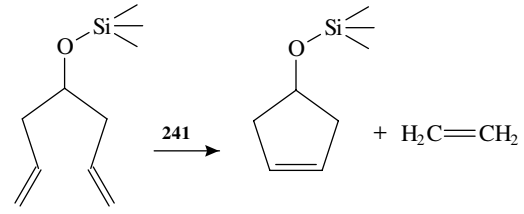


(123)

Metatheses of 1,7-octadienes containing various functional groups are catalysed by ruthenium carbene complexes of the type **248**. For instance, the alcohol **249** (R = CH_2OH), the aldehyde **249** (R = CHO) and the carboxylic acid **249** (R = CO_2H) are all converted into the corresponding cyclohexenes **250** in 82–88% yields (equation 127) and the heterocycles **252** (n = 0, 1 or 2) are efficiently produced from the amides **251** (equation 128)[123].

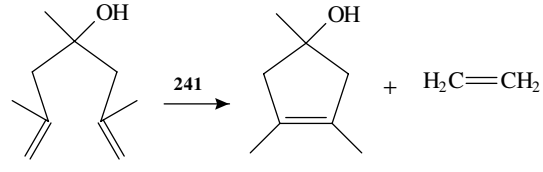


(241)



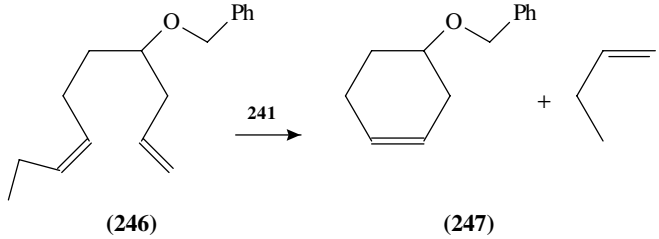
(242) **(243)**

(124)



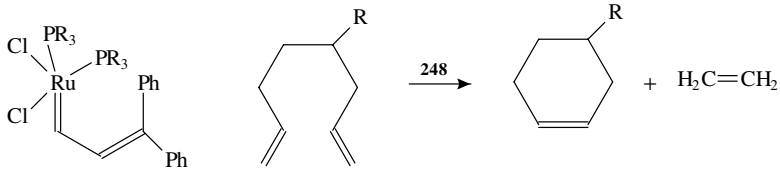
(244) **(245)**

(125)



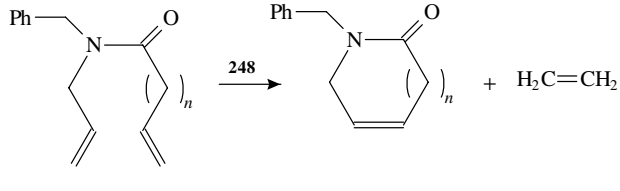
(246) **(247)**

(126)



(248) **(249)** **(250)**

(127)



(251) **(252)**

(128)

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The Chemistry of Dienes and Polyenes. Volume 1
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CHAPTER **12**

The effect of pressure on reactions of dienes and polyenes

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I. INTRODUCTION

Pressure in the range of 1–20 kbar (units of pressure: 1 kbar = 100 MPa = 0.1 GPa = 1013.25 atm) has a strong effect on rate and position of equilibrium of many chemical reactions. Processes accompanied by a decrease of volume are accelerated by pressure and the equilibria are shifted toward the side of products while those accompanied by an increase of volume are retarded and the equilibria are shifted toward the side of

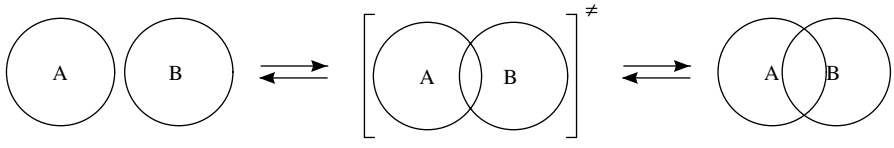
reactants. Therefore, the application of high pressure seems to be particularly useful in controlling the course of competitive and consecutive reactions and can lead to an improvement of chemo-, regio- and stereochemistry. In this chapter our major interest is focused on the effect of pressure on pericyclic reactions of dienes and polyenes in compressed liquid state or in compressed solution, including cycloadditions such as the most important Diels–Alder [4 + 2] cycloadditions of conjugated dienes, [2 + 2] cycloadditions of cumulated dienes, or higher cycloadditions involving trienes and tetraenes, as well as sigmatropic and electrocyclic rearrangements.

Processes with gaseous reactants are excluded here. Due to the large compressibility of gases an increase of pressure (up to 1 kbar) leads essentially only to an increase of gas concentration, and hence to an acceleration of bimolecular processes in which gases are involved as reactants. The effect of pressure on a chemical reaction in compressed solution is largely determined by the volume of reaction (ΔV) and the volume of activation ($\Delta V^{\neq}$). It is not the purpose of this chapter to provide a complete survey of reactions of dienes and polyenes which have been investigated at elevated pressures. There are many excellent monographs (e.g. References 1–4) and reviews (e.g. References 5–16) on this topic which cover the literature up to early 1990. After a short introduction into the basic concepts necessary to understand pressure effects on chemical processes in compressed solutions, our major objective is to review the literature of the past ten years.

II. VOLUME OF ACTIVATION AND REACTION

Static high pressure in the range of 1–20 kbar, frequently used for the investigation of organic reactions in compressed fluids or solids, can be generated with relatively simple devices[1,3]. A list of some suppliers delivering commercially available high-pressure equipment is cited[17]. Pressure influences the physical properties of matter such as boiling and melting point, density, viscosity, solubility, dielectric constant and conductivity. Before carrying out high-pressure experiments it is important to have some knowledge of these effects. The melting points of most liquids used as common solvents are raised by pressure (*ca* 15–20 °C per 1 kbar). Therefore it is necessary for a high-pressure experiment which is planned to be performed in solution, that a solvent is used which does not solidify under the chosen conditions. The solubility of gases in liquids is increased, and that of solids usually decreased, by raising the pressure. Therefore, the solid solutes of saturated solutions may precipitate during the generation of pressure and no longer be accessible for the reaction. The viscosity of liquids increases approximately twofold for each kilobar increase. Knowledge of this effect is particularly important for diffusion-controlled processes. Finally, the compressibility of liquids and solids is usually small compared to that of gases. For that reason experiments with compressed liquids and solids are far less dangerous than those with compressed gases. A detailed discussion of the pressure effect on physical properties of matter can be found in the literature[1].

The effect of pressure on chemical equilibria and rates of reactions can be described by the well-known equations resulting from the pressure dependence of the Gibbs enthalpy of reaction and activation, respectively, shown in Scheme 1. The volume of reaction (ΔV) corresponds to the difference between the partial molar volumes of reactants and products. Within the scope of transition state theory the volume of activation can be, accordingly, considered to be a measure of the partial molar volume of the transition state (TS) with respect to the partial molar volumes of the reactants. Volumes of reaction can be determined in three ways: (a) from the pressure dependence of the equilibrium constant (from the plot of $\ln K$ vs p); (b) from the measurement of partial molar volumes of all reactants and products derived from the densities, d, of the solution of each individual component measured at various concentrations, c, and extrapolation of the apparent molar volume Φ



Forward reaction: decrease of volume (ΔV, $\Delta V^{\neq} < 0$) $\Rightarrow$ accelerated by pressure

Reverse reaction: increase of volume (ΔV, $\Delta V^{\neq} > 0$) $\Rightarrow$ retarded by pressure

$$\Delta V = \left(\frac{\partial \Delta G}{\partial p}\right)_T = \left(\frac{-\partial \ln K_p}{\partial p}\right)_T \cdot RT \qquad \Delta V^{\neq} = \left(\frac{\partial \Delta G^{\neq}}{\partial p}\right)_T = \left(\frac{-\partial \ln k_p}{\partial p}\right)_T \cdot RT$$

ΔV, $\Delta V^{\neq}$: volumes of reactions and activation;
K_p: equilibrium constant at pressure p;
k_p: rate constant at pressure p;
ΔG, $\Delta G^{\neq}$: Gibbs enthalpy and Gibbs enthalpy of activation.

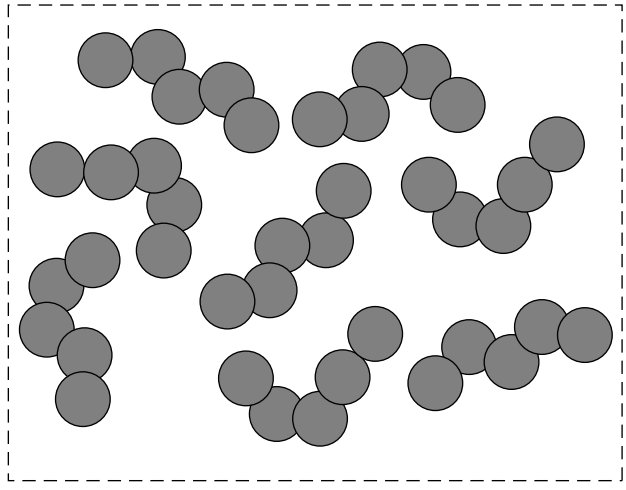
$$\Delta V = V(\mathrm{A-B}) - [V(\mathrm{A}) + V(\mathrm{B})]$$
$$\Delta V^{\neq} = V([\mathrm{A}\text{- - - - - B}]^{\neq}) - [V(\mathrm{A}) + V(\mathrm{B})]$$

SCHEME 1. Volumes of activation and reaction

vs c to $c = 0$. (Scheme 2); (c) from the direct measurement of the difference between the volumes of reactants and products employing dilatometry. To a first approximation the molar volume of neat liquid compounds ($V_M = M/d$) and, hence, the reaction volumes can be calculated with additive group increments which were derived empirically by Exner[18] for many groups such as CH_3, CH_2, or CH from the molar volumes, V_M, easily determined from the known densities for many different types of compounds. This method is comparable to that of the calculation of enthalpies of formation by the use of Franklin[19] or Benson[20] group increments. In all cases where the volume of reaction could be determined by at least two independent methods, the data were in good agreement[21].

Volumes of activation can be unambiguously determined only from the pressure dependence of the rate constants. Attempts to obtain volumes of activation from the correlation of rate constants with the solubility parameter δ[22] or the cohesive energy density parameter (ced)[23], which are related to the internal pressure of solvents, have not led to clear-cut results.

Volumes of activation and reaction are themselves also pressure-dependent as shown for the volume of activation in Figure 1. There is no theory explaining this pressure dependence which would allow the volume of activation or reaction to be determined over a larger range of pressure. Therefore, several empirical relations are employed to fit the pressure dependencies of rate and equilibrium constants[24] from which the least-squares fit [$\ln k(p) = a + b \cdot p$, $\ln k(p = 0) = a$, $\Delta V^{\neq} = -b \cdot R \cdot T$ or $\ln K(p) = a' + b' \cdot p$, $\ln K(p = 0) = a'$, $\Delta V = -b' \cdot RT$] is the simplest and in many cases also the most reliable method of computing $\Delta V^{\neq}$ and ΔV. It is only applicable in the low-pressure range (<2000 bar) where the dependencies of $\ln k(p)$ or $\ln K(p)$ on pressure p are usually linear. Thus, this method requires a very precise measurement of the rate constants at relatively low-pressures (1–2000 bar) where the pressure effect on the rate constants is relatively



V_W: van der Waals volume ($cm^3\,mol^{-1}$)
(intrinsic molar volume of ground and transition structures)

V_M: molar volume ($cm^3\,mol^{-1}$)
(empty space included) $V_M = \dfrac{M}{d}$

V: partial molar volume ($cm^3\,mol^{-1}$) $V = \lim\limits_{c \to 0} \Phi$ $\Phi = \dfrac{M}{d_0} - \dfrac{1}{c} \cdot \dfrac{d - d_0}{d_0}$

η: packing *coefficient* $\eta = \dfrac{V_W}{V_M}$

M ($g\,mol^{-1}$): molar mass of the solute
d ($g\,cm^{-3}$): density of the solution
d_0 ($g\,cm^{-3}$): density of the pure solvent
c (mol^{-1}): concentration of the solute

SCHEME 2. Van der Waals volumes, partial molar volumes and packing coefficients

small. If data over a larger pressure range are to be used, nonlinear least-squares fits have to be applied[24]. Due to the pressure dependence of $\Delta V^{\neq}$ and ΔV we need to select a pressure to which volumes of activation and reaction refer, so that the values can be compared with one another. The choice has universally been that of zero pressure ($p = 0$). The values of activation volumes calculated at $p = 0$ differ only by immeasurably small amounts from those at atmospheric pressure ($p \approx 1$ bar), so that comparison with the reaction volumes, calculated from the partial molar volumes of the reactants and products determined at atmospheric pressure, is feasible.

Processes accompanied by a decrease in volume, such as C−C bond formation, in which the distance between two carbon atoms decreases from the van der Waals distance of *ca* 3.6 Å to the bonding distance of *ca* 1.5 Å, are accelerated by raising the pressure and equilibria are shifted toward the side of products ($\Delta V^{\neq} < 0$, $\Delta V < 0$). The reverse reaction, a homolytic bond cleavage, leads to an increase in volume ($\Delta V^{\neq} > 0$, $\Delta V > 0$). Pressure induces a deceleration of such a process and a shift in equilibrium toward the side of reactants. However, in an ionization, such as an ionic dissociation, the attractive interaction between the ions generated and the solvent molecules leads to a contraction

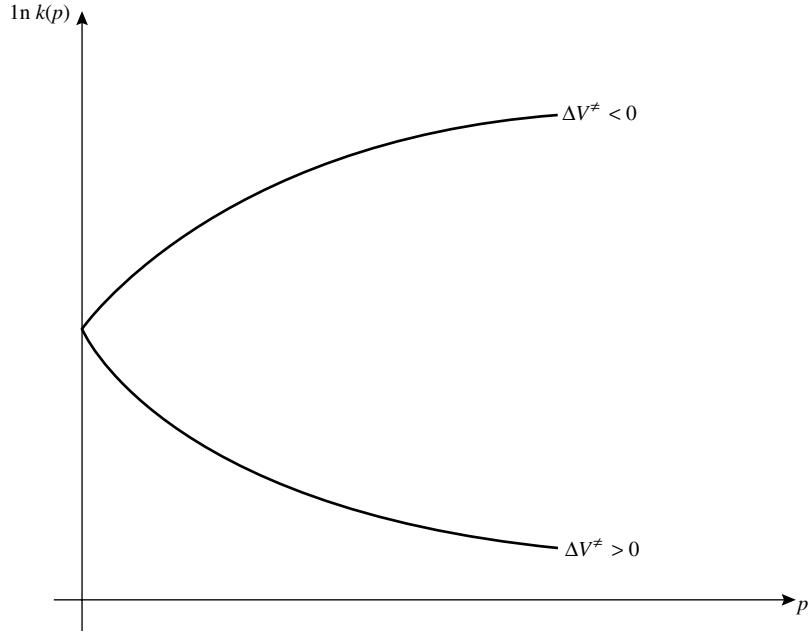


FIGURE 1. Nonlinear slope of the dependence between rate of reaction $\ln k(p)$ and pressure p

of the solvent cage, and hence of the volume, that is generally much stronger than the expansion of volume resulting from the bond dissociation. Thus, the overall dominant effect, called *electrostriction*, leads to negative volumes of activation and reaction ($\Delta V^{\neq} < 0$, $\Delta V < 0$). Neutralization of charges releases the molecules of the solvent cage, leading to positive volumes of activation and reaction ($\Delta V^{\neq} > 0$, $\Delta V > 0$). A similar but less pronounced trend due to the effect of *electrostriction* is observed for charge concentration and charge dispersal, respectively. An increase in steric crowding in the transition or product states results in a volume contraction ($\Delta V^{\neq} < 0$, $\Delta V < 0$). Finally, in the case of diffusion control the rate of reaction depends on the viscosity of the medium. As already pointed out, pressure induces an increase in the dynamic viscosity and, hence, a deceleration of diffusion-controlled processes ($\Delta V^{\neq} > 0$).

As noted earlier for the generation and neutralization of charges, the change in the intrinsic volumes of the reacting molecules is responsible for the overall change in molar volumes observed experimentally only to a minor extent. Similar conclusions can be drawn, e.g., for neutral pericyclic rearrangements, from the comparison of the volumes of activation and reaction determined experimentally with the change in the intrinsic volumes of the reacting molecules discussed in Section IV. The intrinsic volume of a ground or transition structure is defined by the space occupied by the atomic *van der Waals* spheres and can be obtained by numerical integration employing the atomic cartesian coordinates resulting from experimental data, molecular mechanics or quantum mechanical calculations and the *van der Waals* radii [e.g. $R_W(C) = 1.80$ Å, $R_W(H) = 1.17$ Å] derived from crystallographic data[25]. The intrinsic volumes of ground structures can also be calculated from tables of group contributions published by Bondi[26]. The *van der Waals* volume V_W is the intrinsic volume of a ground or transition structure multiplied by

Avogadro's number. The ratio V_W/V_M is defined as the packing coefficient η. The packing coefficients calculated from the V_W and V_M values of simple hydrocarbons[25a] are in the range $\eta = 0.5$ to 0.6. The empty space between the single molecules can be attributed to the so-called void volume and expansion volume required for the thermally induced motions and collisions of the molecules in the liquid state[27]. The importance of change in the packing coefficient and, hence, in the void and expansion volume for the effect of pressure on a reaction will be discussed in the following sections.

III. CYCLOADDITIONS

A. Intermolecular Diels–Alder Reactions

1. Mechanistic aspects

Many Diels–Alder [4 + 2] cycloadditions show a powerful pressure-induced acceleration, which is often turned to good synthetic purpose as discussed in Section III.A.2. Table 1 illustrates the effect of pressure on the Diels–Alder reaction of isoprene with acrylonitrile as a representative example. This reaction is accelerated by a factor of 1650 by raising the pressure from 1 bar to 10 kbar[28].

The activation volumes of many Diels–Alder reactions obtained from the pressure dependence of the rate constants are usually highly negative, $\Delta V^{\neq} \approx -25$ to -50 cm^3 mol^{-1} (Tables 2 and 3); sometimes they are even more negative than the corresponding reaction volumes. For a comparison between volumes of activation and reaction it is necessary to determine both data at the same temperature which is, however, not feasible in most cases. The measurement of pressure dependence of rate constants frequently requires a temperature different from that used for the determination of partial molar volumes of reactants and products (in general, room temperature). Therefore, activation volumes have to be extrapolated to room temperature or the reaction volumes, correspondingly, to the temperature of reaction. The measurement of the temperature dependence of activation volumes requires a large collection of experimental data. To the best of our knowledge only one case, the Diels–Alder dimerization of isoprene, has been reported in the literature[29]. With modern thermostated densimeters it is much easier to determine the temperature dependence of partial molar volumes, and hence of reaction volumes. From these data El'yanov and coworkers[30] extrapolated a generally applicable equation (equation 1) to describe the temperature dependence of activation and reaction volumes. The dependence determined for the isoprene dimerization[29] is in accord with the El'yanov equation.

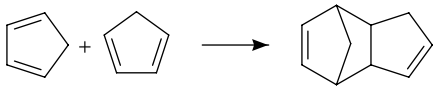
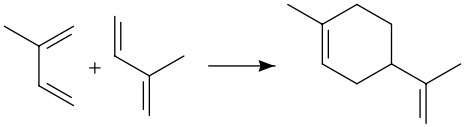
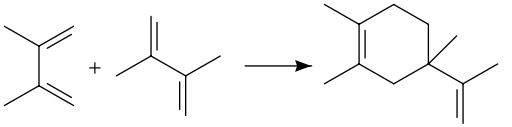
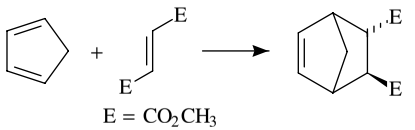
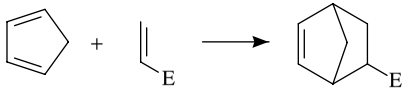
$$\Delta V^{\neq}_{25} = \Delta V^{\neq}_{T}/[1 + 4.43 \times 10^{-3}\ \mathrm{K}^{-1}(T - 25\,^{\circ}\mathrm{C})] \tag{1}$$

In Table 2 Diels–Alder reactions are complied showing ratios of activation volume to reaction volume that are smaller than or close to unity ($\Theta = \Delta V^{\neq}/\Delta V \leqslant 1$) and in Table 3 those that are close to or even larger than unity ($\Theta \geqslant 1$). Within the scope of transition state theory, the activation volume can be considered to be a measure of the partial molar volume of the transition state [$\Delta V^{\neq} = V^{\neq} - \Sigma V$ (reactants)]. Accordingly, the transition state volumes of these reactions are close to or even smaller than the

TABLE 1. Pressure-induced rate acceleration of the Diels–Alder reaction of isoprene with acrylonitrile at 21 °C ($\Delta V^{\neq} = -35.4$ cm^3 mol^{-1}, $\Delta V = -37.0$ cm^3 mol^{-1})[28]

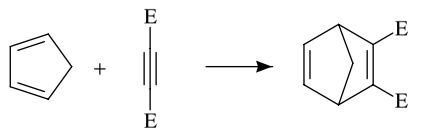
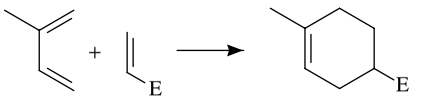
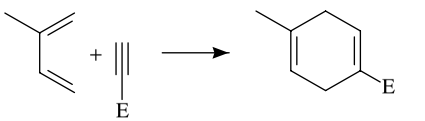
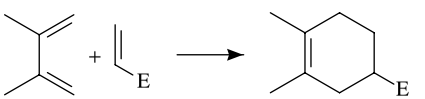
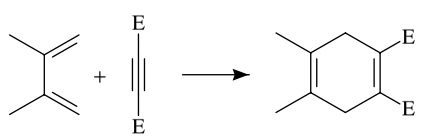
p (bar)	1000	1500	2000	3000	5000	8000	10 000
$k(p)/k$ (1 bar)	3.4	7.0	10.5	24.4	74.4	561	1650

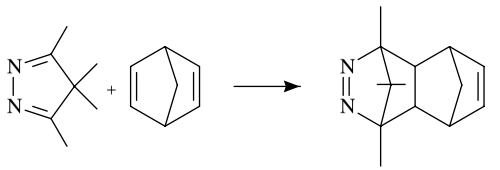
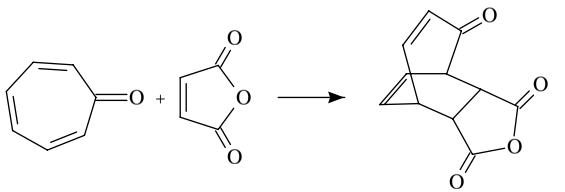
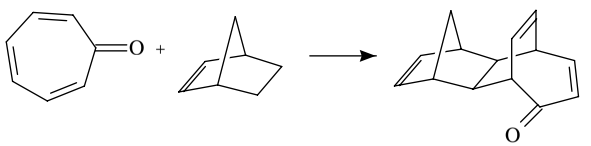
TABLE 2. Volume data of selected Diels–Alder reactions showing ($\Delta V^{\neq}$: ΔV) ratios smaller than unity ($\Theta < 1$)

	Reaction	Solvent	T(°C)	$\Delta V_T^{\neq a}$	$\Delta V_{25}^{\neq a}$	$\Delta V_{25}{}^{a}$	Θ^{b}	Reference
(1)		*n*-BuCl	40	−23.7	−22.2	−33.0	0.67	31
(2)			70	−42.0	−35.0	−47.8	0.73	32
(3)		*n*-BuBr	70	−33.0	−27.5	−44.9	0.61	33
(4)	 E = CO_2CH_3		30	−32.7	−32	−36.7	0.87	31
(5)		*n*-BuCl	40	−30.1	−28.3	−33.5	0.84	31

(*continued overleaf*)

TABLE 2. (*continued*)

	Reaction	Solvent	T(°C)	$\Delta V_T^{\neq a}$	$\Delta V_{25}^{\neq a}$	$\Delta V_{25}{}^a$	Θ^b	Reference
(6)		$MeCO_2Et$	10	−30.2	−32.2	−36.1	0.89	34
(7)		*n*-BuBr	25	−31.5	−31.5	−37	0.85	35
(8)		CH_2Cl_2	82	−43	−34.6	−39.5	0.88	36
(9)		*n*-BuCl	40	−30.2	−28.3	−34.7	0.82	31
(10)		*n*-BuCl	58	−39.1	−34.1	−38.8	0.88	36

(11)		MePh	130	−41.0	−28.0[c]	−28.8[c]	0.97	37
(12)		DMF	105	−16.8	−14.0[d]	−25.5[d]	0.55	38
(13)		*i*-PrPh	135	−30.0	−22.5[d]	−33.5[d]	0.67	38
		DMF	135	−27.8	−20.9[d]	−32.1[d]	0.65	

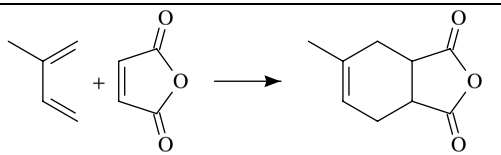
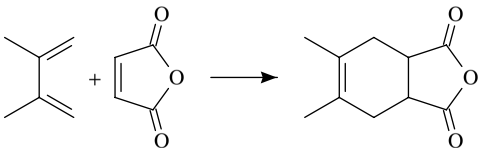
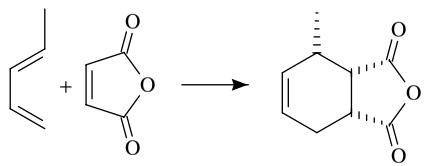
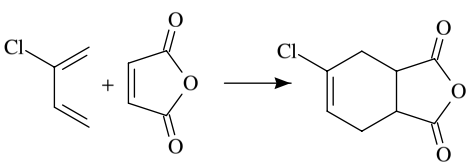
[a] In $cm^3\ mol^{-1}$; $\Delta V_T^{\neq}$ determined from the pressure dependence of the rate constant at temperature T; $\Delta V_{25}^{\neq}$ determined from the temperature dependence of the activation volumes (entry 2) or generally extrapolated by using equation 1.

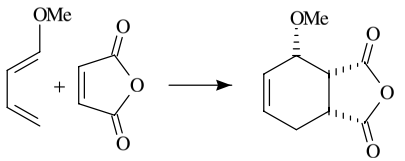
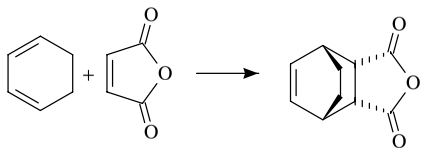
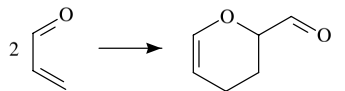
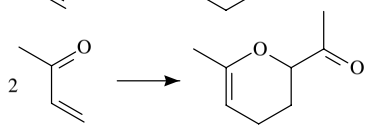
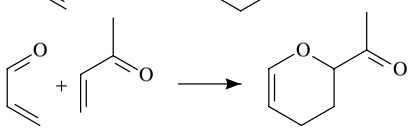
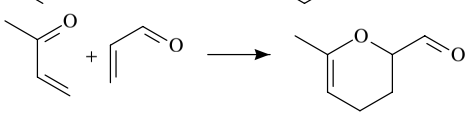
[b] $\Theta = \Delta V_{25}^{\neq} : \Delta V_{25}$.

[c] At 20 °C.

[d] At 60 °C.

TABLE 3. Volume data of selected Diels–Alder reactions showing ($\Delta V^{\neq}$: ΔV) ratios equal to or larger than unity ($\Theta > 1$)

	Reaction	Solvent	T(°C)	$\Delta V_T^{\neq a}$	$\Delta V_{25}^{\neq a}$	$\Delta V_{25}{}^a$	Θ^b	Reference
(1)		$(i\text{-Pr})_2O$		−38.5	−36.9	−38.3	0.96	
		Me_2CO		−39.0	−37.3	−35.9	1.04	
		MeCN		−37.5	−35.9	−34.5	1.04	
		n-BuCl	35	−38.0	−36.4			39
		AcOEt		−37.4	−35.8	−36.8	0.97	
		$ClCH_2CH_2Cl$		−37.0	−35.4	−35.5	0.99	
		CH_2Cl_2		−39.8	−38.1	−33.4	1.14	
(2)		*n*-BuCl	30	−41.3	−40.4	−35.5	1.14	31
(3)		*n*-BuCl	35	−44.7	−42.8	−31.9	1.22	31
(4)		MeCN	65	−41.6	−35.3	−36.9	0.96	31

(5)		MeCN		−32.0	−30.6	−32.4	0.94	
		$(MeO)_2CH_2$		−53.6	−51.3	−32.2	1.6	
		n-BuCl	35	−45.4	−43.5	−35.5	1.23	40
		$MeNO_2$		−43.7	−41.2	−28.2	1.46	
		$ClCH_2CH_2Cl$		−43.7	−41.8	−30.4	1.37	
(6)		CH_2Cl_2	35	−37.2	−35.6			41
(7)		*n*-C_7H_{16}	70	−37.0	−30.8	−28.6	1.08	42
(8)		*n*-C_7H_{16}	70	−41.0	−34.2	−32.3	1.06	42
(9)		*n*-C_7H_{16}	70	−36.5	−30.4			42
(10)		*n*-C_7H_{16}	70	−35.0	−29.2	−29.7	0.98	42

[a] In $cm^3\ mol^{-1}$; $\Delta V_T^{\neq}$ determined from the pressure dependence of the rate constant at temperature T; $\Delta V_{25}^{\neq}$ extrapolated by using equation 1.

[b] $\Theta = \Delta V_{25}^{\neq} : \Delta V_{25}$.

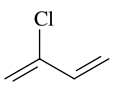
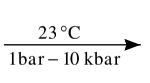
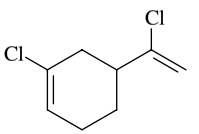
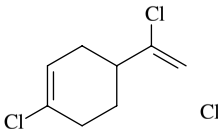
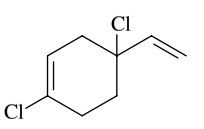
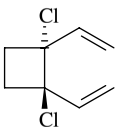
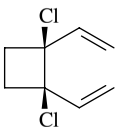
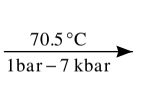
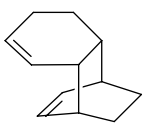
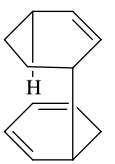
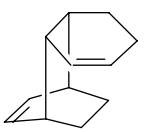
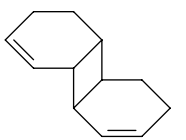
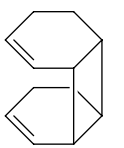
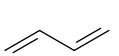
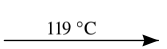
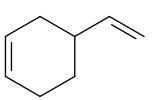
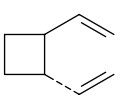
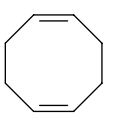
corresponding product volumes. The surprising result, that in some Diels–Alder reactions the transition state is smaller in volume than the product, could be confirmed by the *retro*-Diels–Alder reactions of the furan-acrylonitrile[43] and *N*-benzoylpyrrole-*N*-phenylmaleic imide[44] [4 + 2] cycloadducts which are both accelerated by pressure, having therefore negative volumes of activation ($\Delta V^{\neq} = -2.0$ and -8.3 cm^3 mol^{-1}, respectively). The *retro*-Diels–Alder reaction of dihydrobarrelene (bicyclo[2.2.0]octa-2,5-diene) leading to benzene and ethene is, however, retarded by pressure ($\Delta V^{\neq} = +3.1$ cm^3 mol^{-1})[45].

The finding that in several Diels–Alder reactions the transition state volume is smaller than the product volume is not well understood, and seems to contradict the generally accepted relation between molecular structure and its volume. In the transition state the new bonds between diene and dienophile are only partially formed (according to quantum mechanical calculations, the distance of the newly forming σ bonds in the transition state is in the range between 2.1 and 2.3 Å[46]). Therefore, the van der Waals volumes of the transition states are calculated to be generally larger than those of the products (*vide infra*). Eckert and coworkers[47] gave two explanations for the ratio $\Theta = \Delta V^{\neq}/\Delta V > 1$ in the Diels–Alder reactions with maleic anhydride as dienophile: viz. a larger dipole moment and secondary orbital interactions[48] in the transition state which can only occur in the transition states of *endo*-Diels–Alder reactions. The dipole moment of the transition state in the reaction of isoprene with maleic anhydride (entry 1 in Table 3) was estimated to be 1.6 Debye larger than that of maleic anhydride, but almost equal to that of the product. Thus, the effect of *electrostriction* should be operative to a similar extent in the transition state and product and may not explain the observed difference between $\Delta V^{\neq}$ and ΔV. Therefore, the authors concluded that secondary orbital interactions must be the primary reason for the more negative activation volume. But Seguchi, Sera and Maruyama[49] observed a very small difference between the activation volumes of *endo*- and *exo*-Diels–Alder reactions (e.g. reaction of 1,3-cyclopentadiene with dimethyl maleate: $\delta\Delta V^{\neq} = \Delta V^{\neq}(endo) - \Delta V^{\neq}(exo) = 0.8$ cm^3 mol^{-1}). This finding seems to rule out that secondary orbital interactions are important and induce a large contraction of the transition state volume in the *endo* reaction. Therefore, this issue remains unresolved. As we shall discuss later, the molecular packing of the entire ensemble consisting of solute and solvent molecules and its reorganization during the course of reaction are most important for the magnitude of activation and reaction volume. An effective packing of molecules around the globular transition state (which may also be due to restricted vibrations and rotations) may contribute to the observed differences between $\Delta V^{\neq}$ and ΔV of the Diels–Alder reactions listed in Table 3.

The observation that the transition state volumes in many Diels–Alder reactions are product-like, has been regarded as an indication of a concerted mechanism. In order to test this hypothesis and to gain further insight into the often more complex mechanism of Diels–Alder reactions, the effect of pressure on competing [4 + 2] and [2 + 2] or [4 + 4] cycloadditions has been investigated. In competitive reactions the difference between the activation volumes, and hence the transition state volumes, is derived directly from the pressure dependence of the product ratio, $[4 + 2]/[2 + 2]_p = [4 + 2]/[2 + 2]_{p=1} \cdot \exp\{-\delta\Delta V^{\neq} \cdot (p - 1)/\mathrm{RT}\}$. All [2 + 2] or [4 + 4] cycloadditions listed in Tables 3 and 4 doubtlessly occur in two steps via diradical intermediates and can therefore be used as internal standards of activation volumes expected for stepwise processes. Thus, a relatively simple measurement of the pressure dependence of the product ratio can give important information about the mechanism of Diels–Alder reactions.

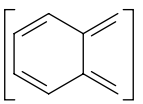
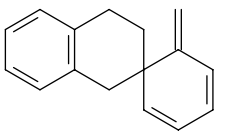
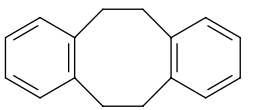
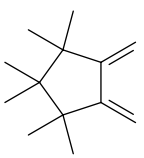
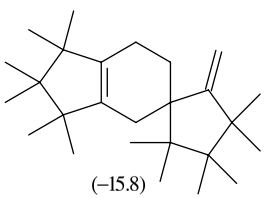
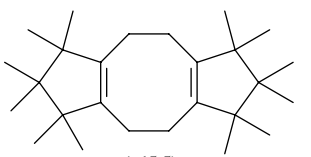
In the thermal dimerization of chloroprene **1** (Table 4, entry 1) the activation volumes for two [4 + 2] cycloadditions leading to **2** and **3** were found to be smaller (more negative) than those of the third [4 + 2] and the [2 + 2] cycloadditions leading to **4**, **5** and **6**, respectively. Stewart[50] explained these results in terms of concerted Diels–Alder

TABLE 4. Activation volumes $\Delta V^{\neq}$ ($cm^3\ mol^{-1}$), given in parentheses, and differences in activation volumes $\delta\Delta V^{\neq}[= \Delta V^{\neq}(4+2) - \Delta V^{\neq}(2+2)]$ ($cm^3\ mol^{-1}$) of competing [4 + 2] and [2 + 2] or [4 + 4] cyclodimerizations

Reaction	[4+2] Cycloadducts ($\Delta V^{\neq}$)	[2+2] or [4+4] Cycloadducts ($\Delta V^{\neq}$)	$\delta\Delta V^{\neq}$	Reference
(1) 2  **(1)**  23 °C, 1 bar – 10 kbar	 **(2)** (–31)  **(3)** (–29)  **(4)** (–22)	 **(5)** (–22)  **(6)** (–22)	–9 –7 0	50
(2) 2  **(7)**  70.5 °C, 1 bar – 7 kbar	 **(8)** (–28)  **(9)**[a] (–32)  **(10)** (–22)	 **(11)** (–18)  **(12)** (–22)	–10[b] –14[c] 0[d]	51
(3) 2  **(13)**  119 °C, 600 – 5300 bar	 **(14)** (–38.4)	 **(15)** (–20.9)  **(16)** (–34.0)	–17.5[e] –4.4[f]	52

(*continued overleaf*)

TABLE 4. (*continued*)

Reaction	[4+2] Cycloadducts ($\Delta V^{\neq}$)	[2+2] or [4+4] Cycloadducts ($\Delta V^{\neq}$)	$\delta\Delta V^{\neq}$	Reference
(4) 2  80 °C, 1–6800 bar			–5	53
(5) 2  79.1 °C, 550–9300 bar	 (–15.8)	 (–15.5)	–0.3	54

[a] [6 + 4]-Ene reaction.
[b] $\Delta V^{\neq}$(**8**) − $\Delta V^{\neq}$(**11**).
[c] $\Delta V^{\neq}$(**9**) − $\Delta V^{\neq}$(**11**).
[d] $\Delta V^{\neq}$(**10**) − $\Delta V^{\neq}$(**12**).
[e] $\Delta V^{\neq}$(**14**) − $\Delta V^{\neq}$(**15**).
[f] $\Delta V^{\neq}$(**14**) − $\Delta V^{\neq}$(**16**).

reactions competing with stepwise [2 + 2] cycloadditions. According to its larger (less negative) activation volume, the third Diels–Alder dimer **4** should be also formed in nonconcerted fashion. Similarly, it can be concluded from the pressure dependence of the 1,3-cyclohexadiene dimerization (Table 4, entry 2) that the *endo*-Diels–Alder dimer **8** and the [6+4]ene product **9** are formed concertedly while the *exo*-Diels–Alder adduct **10** and [2+2] cyclodimers **11** and **12** arise via diradical intermediates. According to the activation volume data, the Diels–Alder dimerization of 1,3-butadiene and *o*-quinodimethane (Table 4, entries 3 and 4, respectively) also fall into the class of concerted processes while the [4 + 2] cyclodimerization of hexamethyl bis(methylene)cyclopentane (entry 5) seems to occur in a stepwise fashion. In Table 5 only the Diels–Alder reaction of 1,3-butadiene with α-acetoxyacrylonitrile (entry 1) seems to proceed concertedly while all other Diels–Alder adducts and *homo*-Diels–Alder adducts are probably formed in stepwise processes comparable to the corresponding competitive [2 + 2] cycloadditions. Stereochemical investigations of the chloroprene and 1,3-butadiene dimerization[52] with specifically deuteriated derivatives [(*E*)-1-deuteriochloroprene and (*Z*, *Z*)-1,4-dideuterio-1,3-butadiene] confirm the conclusions drawn from the activation volumes. As suggested by the activation volumes, the nonstereospecific course of the [4 + 2] dimerization of (*E*)-1-deuteriochloroprene leading to deuteriated **4** provides clear-cut evidence that this reaction proceeds in a stepwise fashion, while the almost stereospecific course of the [4 + 2] dimerization of (*Z*, *Z*)-1,4-dideuterio-1,3-butadiene provides good evidence for a predominant concerted mechanism in competition with a small amount of stepwise reaction, which can be almost completely suppressed by high pressure.

One question that needs to be addressed is: why are the activation volumes of pericyclic reactions smaller (more negative) than those of the corresponding stepwise reactions? In the past it was assumed that the simultaneous formation of two new σ bonds in a pericyclic [4 + 2] cycloaddition leads to a larger contraction of volume than the formation of one bond in the rate-determining transition state of a stepwise process. The interpretation presented[52] is limited by the scope of the Eyring transition state theory where the activation volume is related to the transition state volume, as mentioned above, and does not incorporate dynamic effects related to pressure-induced changes in viscosity[63a,b]. In a very recent study of the pressure effects on the thermal *Z*/*E* isomerization of substituted azobenzenes and *N*-benzylideneanilines in a viscous solvent, T. Asano and coworkers[63c] found that the pressure effects observed in the lower pressure region ($p \leqslant 2$ kbar) were in accordance with transition state theory. At higher pressure, however, the effects of the further increasing viscosity become predominant and all reactions (also those which were first accelerated by an increase of pressure) were retarded.

For the pericyclic and stepwise cycloadditions of ethene to 1,3-butadiene (the prototype of Diels–Alder reactions) the van der Waals volumes V_W of ground and transition structures shown in Table 6 were calculated following the method of Nakahara and coworkers[25a] and compared with the corresponding molar volumes *V* in order to uncover the effect of the different bonding on the volumes of transition states. The packing coefficient η, defined as the ratio V_W/V of cyclohexene, is significantly larger than those of the three isomeric hexadienes. Generally, η is found to be larger for cyclic compounds than for the corresponding acyclic ones.

From the data listed in Table 6 the *van der Waals* volume of the Diels–Alder reaction[13,25,52,65] can be calculated to be with $\Delta V_W = -11.2$ cm^3 mol^{-1} only roughly one-quarter of the experimentally accessible volume of reaction ($\Delta V = -41.7$ cm^3 mol^{-1}) (Scheme 3). Consequently, a significant part of the observed ΔV results from the higher packing of the cyclic product (compared to the acyclic reactants) rather than from the changes in bonding. The difference between the *van der Waals* volume of activation calculated for the pericyclic and stepwise reaction is small ($\delta\Delta V_W^{\neq} = -1.7$ cm^3 mol^{-1}) and is inconsistent with the experimental data listed in Tables 4 and 5. In order to explain

TABLE 5. Activation volumes $\Delta V^{\neq}$ ($cm^3\,mol^{-1}$), given in parentheses, and differences in activation volumes $\delta\Delta V^{\neq}$ ($cm^3\,mol^{-1}$) of competing [4 + 2] and [2 + 2] cycloadditions

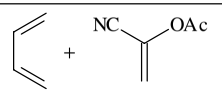
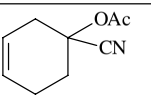
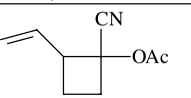
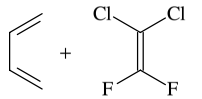
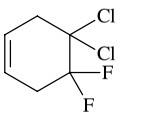
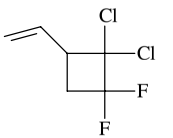
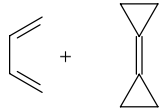
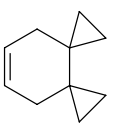
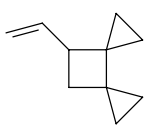
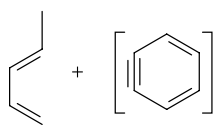
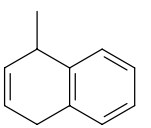
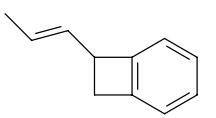
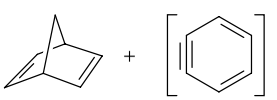
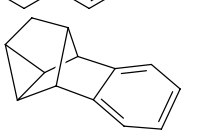
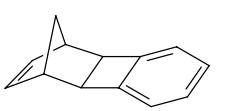
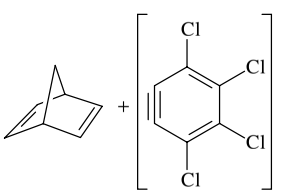
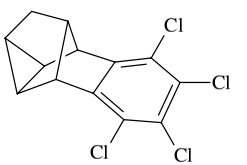
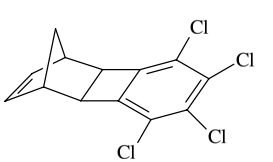
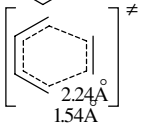
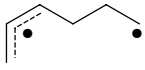
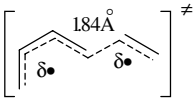
Reaction	[4+2] Cycloadducts	[2+2] or [4+4] Cycloadducts	$\delta\Delta V^{\neq}$	Reference
(1) 			–11.5	55,56
(2) 			0	56,57
(3) 			–2	58,59
(4) 			0	59,60
(5) 			0	59,61
(6) 			–0.7	62

TABLE 6. Comparison between molar volumes V, van der Waals volumes V_w ($cm^3\,mol^{-1}$) and packing coefficients η for selected examples of acyclic and cyclic ground and transition states

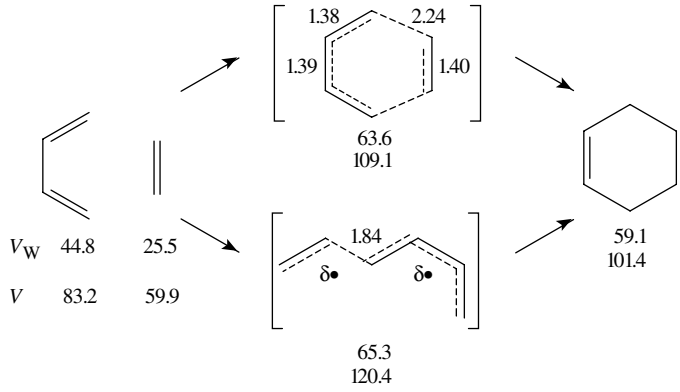
Compound	d	$V = M/d^a$	$V_w^{a,b}$	$\eta = V_w/V$
$CH_2{=}CH_2$		59.9[c]	25.5	0.4257
$CH_2{=}CH{-}CH{=}CH_2$		83.2[c]	44.8	0.5385
$CH_2{=}CH{-}CH_2{-}CH_2{-}CH{=}CH_2$	0.6880	119.4	63.9	0.5354
$CH_2{=}CH{-}CH_2{-}CH{=}CH{-}CH_3$	0.7000	117.7	63.9	0.5443
$CH_2{=}CH{-}CH{=}CH{-}CH_2{-}CH_3$	0.7050	116.5	63.8	0.5475
	0.8102	101.4	59.1	0.5829
		109.1[d]	63.8	0.5829
		118.7[e]	64.4	
		120.4[e]	65.3	0.5424

[a] In $cm^3\,mol^{-1}$.
[b] For the calculation of van der Waals volumes, cartesian coordinates resulting for ground structures from molecular mechanics calculations[64a] and for transition structures from *ab initio* calculations[64b] and the following van der Waals radii were used: $R_w(H) = 1.17$ Å; $R_w(C) = 1.80$ Å.
[c] Calculated with volume increments[18].
[d] With the packing coefficient of cyclohexene ($\eta = 0.5829$).
[e] Calculated with the average of the packing coefficients determined for the three isomeric hexadienes ($\eta = 0.5424$).

the finding that the activation volume of a pericyclic reaction is significantly more negative than that of the corresponding stepwise process, it has been assumed[13,52] that the packing coefficient of the pericyclic transition state is similar to that of the cyclic product, and therefore larger than the packing coefficient of the acyclic transition state of the stepwise process. The difference between the activation volumes calculated by using the packing coefficients of cyclohexene and the average of the three hexadienes (Table 6) for the transition states of the pericyclic and stepwise Diels–Alder reactions, respectively, is with $\delta\Delta V^{\neq} = -11$ $cm^3\,mol^{-1}$ (Scheme 3) well in accord with the experimental findings (Tables 4 and 5). Therefore, the analysis of activation volumes seems to provide important information regarding whether the geometry of a transition state is cyclic or acyclic. The conclusions drawn from this simple analysis are strongly supported by Monte Carlo simulations resulting in activation and reaction volumes for the Diels–Alder reaction of ethene with 1,3-butadiene and the dimerization of 1,3-butadiene[52]. The analysis of packing coefficients also explains why pericyclic rearrangements are accelerated by pressure showing negative volumes of activation (see below).

2. Synthetic application

The powerful pressure-induced acceleration of most Diels–Alder reactions due to their highly negative volumes of activation has been exploited for synthetic purposes. Reviews



$$\Delta V_W = 59.1 - (44.8 + 25.5) = -11.2 \text{ cm}^3 \text{ mol}^{-1}$$
$$\Delta V_W^{\neq} = 63.6 - (44.8 + 25.5) = -6.7 \text{ cm}^3 \text{ mol}^{-1} \text{ (pericyclic process)}$$
$$\Delta V_W^{\neq} = 65.3 - (44.8 + 25.5) = -5.0 \text{ cm}^3 \text{ mol}^{-1} \text{ (diradical process)}$$
$$\delta\Delta V_W^{\neq} = -1.7 \text{ cm}^3 \text{ mol}^{-1}$$

$$\Delta V = 101.4 - (83.2 + 59.9) = -41.7 \text{ cm}^3 \text{ mol}^{-1}$$
$$\Delta V^{\neq} = 109.1 - (83.2 + 59.9) = -34.0 \text{ cm}^3 \text{ mol}^{-1} \text{ (pericyclic process)}$$
$$\Delta V^{\neq} = 120.4 - (83.2 + 59.9) = -22.7 \text{ cm}^3 \text{ mol}^{-1} \text{ (diradical process)}$$
$$\delta\Delta V_W^{\neq} = -11.3 \text{ cm}^3 \text{ mol}^{-1}$$

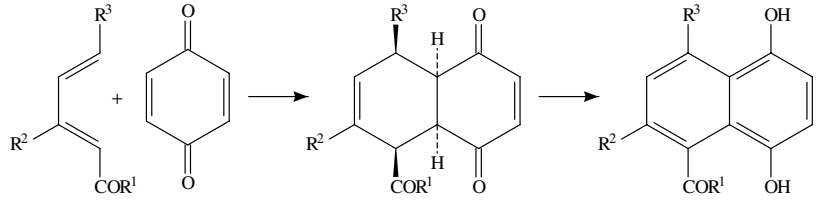
SCHEME 3. Comparison of van der Waals volumes of reaction and activation with the volumes of reaction and activation calculated for a pericyclic and stepwise Diels–Alder reaction of 1,3-butadiene with ethene

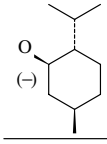
on the synthetic application of pressure-induced Diels–Alder reactions can be found in Chapter 11 on Synthesis by J. Jurczak in Reference 2, in Chapters 9 and 10 by T. Ibata on Diels–Alder reactions of alicyclic and acyclic dienes and of heterocyclic dienes, respectively, in Reference 3 and in References 9 and 11. In this chapter we only survey the more recent literature.

At atmospheric pressure the Diels–Alder adducts of 1,4-benzoquinones are often not stable under the conditions of reaction and undergo an isomerization leading to the corresponding hydroquinones (Scheme 4). Due to the acceleration at high pressure the temperature of reaction can be lowered so that the secondary isomerization does not proceed and the primary Diels–Alder adduct can be isolated in good yields. The diastereoselectivity at high pressure induced by a chiral auxiliary, however, is with a diastereomeric excess of d.e. = 36%, only moderate.

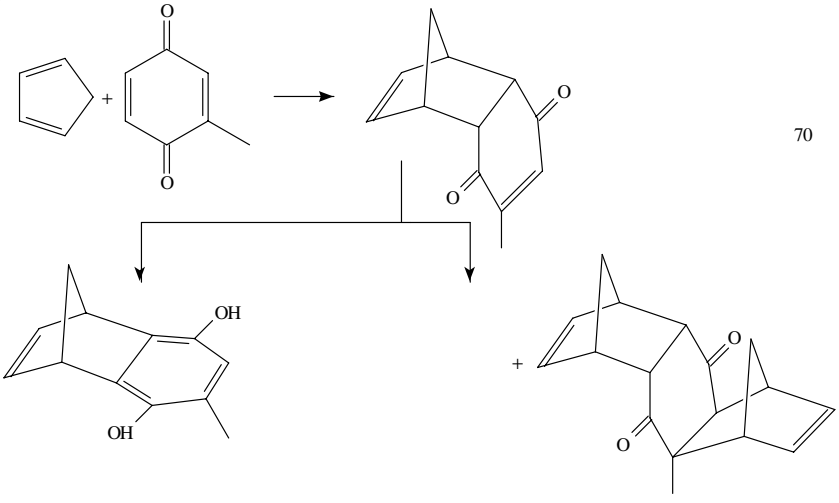
Diels–Alder reactions with acyclic and carbocyclic dienes are compiled in Scheme 5. The comparison between the Lewis-acid catalyzed and pressure-induced reaction (entry 1) shows that the application of high pressure, particularly in acid-sensitive systems, can sometimes lead to a better yield. Furthermore, pressure may shift the product ratio, if the activation volumes of the competing reactions are different, so that the application of pressure may also be useful in highly reactive systems, e.g. the reactive indenone **17** as dienophile, provided that a shift in the product ratio is desired. At atmospheric

(1)



R^1	R^2	R^3		Yield		Reference
OMe	Et	H	1 bar, 80 °C, 65 h	–	only product to be isolated	66
			15 kbar, 20 °C, 3 h	60%		67, 68
OEt	H	CH_2OSiMe_3	15 kbar, 20 °C, 65 h	84%		
OEt	H	Me	1 bar, 80 °C, 24 h	no reaction		67, 68
			15 kbar, 20 °C, 18 h	92%		
 (–)	H	H	15 kbar, 20 °C, 22 h	58%; d.e. 36%		69

(2)



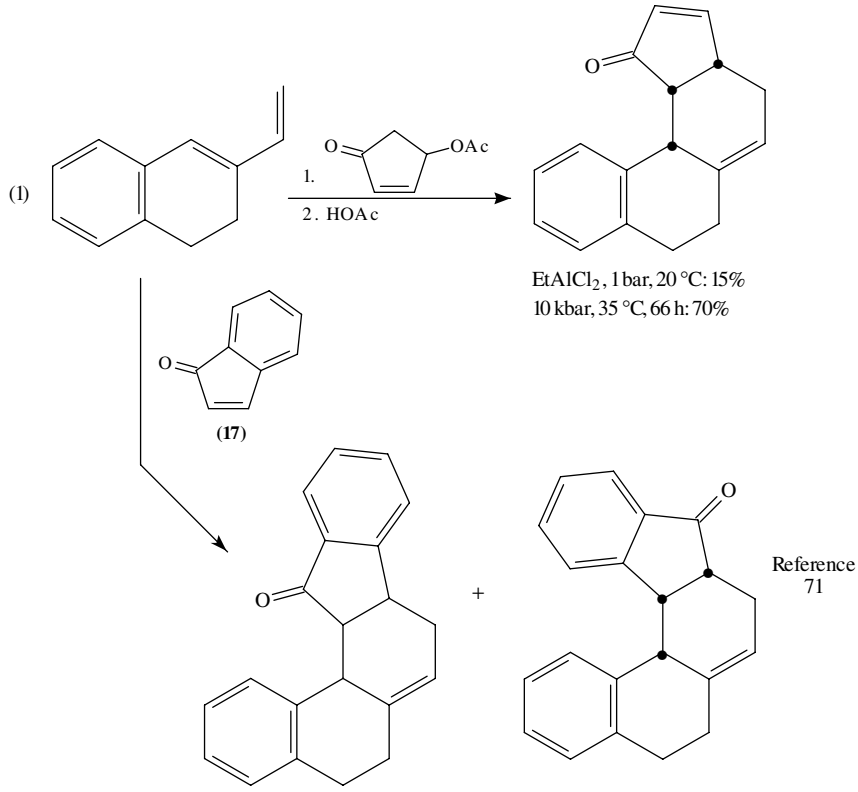
70

7-8 kbar, 75-80 °C;	4	:	1
1bar, 75-80 °C;	no bisadducts		

SCHEME 4. Diels–Alder reactions with 1,4-benzoquinones as dienophiles

pressure and 130 °C the Danishefsky diene[79] reacts with the polyfunctional dienophile (entry 2) in the fashion of a *hetero*-Diels–Alder reaction leading, after elimination of methanol during the work-up, to dihydropyrones as major products. At 10 kbar a reaction, leading, however, to a carbocyclic adduct, proceeds readily at room temperature. The example in entry 2 illustrates that pressure can be an important tool to control selectivity

in competitive processes. The next example in entry 3 shows that this can also be the case for consecutive reactions. Cyanoacetylene is only a moderate dienophile reacting, for example, with 1,3-cyclohexadiene only at a temperature of *ca* 100 °C at which the primary Diels–Alder adduct is thermally not stable and undergoes a *retro*-Diels–Alder reaction, producing benzonitrile and ethene. At high pressure the reaction occurs already at lower temperatures. Under these conditions the primary adduct is stable and can be isolated in good yields. A similar effect of pressure was observed in the thermal trimerization of cyanoacetylene producing 1,2,4- and 1,2,3-tricyanobenzene as major products at 160 °C and atmospheric pressure[80]. At 12 kbar the trimerization occurs already at 40 °C, leading to the thermally labile 2,3,5-tricyano-Dewar benzene as major product which isomerizes to 1,2,4-tricyanobenzene upon heating to a temperature ⩾50 °C. The high-pressure results are good evidence that the thermal trimerization of cyanoacetylene occurs by a sequence of reactions consisting of a [2 + 2] cycloaddition (producing the

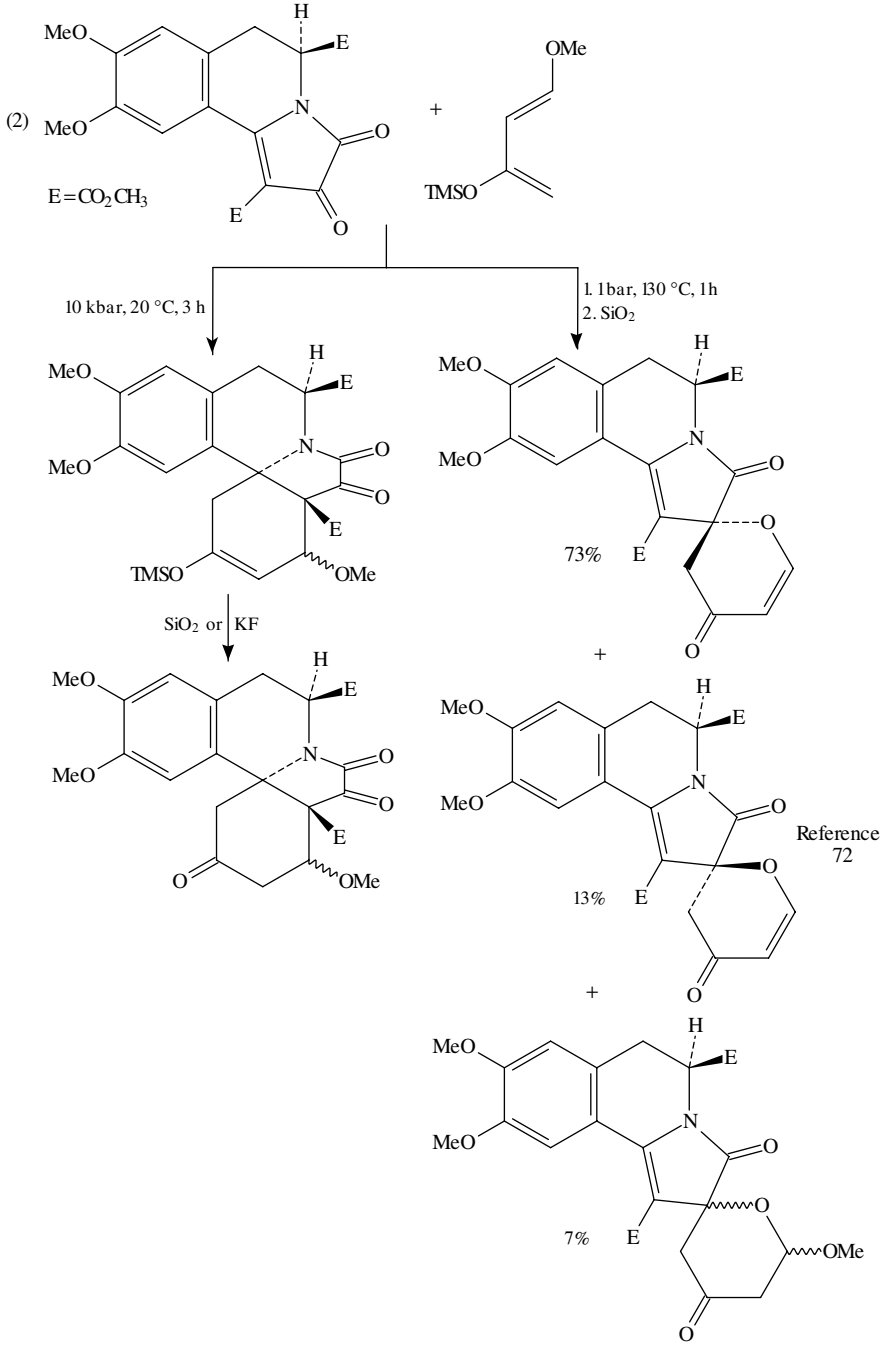


17[a], 1 bar, CCl_4 (reflux), 3 h:	1	:	5	(76%)
17[a], 7 kbar, CCl_4 (reflux), 3 h:	1	:	3	(75%)
17[b], 7 kbar, CCl_4, 50 °C, 3 h:	1	:	1	(70%)

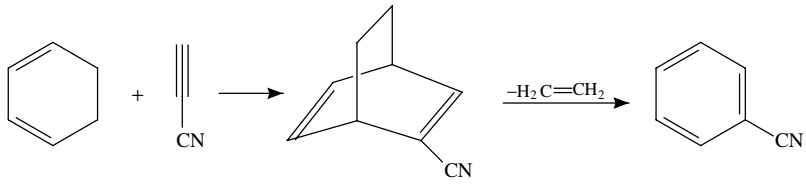
[a]Generated in situ from 2-bromindanone and Et_3N.

[b]Isolated **17** as starting material.

SCHEME 5. Diels–Alder reactions with acyclic and carboxyclic dienes

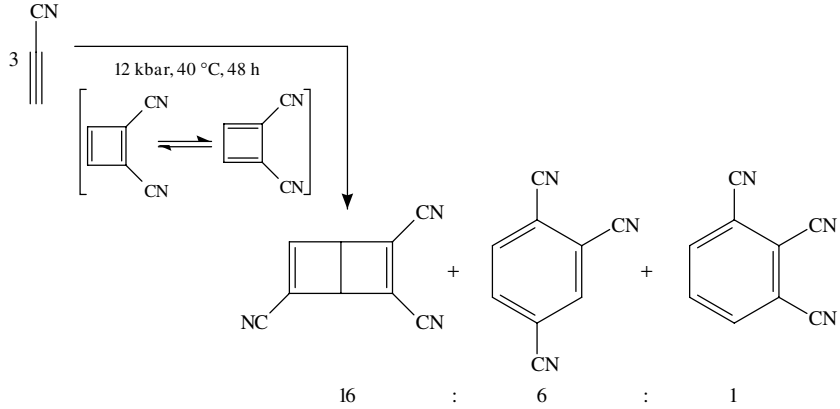


SCHEME 5. (*continued*)



1 bar, 100 °C, 24 h: 6% 68%
9.4 kbar, 50 °C, 24 h: 87% 0%

(3) Reference 73



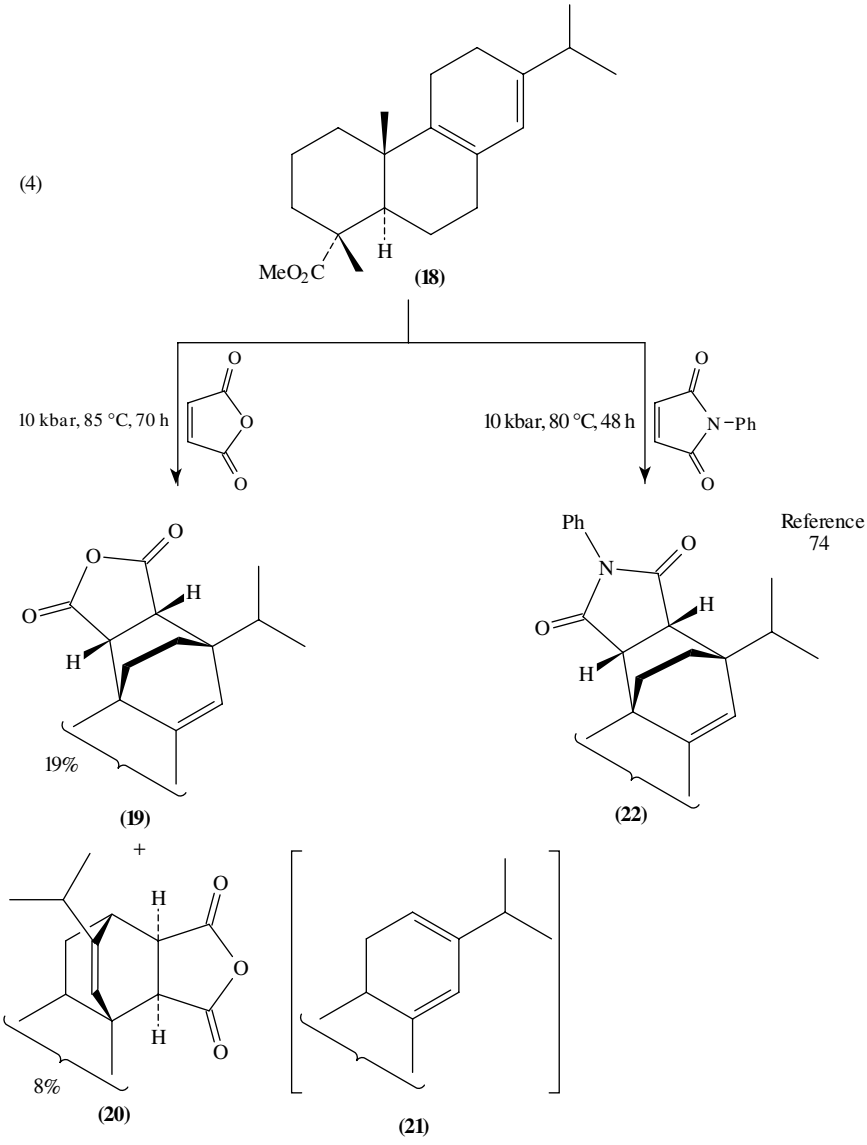
16 : 6 : 1

SCHEME 5. (*continued*)

highly reactive 1,2-dicyanocyclobutadiene), a Diels–Alder reaction of the cyclobutadiene intermediate with an excess of cyanoacetylene (leading to Dewar benzenes like the isolated 2,3,5-tricyano derivative) and an aromatization of Dewar benzenes yvia orbital symmetry-forbidden electrocyclic ring-opening.

The partially hydrogenated phenanthrene derivative **18** (entry 4) is a very moderate diene due to the steric crowding caused by the substituents and the anulated rings, and it reacts even with highly reactive dienophiles such as maleic anhydride (MA) or N-phenylmaleic imide only at high pressure. The minor product **20** in the reaction with MA obviously stems from diene **21**. This can be explained by a double-bond isomerization **18** → **21** prior to the cycloaddition, certainly catalyzed by traces of acid present in the MA. In the absence of acid only the Diels–Alder adduct **22** derived from diene **18** was observed. In the reaction of diene **23** with MA (entry 5) a similar sequence of steps was observed. A [1,5] shift of the C−O bond in **23**, again certainly acid-catalyzed, produces the diene **26** followed by the Diels–Alder reaction with MA to give **24** and **25**.

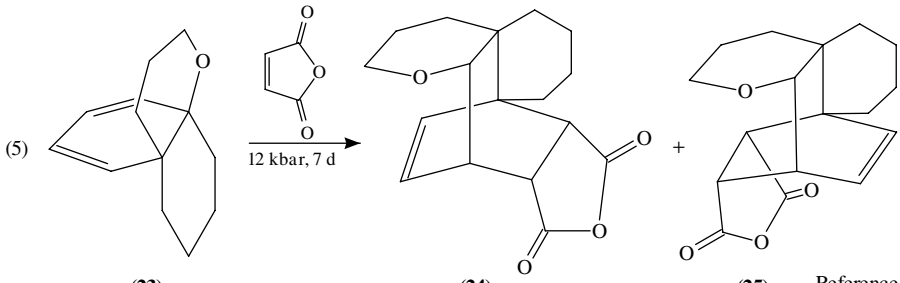
The effect of pressure on pericyclic additions of cycloheptatriene (entry 6) to various olefins [such as tetracyanoethene (TCNE), acrylonitrile, dimethyl acetylenedicarboxylate (DMAD), methyl propiolate and diethyl azocarboxylate] reacting as dienophiles or enophiles was studied by Jenner and Papadopoulos.[76,77] All reactions are strongly accelerated by pressure and show a larger selectivity at high pressure than at atmospheric pressure. At high pressure generally the Diels–Alder adducts derived from the valence tautomeric norcaradiene form are favored over the adducts resulting from an initial ene reaction to the cycloheptatriene followed by a valence bond isomerization and a subsequent Cope rearrangement, as shown for the reaction of cycloheptatriene with DMAD. In this case the preference of the Diels–Alder reaction at high pressure can be



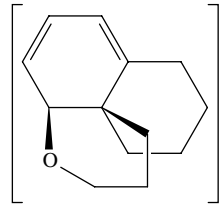
SCHEME 5. (*continued*)

rationalized by the observation that in the Diels–Alder reaction the volume of activation is more negative because the number of cyclic interactions is larger in the transition state of the Diels–Alder reaction than in that of the ene reaction (*vide infra*).

Generally, benzene and naphthalene derivatives show only little reactivity as dienes in Diels–Alder synthesis, contrary to anthracene and the higher acene derivatives which are frequently used as dienes. Exceptions are the reactions of benzene and naphthalene derivatives with highly reactive dienophiles such as dicyanoacetylene (DCA), which



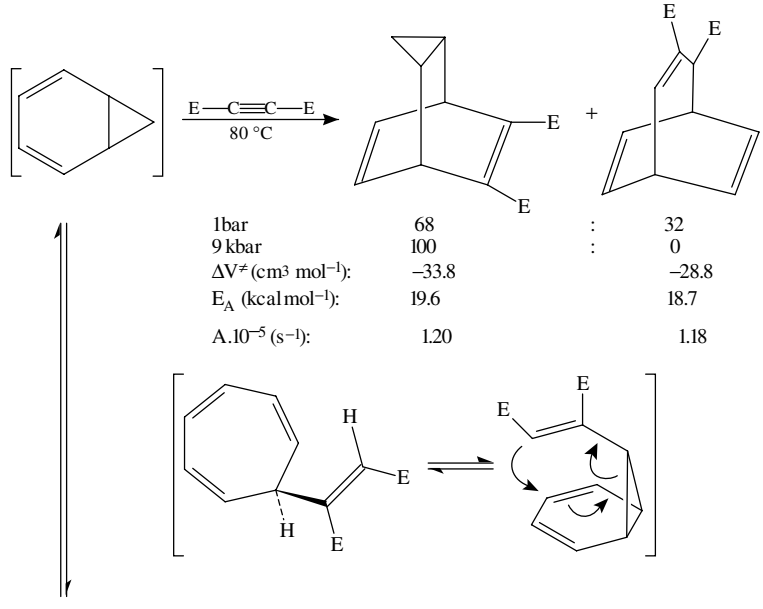
(23) **(24)** 19% **(25)** 34% Reference 75



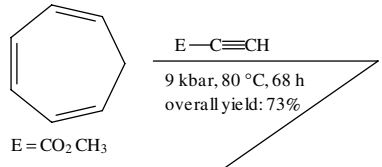
(26)

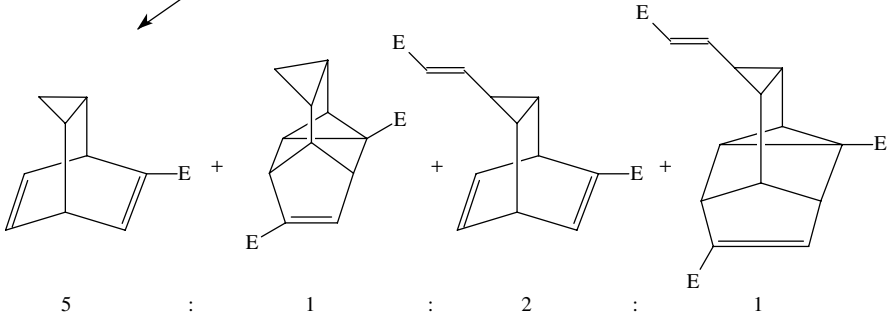
SCHEME 5. (*continued*)

require either high temperatures (180 °C) or a Lewis-acid catalyst ($AlCl_3$) at 25 °C[80,81]. Strained benzene derivatives like [2.2]paracyclophane react with DCA thermally at lower temperatures (120 °C)[81,82]. One reason why Diels–Alder reactions with benzenoid aromatics are rare is probably the unfavorable $T\Delta S$ term which causes the equilibrium to be shifted toward the reactants at the high temperatures which are necessary in these cases for the progress of the reaction. High pressure has two favorable effects on these reactions: the equilibrium is shifted by pressure toward the products due to the highly negative volumes of reaction, and the rate of reaction is enhanced due to the highly negative volumes of activation so that the temperature of the reaction can be lowered and the unfavorable $T\Delta S$ term becomes less important. An early example is the Diels–Alder cycloaddition of naphthalene to maleic anhydride (MA) leading to a mixture of *endo*- and *exo*-adduct which proceeds only at high pressure[83]. According to a more recent investigation, the precipitation of the adducts under the high-pressure conditions seems to be the main reason why this reaction is shifted toward the adducts which can be isolated in high yields[84]; [2.2]paracyclophane (Scheme 6: entry 1) reacts with MA and various maleic imide derivatives to give the *endo*- and *exo*-(1:2)-Diels–Alder adducts only at high pressure. At atmospheric pressure no reaction was observed up to 180 °C. An interesting case is the reaction of azulene and its derivatives **27** with DMAD (entry 2) which occurs at atmospheric pressure only at temperatures of about 200 °C to produce the diester-substituted heptalenes of type **29** in some reactions. At high pressure azulenes **27** already react with DMAD between 30 and 50 °C to give Diels–Alder adducts of type **28** which undergo rearrangement to the heptalenes **29** and cycloreversion to **27** as well. According to a recent investigation by Hansen and coworkers[88], the rearrangement **28** → **29** proceeds through the zwitterionic and tricyclic intermediates **30** and **31** and not through a diradical intermediate as proposed in the original publications[86,87]. Azulenes **32** and **33** were formed in few cases. The highly reactive benzyne adds to azulene in a Diels–Alder



(6) Reference 76–78

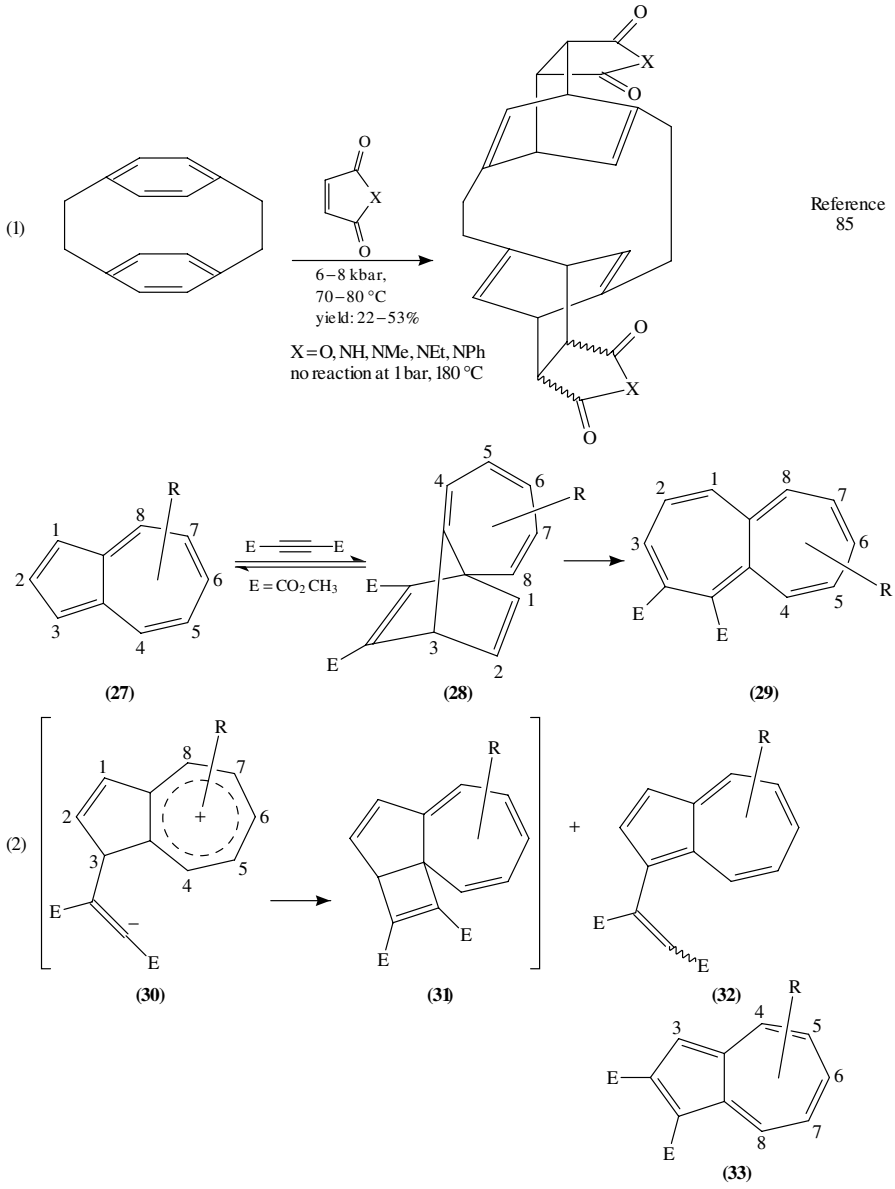




SCHEME 5. (*continued*)

fashion already at atmospheric pressure[89]. The Diels–Alder adducts of type **28** contain an almost planar cycloheptatriene ring. Therefore, they are also interesting for structural purposes concerning, for example, the question of homoaromaticity[90].

11-Methylene-1,6-methano[10]annulene **34** reacts with dicyanoacetylene (DCA) at 60 °C and atmospheric pressure producing the (1:1) Diels–Alder adduct at low conversion (<10%). The latter is not stable under the conditions of the reaction and undergoes a



SCHEME 6. Diels–Alder reactions with benzoid and nonbenzoid aromatic carbocycles as diene

cycloreversion leading to phthalonitrile and phenylacetylene as final products (Scheme 7). The strained methylenecyclopropabenzene **35** suggested as one primary product of the cycloreversion could not be detected. At 7 kbar the (1:1) adduct shows entirely different reactions leading to the formation of two (2:1) adducts **36** and **37** and no cycloreversion. The pressure-induced addition of DCA to the (1:1) adduct is obviously controlled by the

Compound	R	Conditions of reaction	Yields (%) (related to the turnover of the azulene)		Reference
			28	**29**	
27a	H	7 kbar, 50 °C, 67 h	39	11	86, 87
27b	1-Me	6.9 kbar, 50 °C, 67 h	50	13	86, 87
		7 kbar, 30 °C, 68 h	24	—	88
27c	4,6,8-Me_3	6.5 kbar, 50 °C, 68 h	—	30[a]	86, 87
27d	3,6-Me_2	7 kbar, 30 °C, 48 h	25		88
27e	1,4,6-Me_3	7 kbar, 30 °C, 48 h	7		88
27f	1,5,7-Me_3	7 kbar, 30 °C, 61 h	22		88
27g	1,4,6,8-Me_4	7 kbar, 30 °C, 69 h	41[b]		88
27h	1,4-Me_2, 7-*i*-Pr	5.5 kbar, 30 °C, 95 h	62[c]	8	88
27i	1,2,4,6,8-Me_5	7 kbar 30 °C 42 h	38		88
27k	1,2,4,8-Me_4, 6-*t*-Bu	7 kbar, 30 °C, 66 h	40		88

[a] 40% of **32c** and 4% of **33c**
[b] 8% of **32g**
[c] 15% of **32h**.

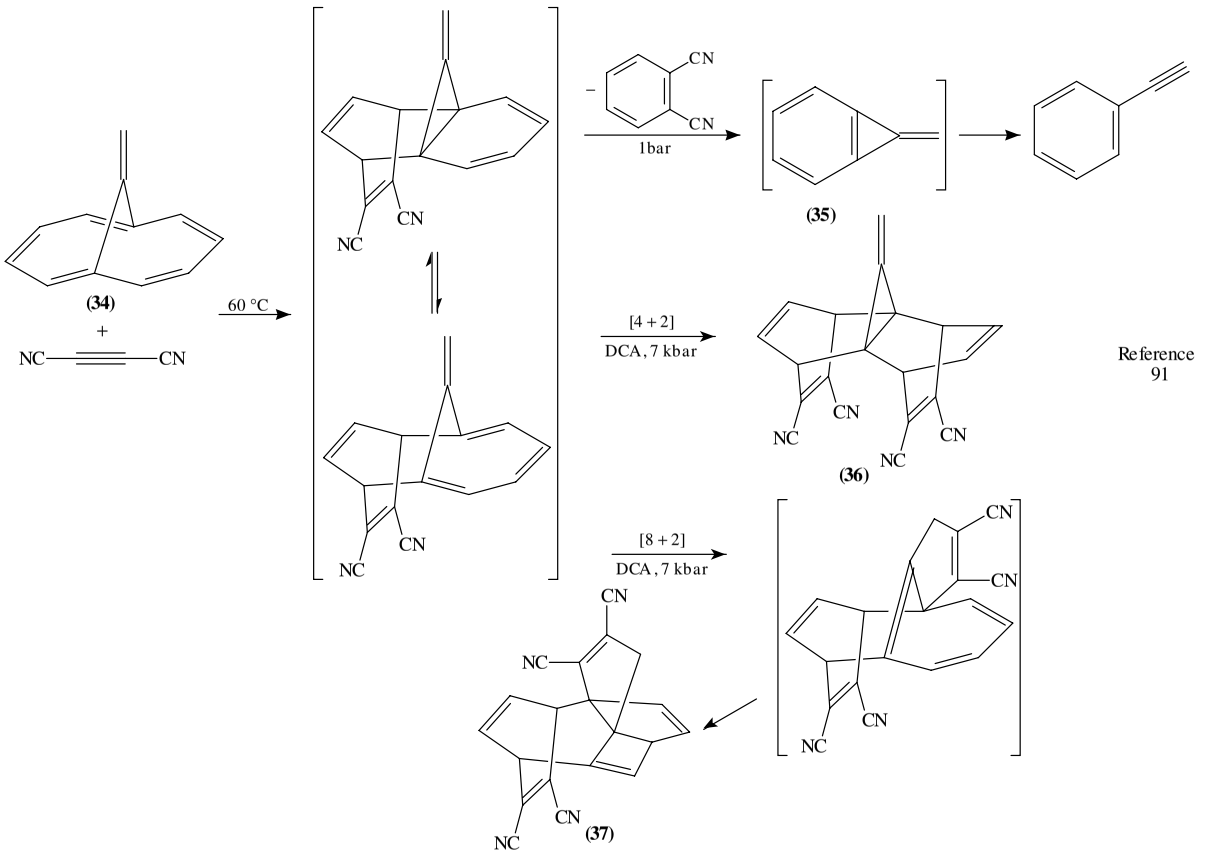
SCHEME 6. (*continued*)

(with respect to the NMR time scale) rapid equilibrium between the valence tautomeric bridged norcaradiene and the heptafulvene structure. [4 + 2] cycloaddition of DCA to the norcaradiene moiety leads to the symmetrical (2:1) adduct **36**, while [8 + 2] cycloaddition of DCA to the heptafulvene moiety followed by an electrocyclization leads to the unsymmetrical adduct **37**.

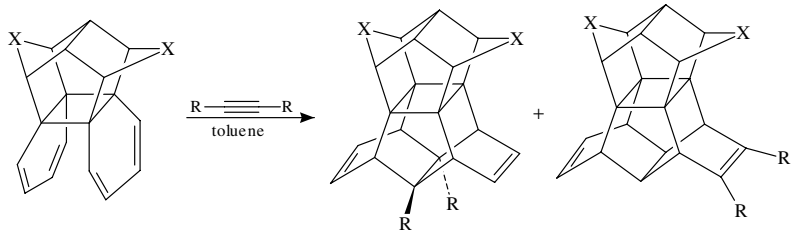
Scheme 8 shows examples of competitive 'pincer' and 'domino' cycloadditions with *syn-o,o′*-dibenzene derivatives **38**. The selectivity depends strongly on the nature of the acetylenic dienophile as well as of the *syn-o,o′*-dibenzene derivative. Preferential formation of the 'pincer' **39** adduct and of the 'domino' adduct **40** occurs, respectively, with DCA (entry 1) or DMAD (entry 2). The approach of the linear DCA to the center of the two cyclohexadiene rings may be supported by noncovalent interaction between the orthogonal π-bonds of DCA and the inner faces of the electron-rich cyclohexadiene units while the sterically larger ester groups may prevent this orientation. Thus, DMAD approaches preferentially from the outer face of one cyclohexadiene unit. In the reaction of DCA with the dibenzo-substituted bis-diene (entry 3), one of the benzene rings can successfully compete with one cyclohexadiene ring to complex DCA, so that the formation of the 'domino' adduct **40** is favored. High pressure induces a large rate enhancement but no significant change in selectivity. This finding supports the conclusion that either the 'pincer' or the 'domino' cycloaddition consists of two consecutive Diels–Alder reactions.

The synthesis of the macrocycles **43** (Scheme 9) is an example of repetitive, highly stereoselective Diels–Alder reaction between bis-dienes **41** and bis-dienophiles **42**, containing all oxo or methano bridges *syn* to one another. The consecutive inter- and intramolecular Diels–Alder reactions only succeed at high pressure. Obviously, both reactions are accelerated by pressure. The macrocycles are of interest in supramolecular chemistry (host–guest chemistry) because of their well-defined cavities with different sizes depending on the arene spacer-units.

If the oxo (or methano) bridges are not exclusively *syn* to one another in either the bis-dienophiles or bis-dienes, then the pressure-induced repetitive Diels–Alder reactions (proceeding again highly stereoselectively) produce rigid ribbon-type oligomers on a nanometer scale (Scheme 10: entry 1). Bis-diene **45** reacts less stereoselectively than bis-diene **44** and forms with bis-dienophiles such as **46** the ribbon-type oligomers **47**



SCHEME 7. Competition between cycloadditions and *retro*-Diels–Alder reactions in the reaction of dicyanoacetylene and 11-methylene-1,6-methano[10]annulene



(38) 'pincer' **(39)** 'domino' **(40)**

		T(°C)	time (h)	**39**	:	**40**
(1)	X = CH_2, R = CN					
	1 bar	100	4	74	:	26
	12 kbar	25		85	:	15
(2)	X = CH_2, R = CO_2CH_3					
	1 bar	100	80	3	:	97
	14 kbar	25		3	:	97
(3)	X = *o*-C_6H_4, R = CN					
	1 bar	25		0	:	100
	1 bar	80		4	:	96
	1 bar	100		12	:	88
	14 kbar	25		0	:	100

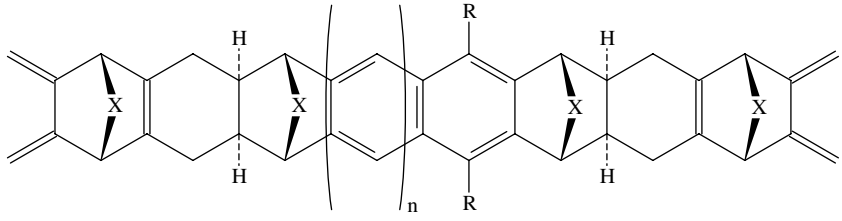
SCHEME 8. Competition between 'pincer' and 'domino' Diels–Alder reactions in the synthesis of pagodane precursurs[92]

with long chain-lengths (Scheme 10: entry 2). The more flexible ribbon-type structures **50** can be obtained by repetitive Diels–Alder reactions of bis-diene **48** with DMAD as bis-dienophile (Scheme 10: entry 3). The cage compound **49** is formed in an undesired side-reaction. The application of high pressure leads here to a larger conversion of starting materials and to a higher degree of polymerization.

All Diels–Alder reactions of tropones **51** as dienes with different types of dienophiles shown in Scheme 11 are accelerated by pressure, so that in some cases the desired cycloadducts are only formed at high pressure. An interesting synthetic equivalent of the unreactive acetylene in Diels–Alder syntheses is the oxanorbornadiene derivative **52** (Scheme 11: entry 2). **52** reacts with tropones forming the adducts **53, 54** and **55**, which undergo a *retro*-Diels–Alder reaction leading to **56** and **57**, the formal [4+2] cycloadducts of tropones to acetylene.

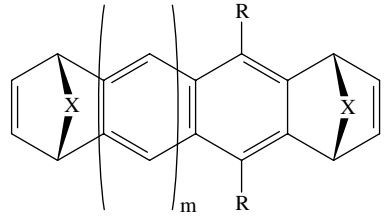
Buckminsterfullerene C_{60} generally reacts as electron-deficient dienophile or dipolarophile in numerous Diels–Alder or 1,3-dipolar cycloadditions[103]. The rates of reaction are again enhanced by an increase of pressure so that the yields are usually better at high pressure than at atmospheric pressure (Scheme 12).

The heteroaromatic compounds like furans, pyrroles or thiophenes cannot be generally used as dienes in Diels–Alder syntheses, because at the higher temperature required for the addition of less reactive dienophiles, the equilibrium is on the side of the starting materials due to the unfavorable $T\Delta S$ term comparable to the benzenoid aromatic compounds as mentioned. High pressure again shows the two effects already discussed: the shift of the equilibrium toward the products and the enhancement of the rate of reaction which allows the temperature of reaction to be lowered. One



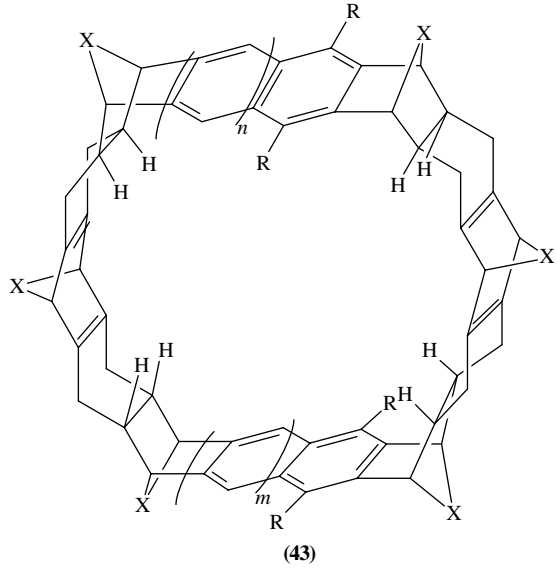
(41)

X = O, CH_2
R = H, OCH_3
n = m = 0, 1
n = 1, m = 0



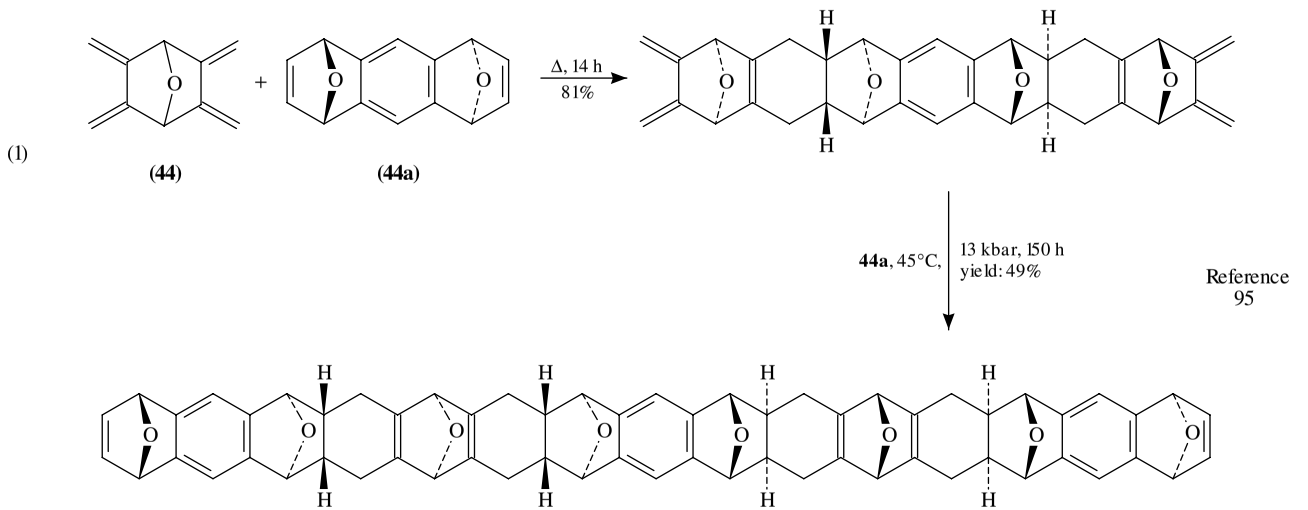
(42)

8 – 12 kbar

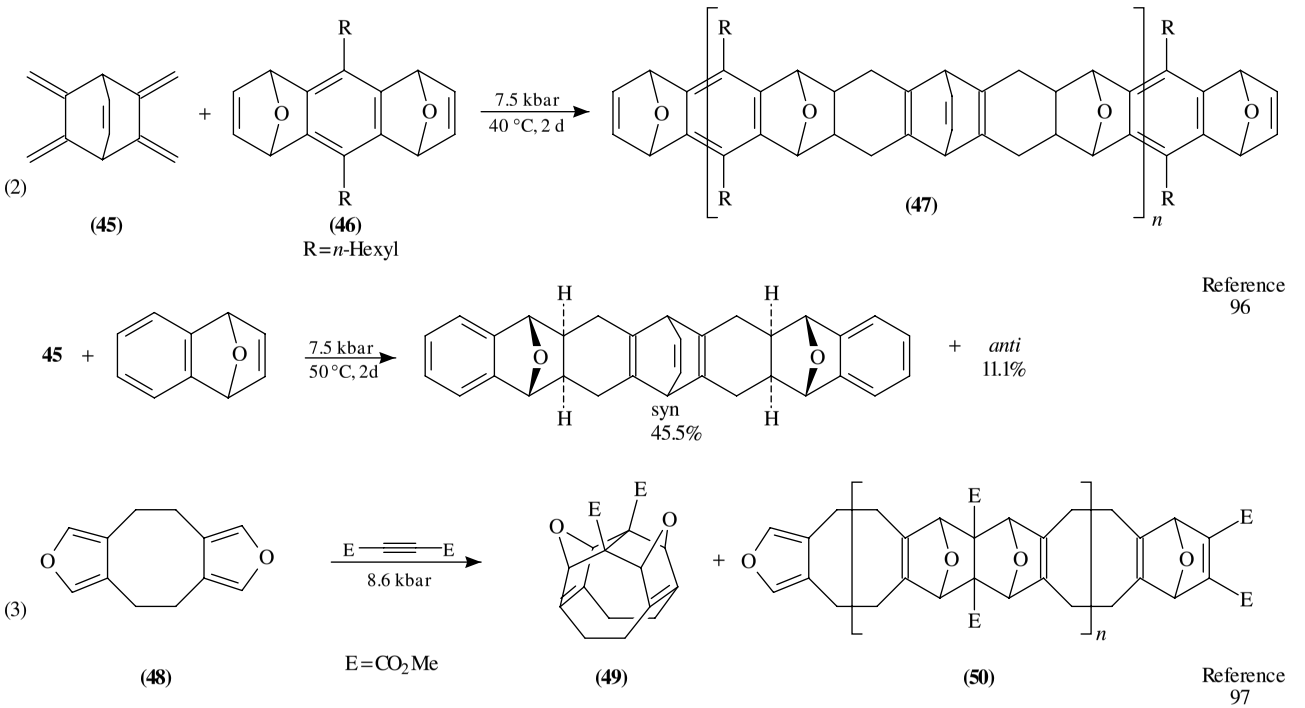


(43)

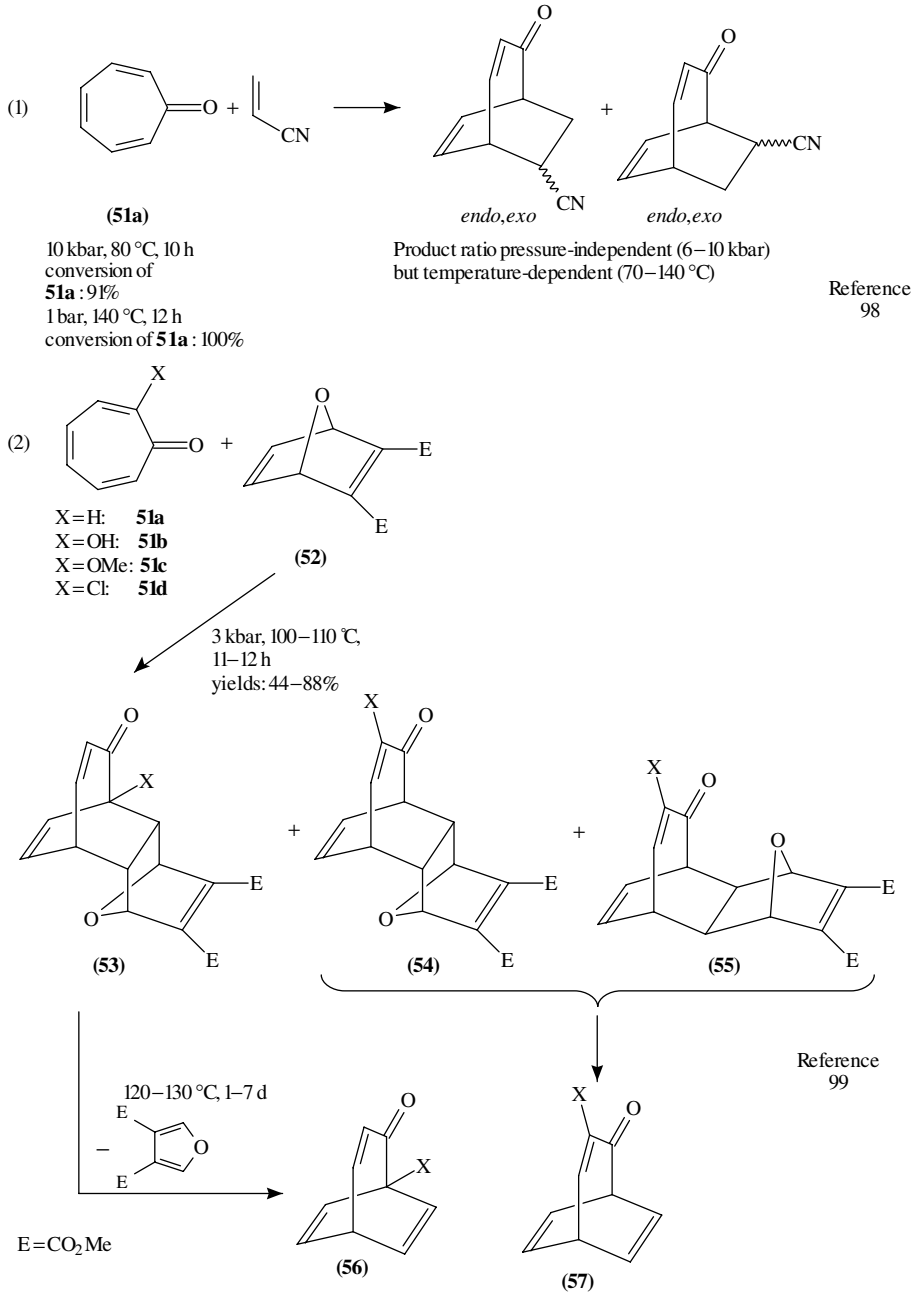
SCHEME 9. Repetitive Diels–Alder reactions in the synthesis of macrocycles having cavities of different size[93,94]



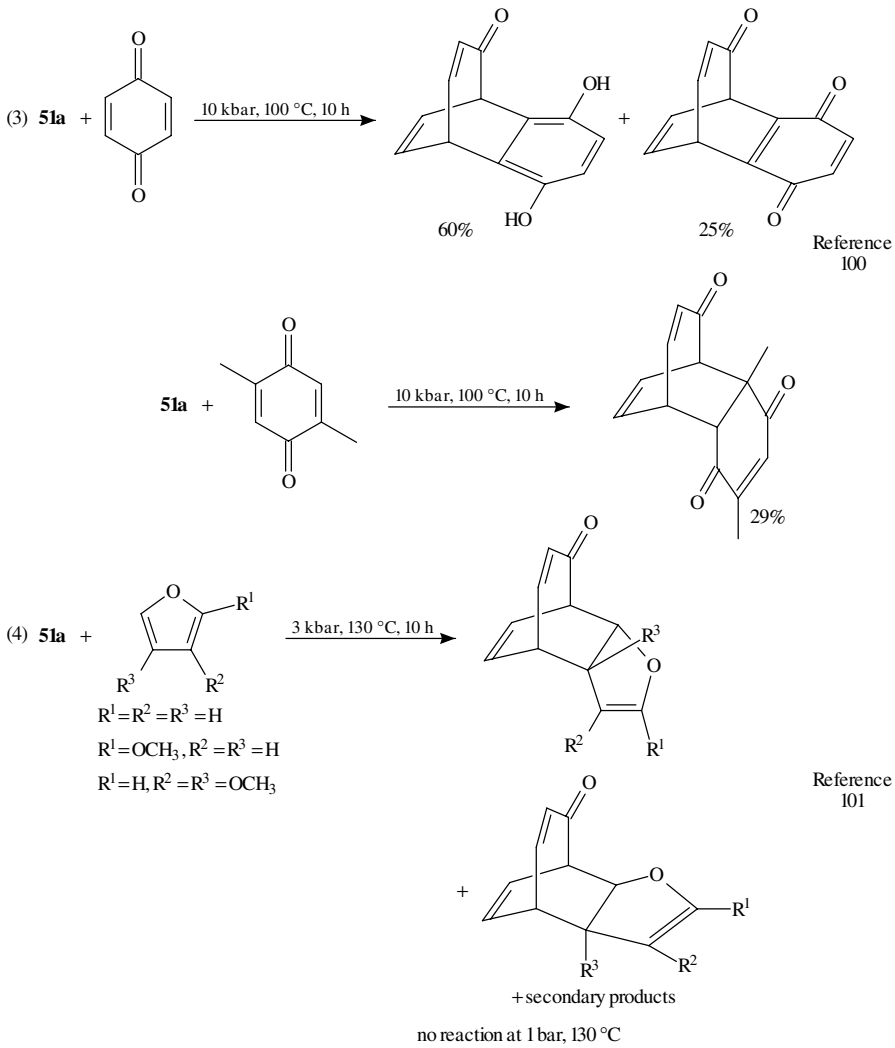
SCHEME 10. Ribbon-type oligomers and polymers via repetitive Diels–Alder reactions



SCHEME 10. (*continued*)

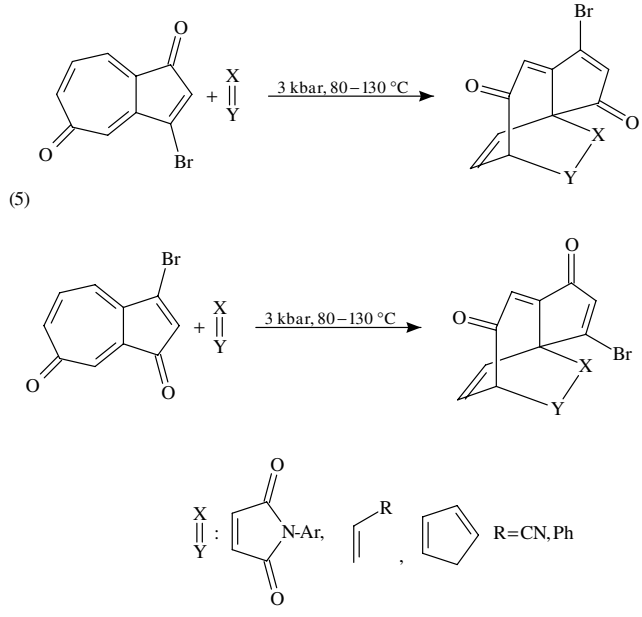


SCHEME 11. Diels–Alder reactions of tropones as dienes



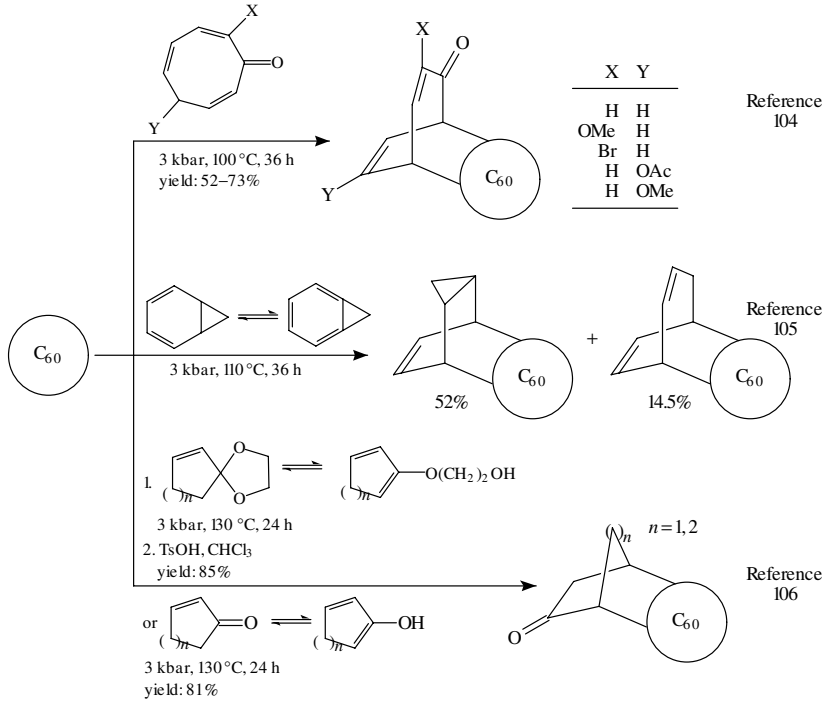
SCHEME 11. (*continued*)

of the most prominent examples is the synthesis of a cantharadine precursor by the cycloaddition of furan to the substituted maleic anhydride shown in Scheme 13, entry 1, which occurs only at high pressure or when catalyzed by $LiClO_4$. Other examples of pressure-induced Diels–Alder reactions with five- and six-membered heterocyclic dienes such as furans, pyrroles, oxazoles, isopyrazoles, phospholes, α-pyrones and pyridones are depicted in Scheme 13. High pressure is here not only useful for synthetic purposes, but also provides important information concerning the course of reaction. One example is the addition of cyanoacetylene to furan and furanobenzocyclophane **63** (Scheme 13: entries 4 and 5) leading to the (2:1) adducts **61** and **66**, respectively, as the major products at 160 °C and atmospheric pressure. In analogy to the trimerization of cyanoacetylene (Scheme 5: entry 3) and the addition of



(5)

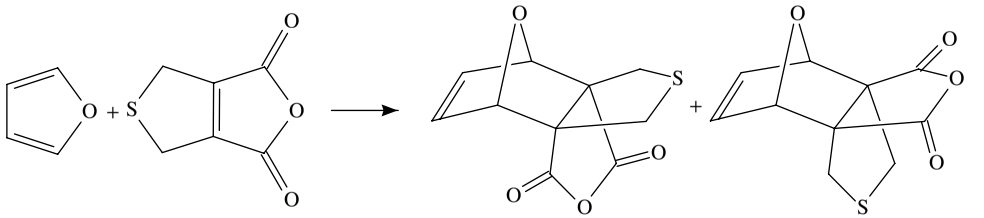
SCHEME 11. (*continued*)



SCHEME 12. Diels–Alder reactions with fullerenes as dienophiles

(a) Furans

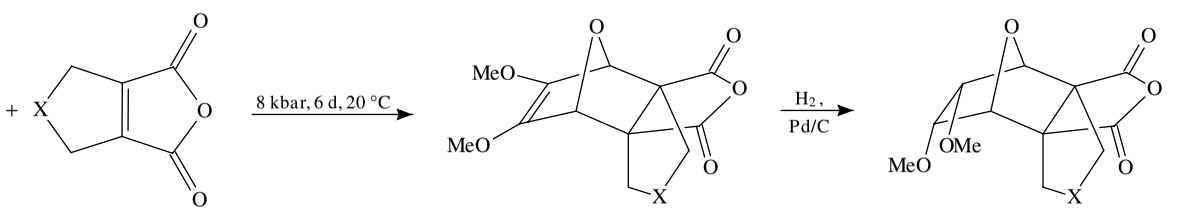
(1)



4–15 kbar, 20 °C, 40–100% conversion — 1 : 4 (pressure independent)

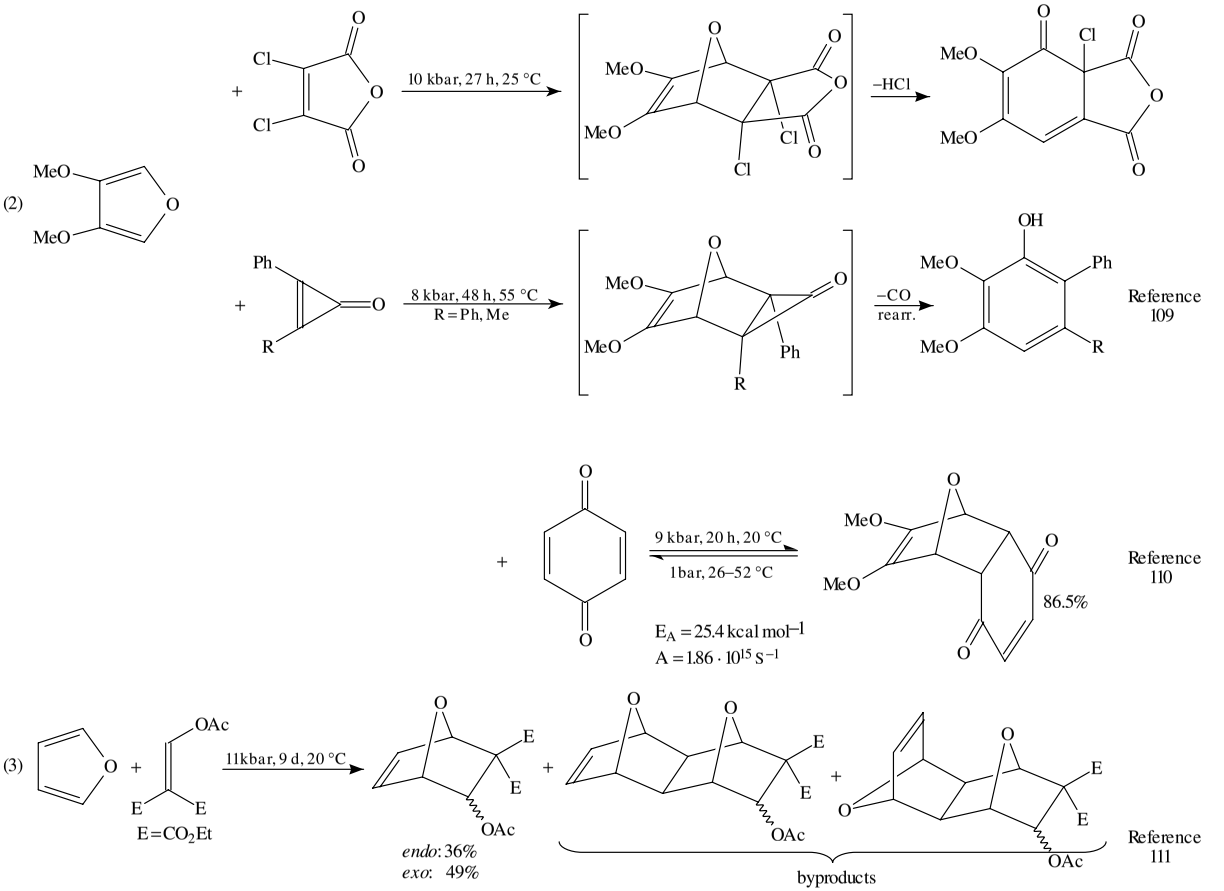
5 M $LiClO_4$, Et_2O, 20 °C, 10 h, yield: 70% — 1 : 5.7

Reference 107



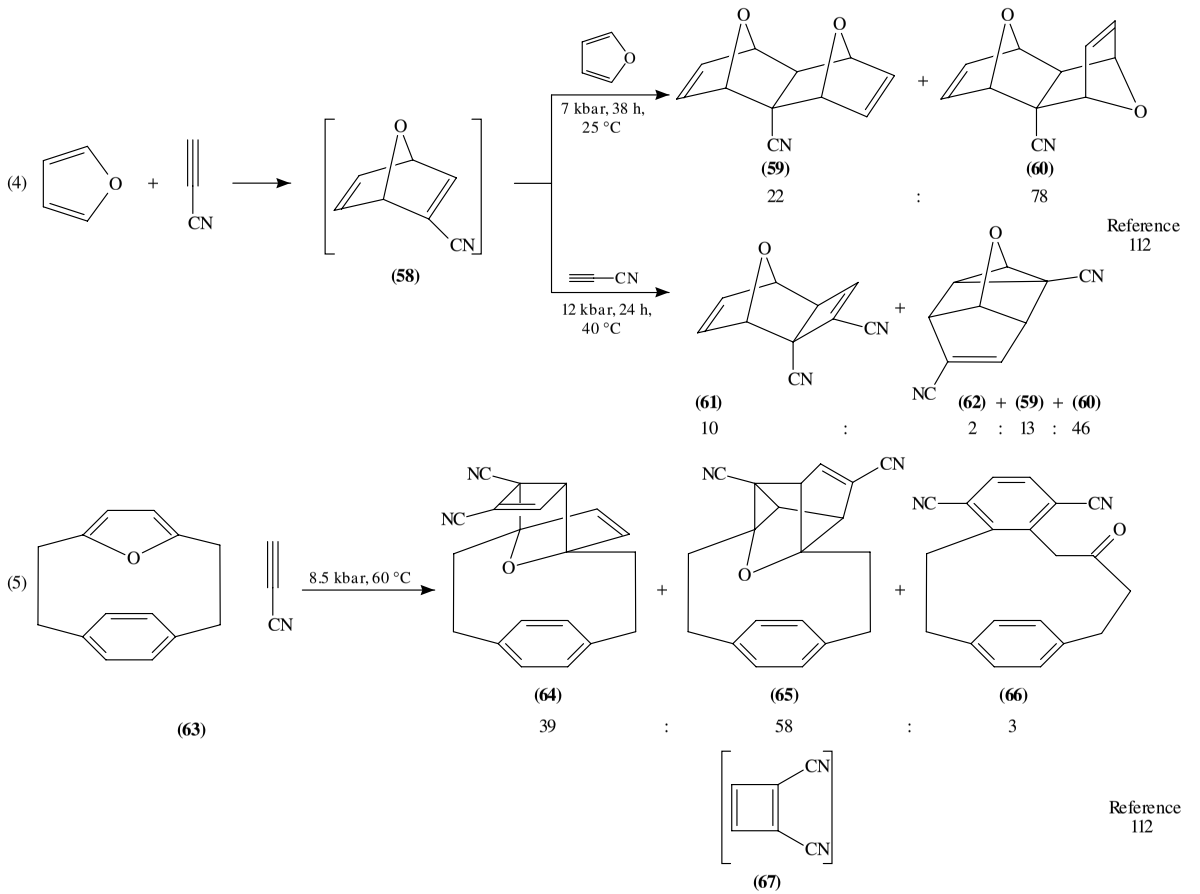
X: CH_2CH_2, $CHMeCH_2$, $CHMeCHMe$, CH_2
yields: 18–28%

Reference 108

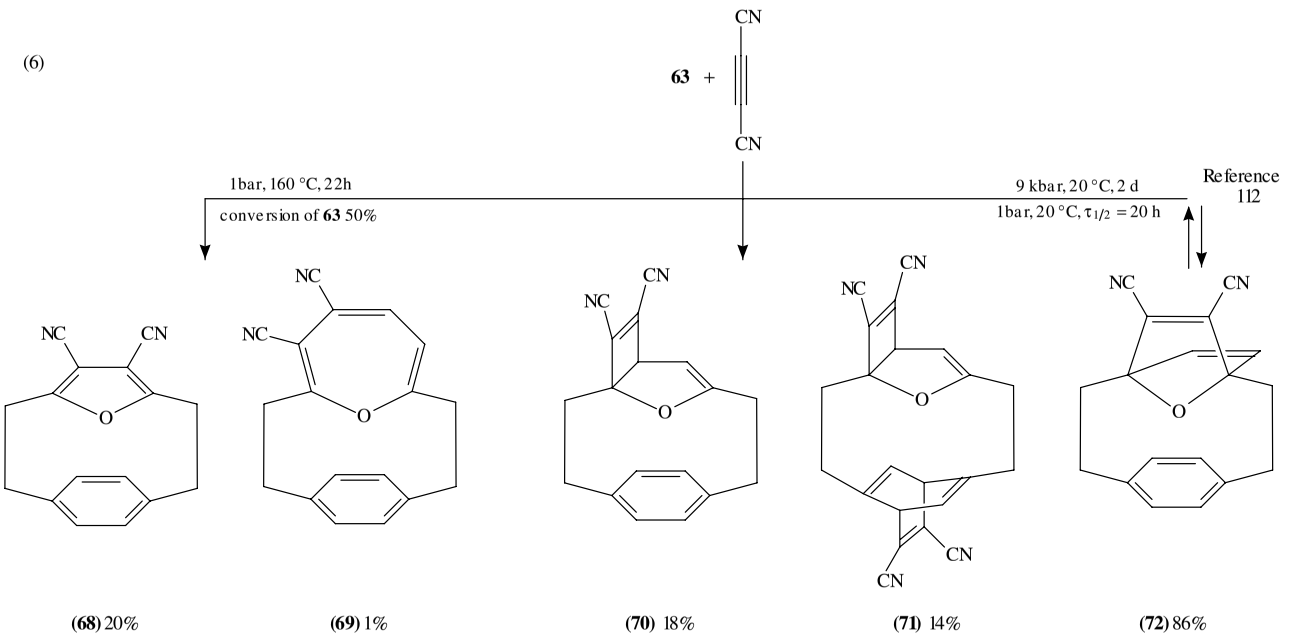


SCHEME 13. Diels–Alder reactions with heterocyclic dienes

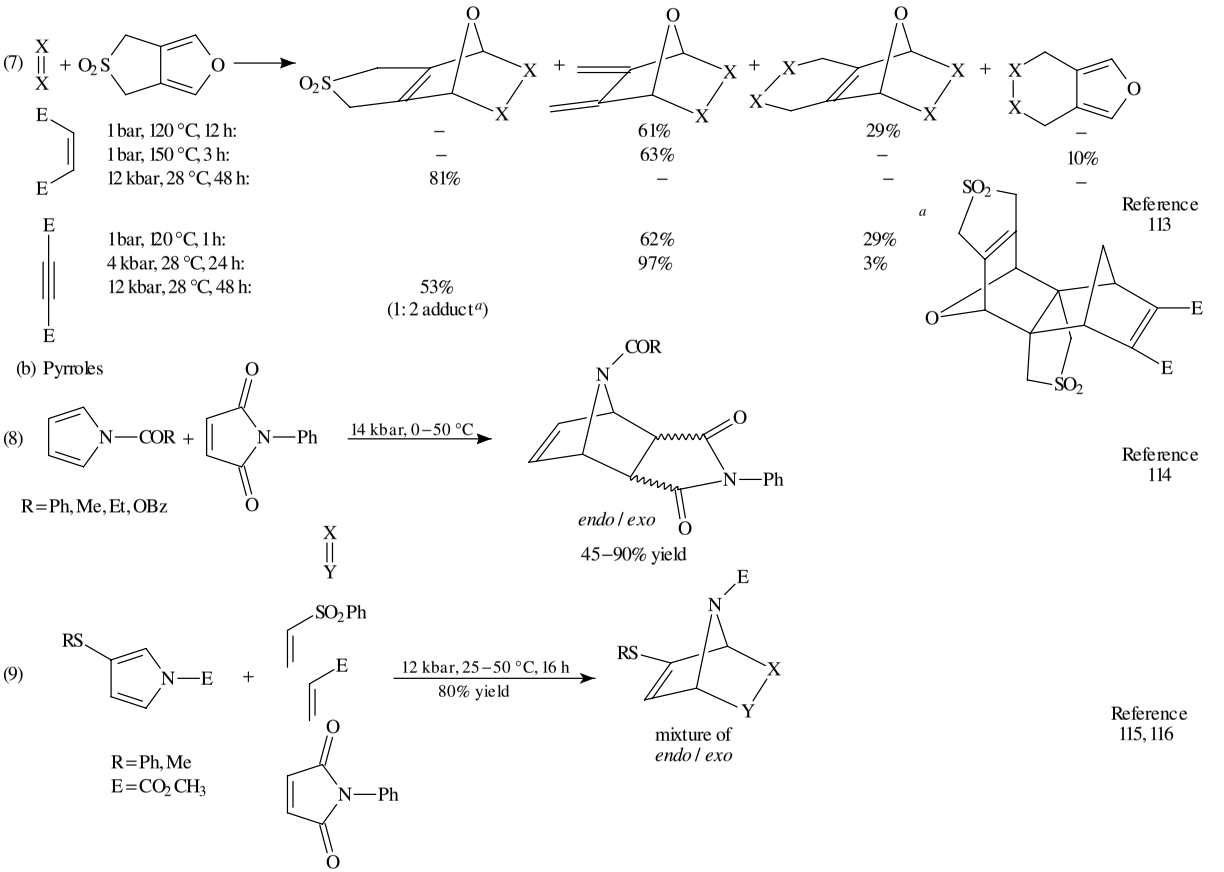
(*continued*)



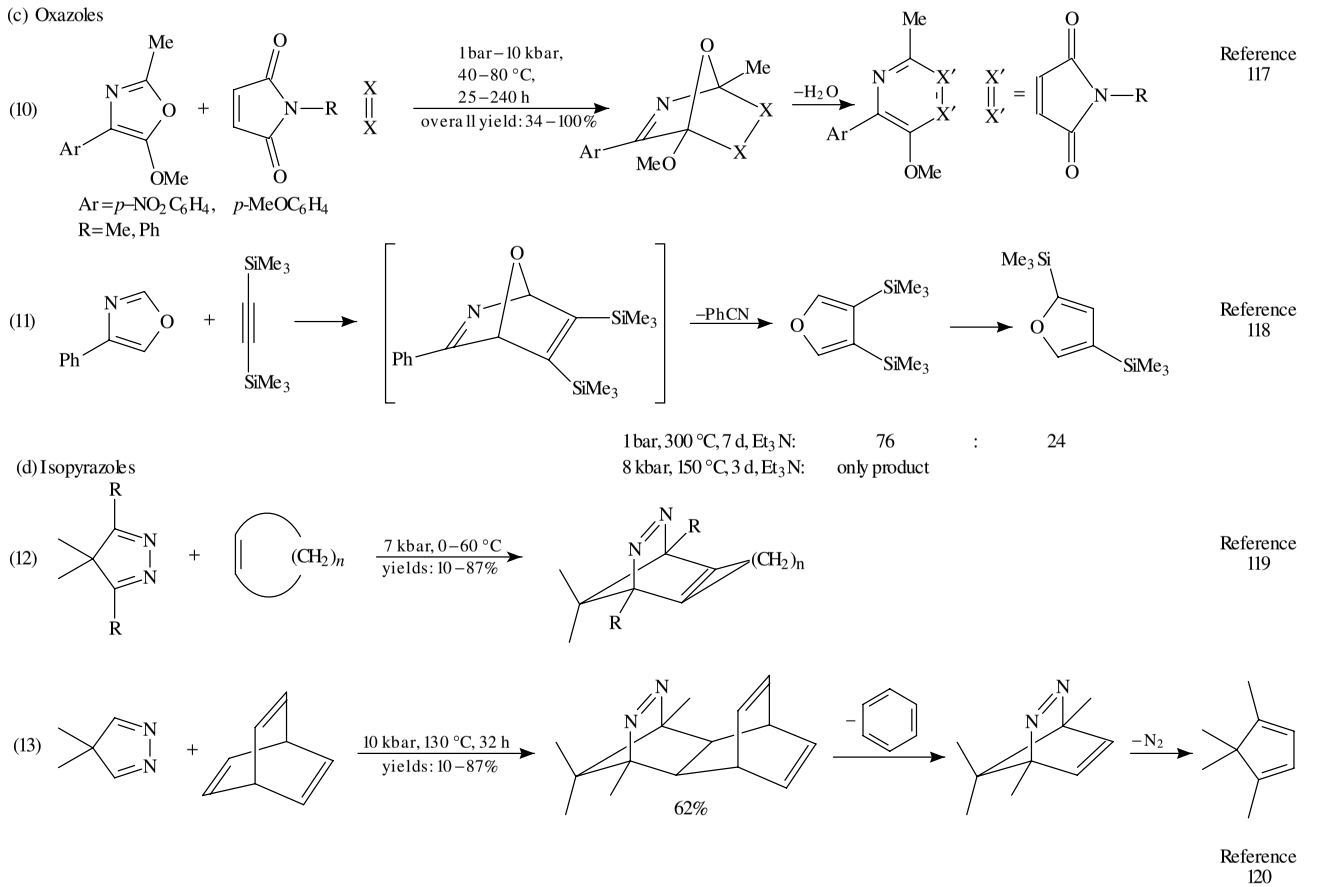
SCHEME 13. (*continued*)



SCHEME 13. (*continued*)



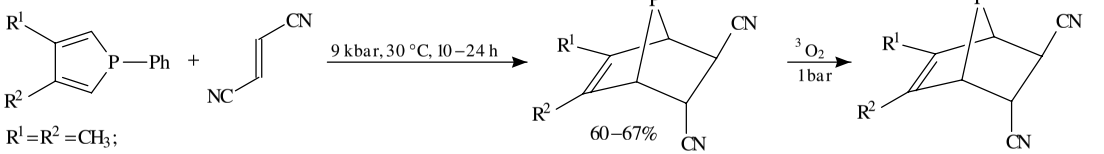
SCHEME 13. (*continued*)



SCHEME 13. (*continued*)

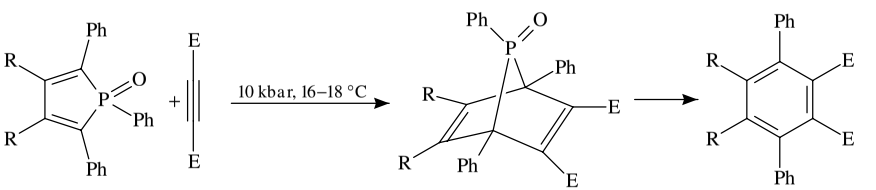
(e) Phospholes

(14)

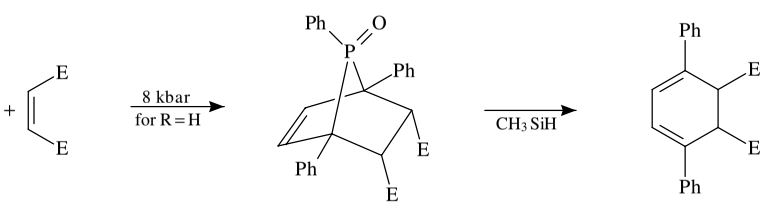


$R^1 = R^2 = CH_3$;
$R^1 = H, R^2 = CH_3$;
$R^1 = R^2 = H$

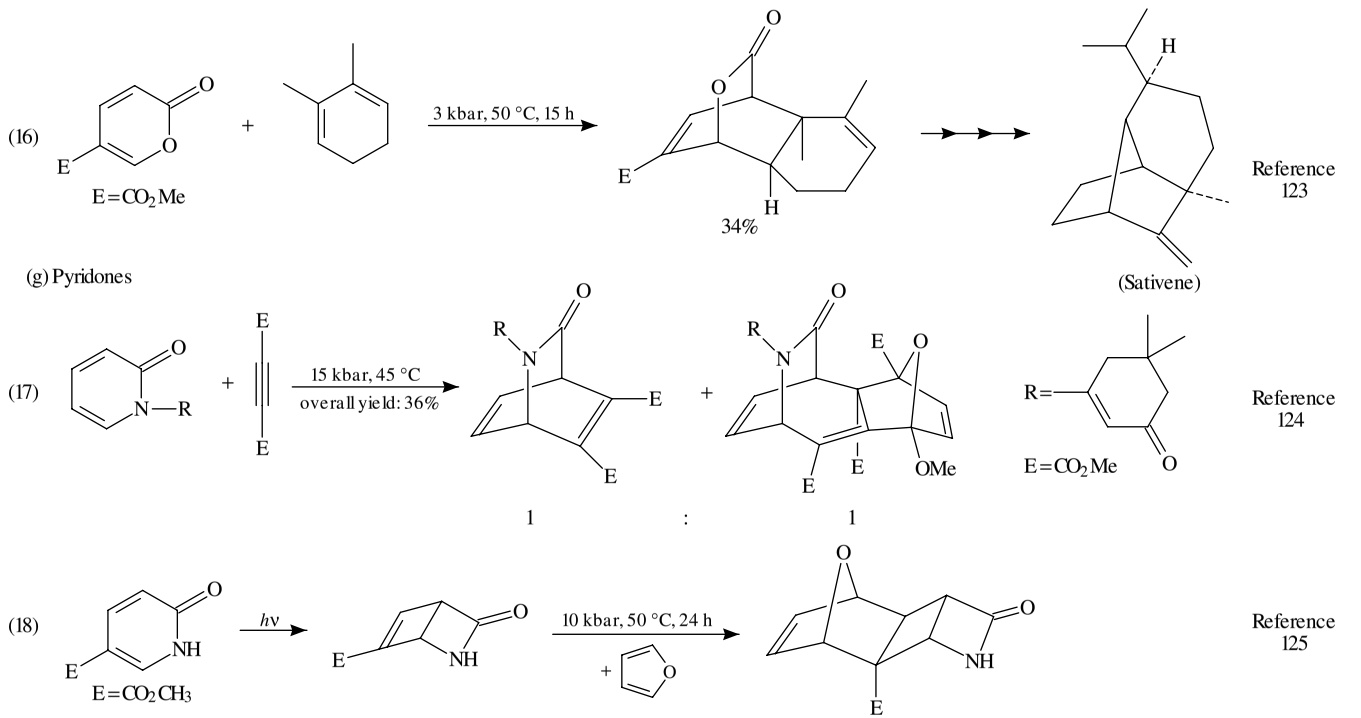
Reference 121



(15) R = Ph, H E = CO_2Me, COBu-t, COAr

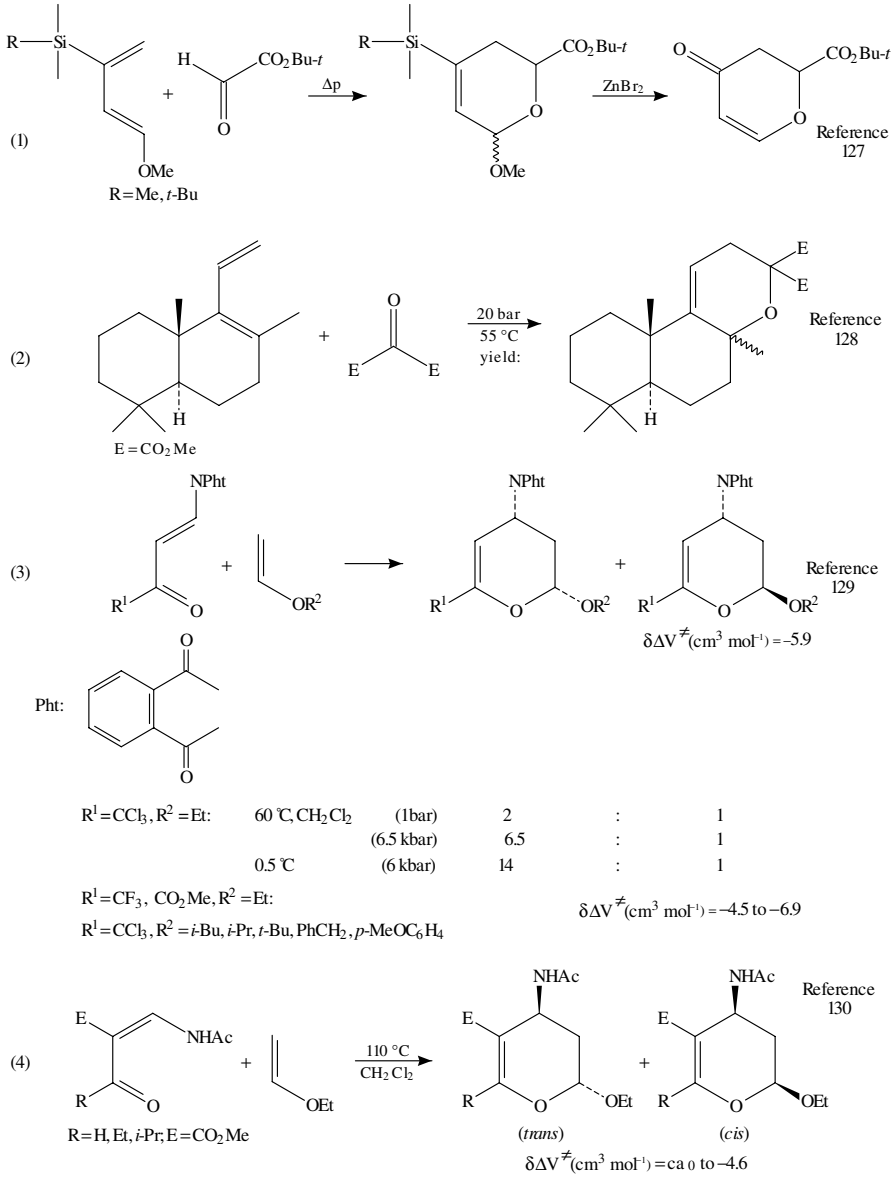


SCHEME 13. (*continued*)



SCHEME 13. (*continued*)

cyano acetylene to [2.2]paracyclophane[126] the cyclobutadiene **67**, the [2 + 2] cyclodimer of cyanoacetylene, was assumed to be the intermediate in these reactions. From the investigation of the pressure effect it could be concluded that oxanorbornadienes such as **58** and not cyclobutadiene **67** are intermediates in the formation of **61** and **62** or **64** and **65** whereas **67** is indeed an intermediate on the reaction path from **63** to **66**. In the



SCHEME 14. Diels–Alder reaction with acyclic heterodienophiles and heterodienes

reaction of **63** with dicyanoacetylene (DCA) (Scheme 13: entry 6) which gives **68** and **69** at 1 bar, the effect of pressure reveals that the [4+2] cycloadduct **72** formed in a kinetically controlled reaction is less stable than the [2+2] cycloadduct **70**, the precursor of the oxepin **69**. In reaction of **63** with DCA catalyzed by $LiClO_4$, only the thermodynamically more stable [2+2] cycloadduct **70** is obtained at 8.5 kbar and 60 °C both **69** and **70** are formed, whereas at 9 kbar and 20 °C the [4 + 2] adduct **72** can be observed.

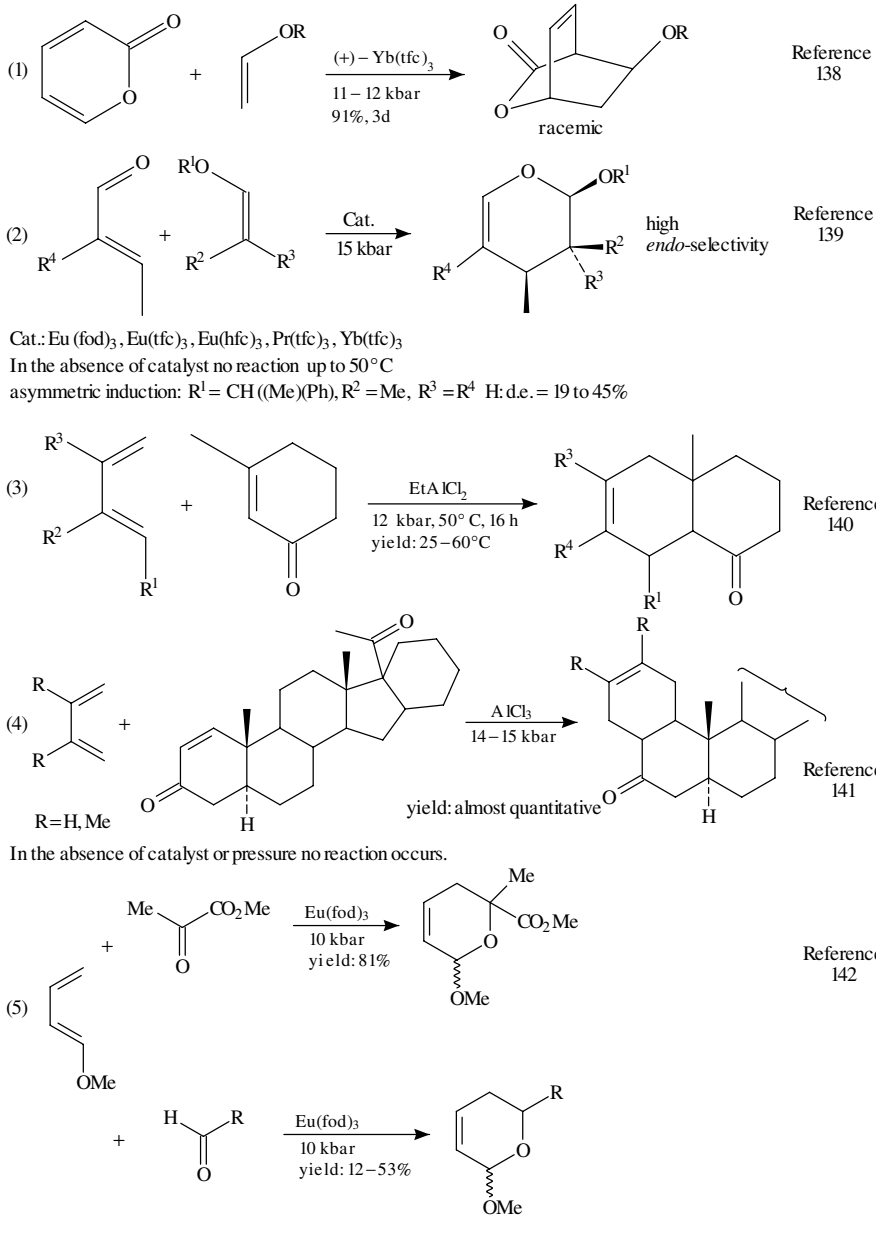
In Scheme 14 the effect of pressure on Diels–Alder reactions with acyclic heterodienophiles or heterodienes is presented. The application of high pressure leads also in these reactions to an enhancement of rates and improvement of yields. The hetero-Diels–Alder reaction (entry 3) is a good example of the interplay between pressure and temperature. At high pressure the rate of reaction as well as the diastereoselectivity are increased. The pressure-induced acceleration allows the temperature of reaction to be lowered, which leads to a further increase of diastereoselectivity.

Breslow[131], Grieco and coworkers[132] and Engberts and coworkers[133] have found that the rates of cycloadditions can be strongly enhanced by conducting them in water or in saturated $LiClO_4$–diethyl ether solution. These enhancements are comparable to the enhancement of rates of reaction by high pressure in conventional organic solvents. Suggested origins of these effects are high internal solvent pressure, hydrophobic association, micellar catalysis, solvent polarity and hydrogen bonding. Blake and Jorgensen[134] found in a Monte Carlo simulation of the solvent effect on the Diels–Alder reaction between 1,3-cyclopentadiene (CP) and methyl vinyl ketone (MVK) that the interaction between water and the transition state leads to a substantial stabilization whereas the interaction between water and the reactants or adduct is small. Propane as solvent has accordingly no significant influence on the stability of the transition state, the reactants or the adduct. The authors concluded that the aqueous acceleration of the reaction between CP and MVK is due to the hydrophobic association, as well as to a nonhydrophobic component stemming from enhanced polarization of the transition state that lead *inter alia* to stronger hydrogen bonds at the carbonyl oxygen. The various methods for acceleration and selectivity enhancement of Diels–Alder reactions were recently reviewed by Pindur and coworkers[135].

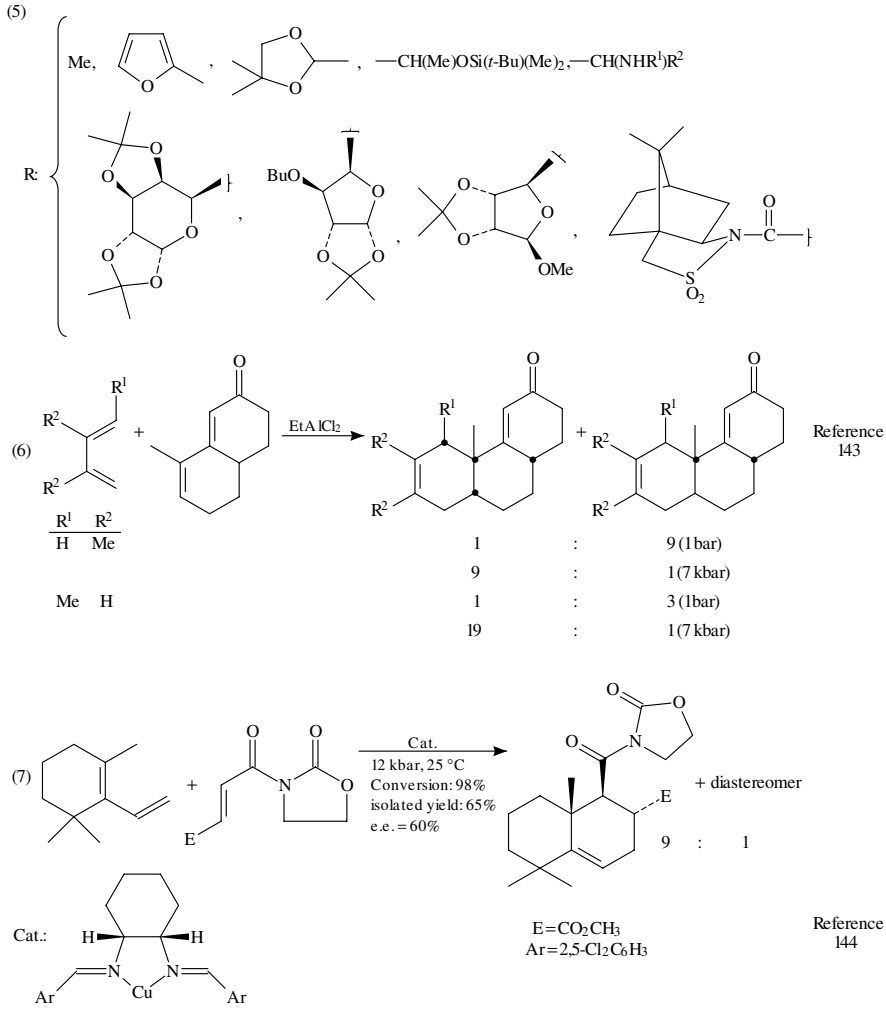
A study of the pressure effect on reactions in H_2O by Jenner[136] showed that the Diels–Alder cycloaddition of furan or 1-methylfuran to acrylic acid derivatives is less sensitive to pressure in aqueous solution than in an organic solvent such as CH_2Cl_2. Isaacs and coworkers[137] found, however, that the pressure effect on the Lewis-acid or $LiClO_4$ catalyzed Diels–Alder reaction of isoprene with N-phenylmaleic imide is larger (more negative activation volume) than that on the corresponding uncatalyzed reaction. Similar results were also obtained for the Diels–Alder reaction between 9-anthranceneethanol and N-ethylmaleic imide. The Diels–Alder reactions shown in Scheme 15, entries 1–4, illustrate that the combination of high pressure and Lewis-acid catalyst can have a synergetic effect. The reactions are observed only at high pressure in the presence of the catalysts. The examples shown in Scheme 15, entries 5 and 6, demonstrate that pressure can have a strong effect on the diastereoselectivity of catalyzed reactions. In one case (entry 6) the selectivity is reversed by pressure. In another case, the intramolecular Diels–Alder reaction catalyzed by a chiral titanium complex (entry 8), the enantioselectivity is increased by pressure from 4.5%ee at 1 bar to 20.4%ee at 5 kbar.

B. [2 + 2] Cycloadditions of Cumulated Dienes

[2 + 2] Cycloadditions involving ketene derivatives as one or both reaction partners are assumed to be rare examples of concerted $[\pi_s^2 + \pi_a^2]$ cycloadditions[146]. The activation volumes determined for the [2 + 2] cyclodimerization and the [2 + 2] cycloadditions

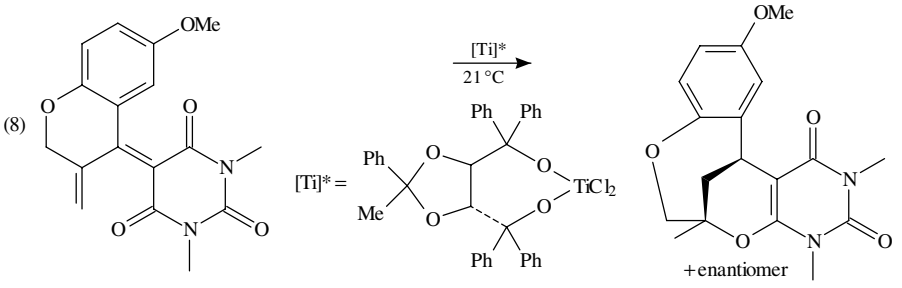


SCHEME 15. Catalyzed Diels–Alder reactions

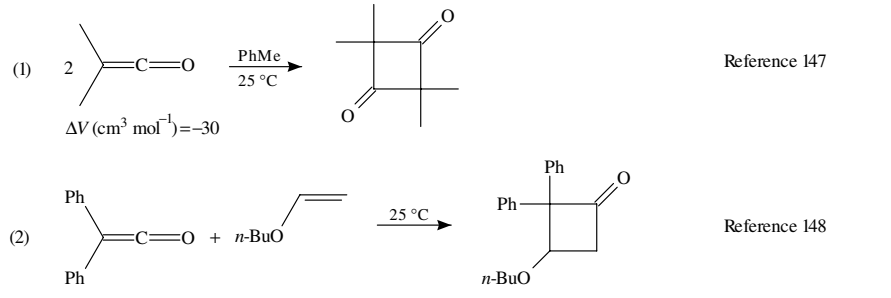


SCHEME 15. (*continued*)

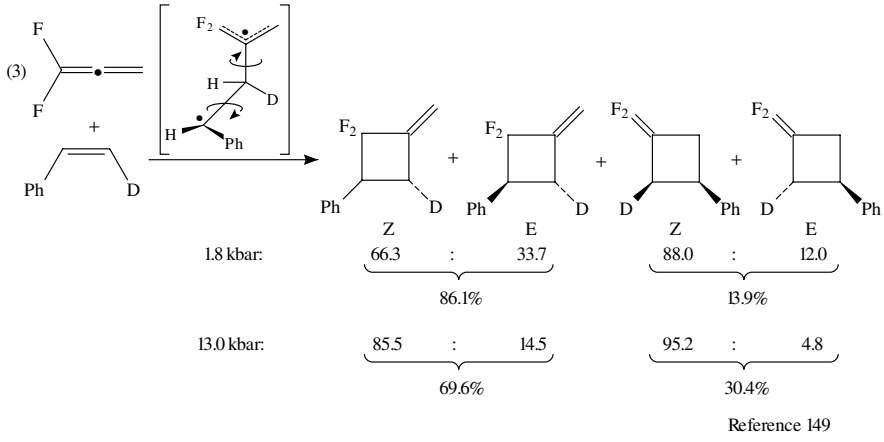
of diphenylketene to various enol ethers turned out to be highly negative (Scheme 16: entries 1 and 2). Kelm, Huisgen and coworkers studied the mechanism of the reaction of diphenylketene with *n*-butyl vinyl ether in great detail. Although the rate constants at atmospheric pressure could be successfully correlated with the term $[(\varepsilon - 1)/(2\varepsilon + 1]$ containing the dielectric constants (ε) of the solvents used, indicating an increase of polarity during the reaction, the very large solvent dependencies of $\Delta V^{\neq}$ and ΔV were erratic and not understandable. The authors found a fairly good correlation between the partial molar volumes of the reactants and the solvent cohesion energy density (ced), but the correlation failed for those of the transition state and the product. Thus, the effect of pressure leads to a powerful acceleration of these [2 + 2] cycloadditions comparable to that of Diels–Alder reactions, which may be useful for synthetic purposes but does not provide further insight into the mechanism of this reaction.



SCHEME 15. (*continued*)

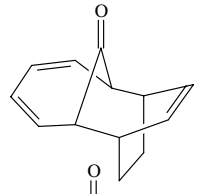
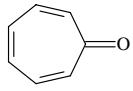
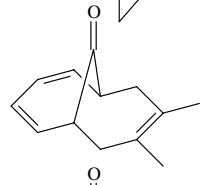
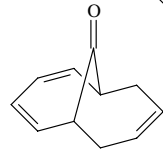
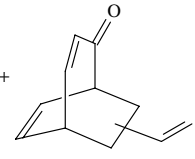


Solvent	$\Delta V^{\neq}$ (cm^3 mol^{-1})	ΔV (cm^3 mol^{-1})
PhCN	–22	–10.4
c-C_6H_{12}	–26	–31.3
CH_2Cl_2	–29	–26.2
PhCl	–30	–26.4
PhH	–44	–23.0
PhMe	–52	–29.0

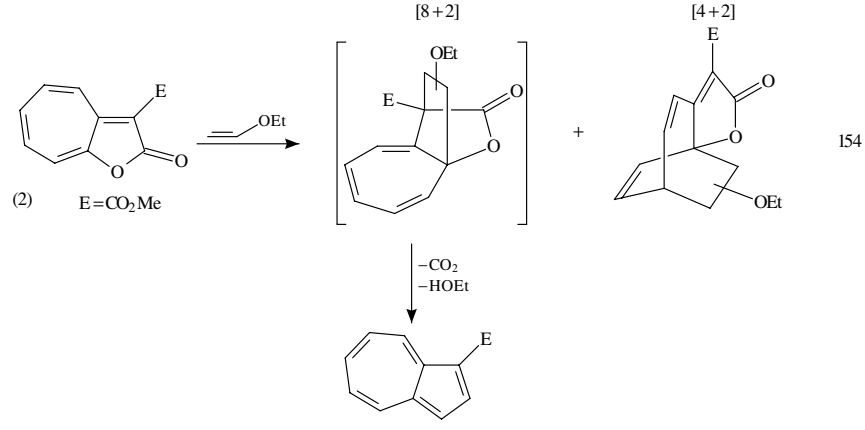


SCHEME 16. [2 + 2] Cycloadditions of cumulated dienes

Dolbier and Weaver[149] investigated the effect of pressure on the stereo- and regioselectivity in a certainly stepwise [2 + 2] cycloaddition of 1,1-difluoroallene to (*Z*)-*β*-deuteriostyrene (Scheme 16: entry 3). In order to explain the pressure-induced increase in stereoselectivity the authors concluded that, in the diradical intermediate at high pressure, the ring-closure reactions leading to the (*Z*)-configured methylenecyclobutane derivatives are favored over bond rotation, which is a prerequisite for the formation of (*E*)-configurated methylenecyclobutanes.

Reaction					$\Delta V^{\neq a}$	ΔV^{a}	Reference
	i-PrPh, 80 °C				–37.6[b]	–36.1[c]	151
(1) 	*i*-PrPh, 80 °C				–33.1[b]	–34.9[c]	151
	MePh, 50 °C		+		–31.0[d]	–33.6[c]	152
		[6+4]		[4+2]			
product ratio	(p = 0.9 kbar)	10.0	:	1			
	(p = 6.9 kbar)	10.8	:	1			
	$\delta\Delta V^{\neq a)} = \Delta V^{\neq}$ [6+4] $- \Delta V^{\neq}$ [4+2] = –0.3						

[a] In cm^3 mol^{-1}. [b] At 80 °C. [c] At 60 °C[153]. [d] At 50 °C.



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SCHEME 17. [6 + 4] and [8 + 2] Cycloadditions of tropone and a heptafulvene derivative

C. Higher Cycloadditions Involving Trienes and Tetraenes

The pressure dependence of the orbital symmetry-allowed [6 + 4] cycloaddition of tropone with 1,3-dienes was first studied by le Noble and Ojosipe[150], who reported extremely small absolute values of $\Delta V^{\neq}$ and ΔV. A reinvestigation by Takeshita and his coworkers[151] showed, however, that the activation and reaction volumes of these cycloadditions are of the same order of magnitude as those of Diels–Alder reactions (Scheme 17: entry 1). Dogan[152] confirmed this finding with a study of the reaction between 1,3-butadiene and tropone in which a [6 + 4] cycloaddition competes with a [4 + 2] Diels–Alder reaction. The activation volume of the overall reaction was again found to be highly negative. However, the ratio between the [6+4] and [4+2] cycloadduct turned out to be almost pressure-independent, which means that the difference between the activation volumes ($\delta\Delta V^{\neq}$) is almost zero and hence the activation volumes of both reactions are of the same value.

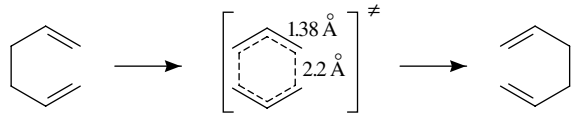
Tropone can also react as a tetraene component in [8 + 2] cycloadditions including the C=O double bond. Tropone reacts, e.g., with 1,1-diethoxyethene (at 120 °C, 10 h, 1 bar) to give the corresponding [4 + 2], [8 + 2] and [6 + 4] cycloadduct in yields of 1.1, 9.1 and 3.1%, respectively (conversion of tropone: 16%). At 3 kbar, 120 °C, only the [4 + 2] and [8 + 2] cycloadducts were formed in yields of 13 and 17%, respectively (conversion of tropone: 30%)[155]. Tropone reacts with 2,3-dihydrofuran in a similar fashion leading to the corresponding [8 + 2] and [4 + 2] cycloadducts. The product ratio is again pressure-dependent[156]. The heptafulvene derivative shown in Scheme 17 can undergo a [8 + 2] cycloaddition leading to methyl azulene-1-carboxylate, obviously after elimination of CO_2 and ethanol from the undetected primary cycloadduct. The [8+2] cycloaddition competes with [4 + 2] cycloadditions. Study of the pressure effect on the competitive reactions showed that the formation of the [4 + 2] cycloadduct is reversible even at 10 kbar, and that the [4 + 2] cycloadduct is not directly converted to methyl azulene-1-carboxylate. Thus, the azulene formation can only occur via the intermediate [8 + 2] cycloadduct.

IV. PERICYCLIC REARRANGEMENTS

Many pericyclic rearrangements show a pressure-induced acceleration which is characterized by a negative volume of activation[157]. The effect, which is usually smaller than that of intermolecular cycloadditions, may be explained with different packing coefficients of cyclic and acyclic states as already discussed for the pericyclic and stepwise cycloadditions.

A. Sigmatropic [3.3] Shifts: Cope and Claisen Rearrangements

On the basis of stereochemical and kinetic investigations, most Cope rearrangements are regarded as being pericyclic processes[158]. The van der Waals volumes calculated for the parent 1,5-hexadiene and the pericyclic transition state are approximately the same (Scheme 18). This is understandable since in the symmetrical transition state the bond breaking and making have proceeded to the same extent so that the effects of the two processes on the van der Waals volume compensate each other and no great overall effect of pressure on the Cope rearrangement is to be expected. If it is assumed that, by analogy with the pericyclic and stepwise cycloadditions already discussed, the transition state here also exhibits a larger packing coefficient because of its cyclic geometry, the activation volume ought to be negative. The activation volume can be estimated at approximately $-10\ \mathrm{cm^3\,mol^{-1}}$ if the packing coefficient determined for cyclohexene is used for the unknown packing coefficient of the transition state. In fact, negative activation volumes of the expected size were found for the Cope rearrangements and related Claisen



V_W	63.9	63.6	$\Delta V_W^{\neq} = -0.3$
V	119.4	109.1	$\Delta V^{\neq} = -10.3$

All volumes are given in $cm^3\ mol^{-1}$. The structural parameters necessary for the calculation of the van der Waals volume for the transition state (TS) were taken from *ab initio* calculations[159,160]. The partial molar volume for the TS was calculated from the equation:

$$V(\mathrm{TS}) = V_W(\mathrm{TS})/\eta(\text{cyclohexene});\ \eta V_W/V = 0.5829(\text{cyclohexene})$$

SCHEME 18. van der Waals volume of activation $\Delta V_W^{\neq}$ and volume of activation $\Delta V^{\neq}$ calculated for degenerate Cope rearrangement of 1,5-hexadiene

rearrangements shown in Scheme 19. However, the reacting compounds are highly polar, so the negative activation volumes could also be due to electrostriction effects rather than as a consequence of the cyclic transition states.

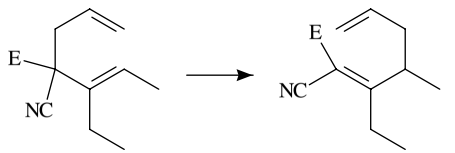
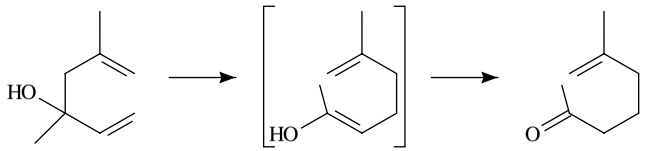
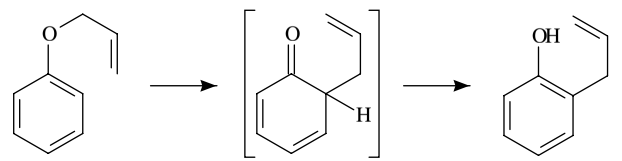
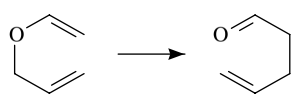
The activation volumes obtained from the pressure dependence of the Cope rearrangements in pure hydrocarbons, in which electrostriction effects caused by polar substituents should be negligible, were in good agreement with that predicted for the parent system (Scheme 20: entries 1–4). This concept elucidates why the degenerate Cope rearrangement in bullvalene, investigated by Merbach, le Noble and coworkers[166] with pressure- and temperature-dependent NMR spectroscopy, shows no significant pressure effect ($\Delta V^{\neq} = -0.5\ cm^3\ mol^{-1}$) (Scheme 20: entry 5). As a result of the fixed stereochemistry due to the rigid bullvalene skeleton no new cyclic interaction, in the sense discussed here, appears in the transition state.

B. Potential Sigmatropic [1.*n*] Shifts (Hydrogen, Carbon, Silicon)

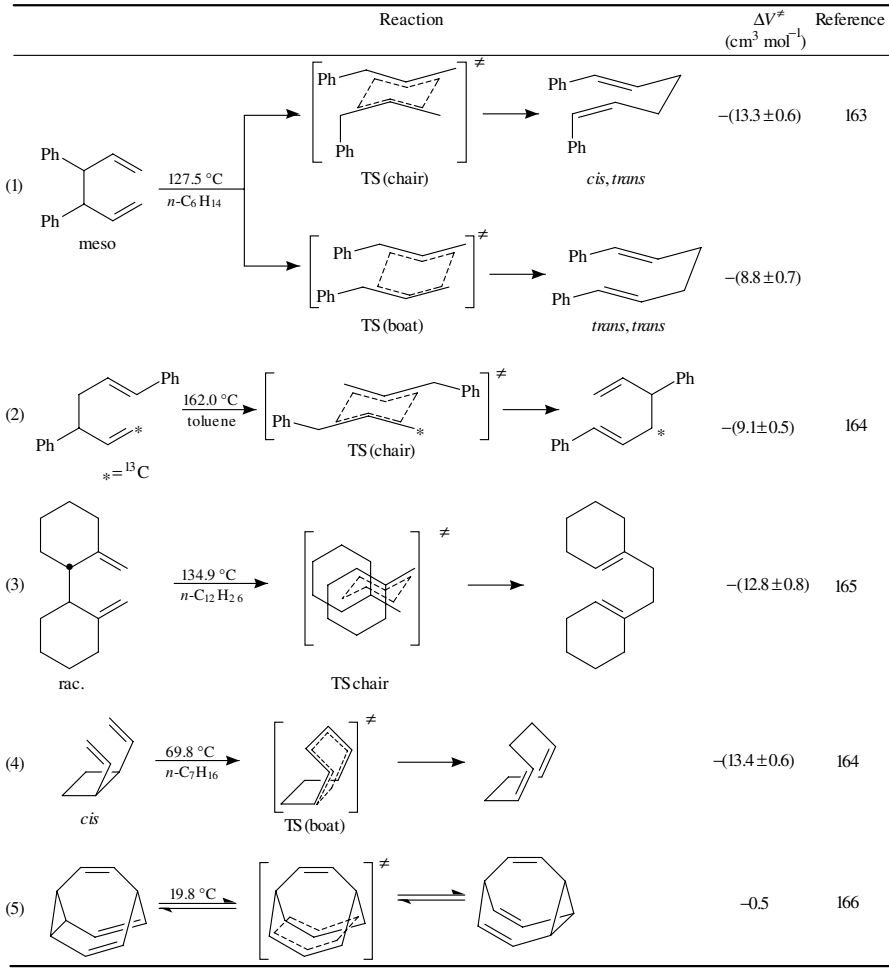
In Scheme 21 the activation volume data for some potential sigmatropic [1,*n*] carbon, silicon or hydrogen shifts ($n = 3$–9) are summarized. Analogously to the Cope rearrangement (sigmatropic [3,3] carbon shift) the activation volumes turned out to be negative in cases of pericyclic mechanism while the activation volumes are positive in cases of dissociative mechanism. The [1,4] shift of a benzyl or benzhydryl group in 1-alkoxypyridine-N-oxides (Scheme 21: entry 3), is particularly instructive. From the completely different pressure response of the two reactions, le Noble and Daka[169] concluded that the shift of the benzyl group occurs via a pericyclic mechanism while that of the benzhydryl group proceeds via a dissociative radical-pair mechanism. The conclusion drawn from the different activation volumes is in full accord with the stereochemical finding of retention of configuration in the PhCHD migration and the observation of a CIDNP (Chemically Induced Dynamic Nuclear Polarization) effect in the Ph_2CH migration[173].

C. Electrocyclic Rearrangements

In the transition state of the electrocyclization of (*Z*)-1,3,5-hexatriene to 1,3-cyclohexadiene (Scheme 22: entry 1) a new six-membered ring develops analogously

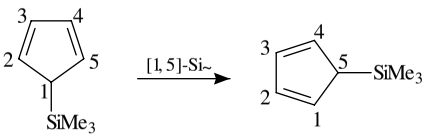
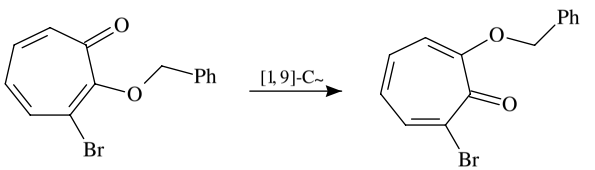
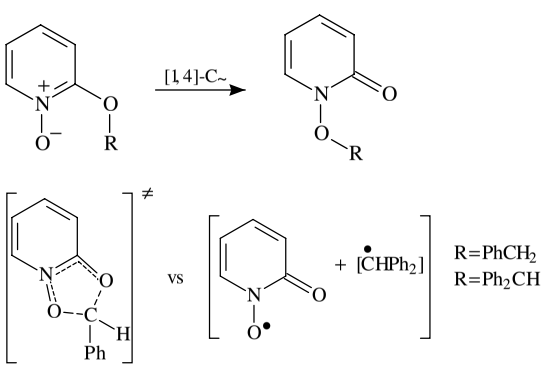
	Reaction	T(°C)	Solvent ($cm^3\ mol^{-1}$)	$\Delta V_T^{\neq}$	Reference
(1)		119	decalin	−6.7	161
(2)		180	*N*-methyl-pyrrolidone	−9.7	162
(3)		160	decalin	−7.7	161
(4)		130.4	neat	−18	161

SCHEME 19. Activation volumes of Cope and Claisen rearrangements in polar 1,5-hexadiene systems

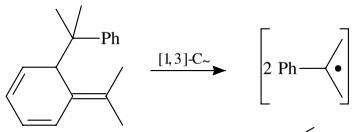
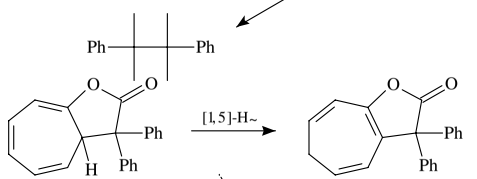
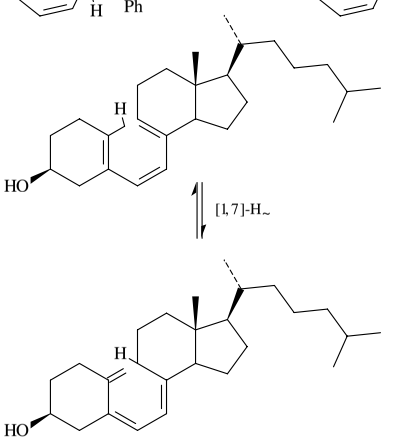


SCHEME 20. Activation volumes of Cope rearrangements in unpolar 1,5-hexadiene systems

to that of the Cope rearrangement. The electrocyclization is accelerated by an increase in pressure. The activation volume determined at different temperatures listed in Scheme 22 is about $-10\ cm^3\ mol^{-1}$ and corresponds to those of the Cope rearrangements (Scheme 20). Over the temperature range of about 20 °C investigated the activation volume does not show any significant temperature dependence within the experimental limits of error $\pm 1\ cm^3\ mol^{-1}$. From the volume data shown in Scheme 22, the packing coefficient of the transition state is calculated to equal approximately that of the cyclic product and differs substantially from that of the acyclic reactant. This result provides good evidence for the assumption used in the explanation of the pressure effect on pericyclic reactions. From the complete volume data set of the (*Z*)-1,3,5-hexatriene → 1, 3-cyclohexadiene isomerization, the activation volume of the reverse reaction, the electrocyclic ring-opening 1,3-cyclohexadiene → (*Z*)-1,3,5-hexatriene can be extrapolated to be slightly positive ($\Delta V^{\neq} = +4\ cm^3\ mol^{-1}$). The electrocyclic

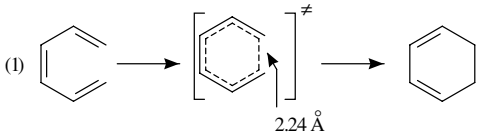
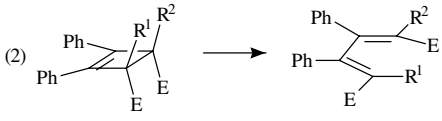
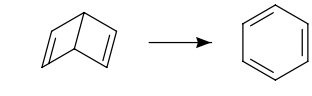
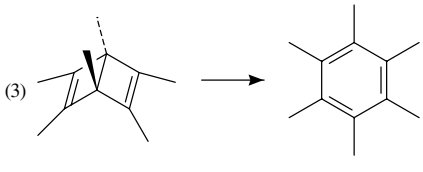
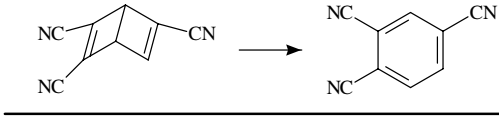
	Reaction	T(°C)	Solvent	$\Delta V_T^{\neq}$ (cm^3 mol^{-1})	Reference
(1)		68	Benzene-freon	−12.5	167
(2)		130	*i*-Pr-Ph	−11.1	168
(3)		100	diglyme	−30 +10	169

SCHEME 21. Activation volumes of potential sigmatropic [1,*n*] shifts (n = 3,4,5,7,9)

	Reaction	T(°C)	Solvent	$\Delta V_T^{\neq}$ ($cm^3\ mol^{-1}$)	Reference
(4)		20	cyclohexane	+6	170
(5)		130	n-Bu_2O	−2.2	171
(6)		20	benzene/ toluene	$< -5^a$	172

[a] Estimated from two experiments at 1 bar and 15 kbar.

SCHEME 21. (*continued*)

Reaction	T(°C)	$\Delta V_T^{\neq a}$	ΔV_T^{a}	θ	Reference
(1) 	101.2	–9.8	–14.4	0.68	
	108.1	–10.8	–14.8	0.73	
	117.5	–10.9	–15.2	0.72	174
	122.4	–10.3	–15.4	0.67	
V_W^a 61.2 58.6 57.0					
V^b 118.7 107.9 103.9					175
η 0.5156 0.5431 0.5486					
(2) 					176, 177
R^1=H, R^2=H		–1 to –2			
R^1=R^2=Me		–7			
R^1=H, R^2=Me	70	–12.7	–23[c]		
	20	+5			178
(3) 	140	–12	–22		178, 179
	51.3	≈0			180

[a] In $cm^3\,mol^{-1}$; the reaction volume ΔV_T was calculated from the partial molar volumes V_T determined by the temperature dependence of the densitites of reactant or product according to Scheme 2.

[b] 108.1 °C in toluene.

[c] In toluene.

SCHEME 22 Activation and reaction volumes of electrocyclic rearrangements

ring-opening of heavily substituted cyclobutene derivatives, however, shows negative activation volumes of different size depending on the substitution pattern (Scheme 22: entry 2). This result indicates that other effects, such as an increase of steric crowding, contribute to the activation volume, overcompensating the effect of ring-opening. A clear-cut example is the ring-opening of Dewar benzene to benzene. The isomerization of the parent Dewar benzene is retarded by pressure ($\Delta V^{\neq} = +5\ cm^3\,mol^{-1}$) (Scheme 22: entry 3) whereas the isomerization of the hexamethyl derivative is accelerated by pressure ($\Delta V^{\neq} = -12\ cm^3\,mol^{-1}$). The negative volume of activation of the latter isomerization can be again explained by steric crowding of the six methyl groups which is larger in the planar hexamethylbenzene than in the nonplanar precursor, overcompensating the volume-increasing effect of ring-opening.

D. Intramolecular Diels–Alder Reactions

In intramolecular Diels–Alder reactions, two new rings are formed. There are examples of relatively large pressure-induced accelerations which can be exploited for preparative purposes (Scheme 22: entries 1–5). These compounds, without exception, contain polar groups and are therefore not very suitable for the analysis of the relation between pressure effect and ring formation. The strong solvent dependence of the activation volume of the intramolecular Diels–Alder reaction shown in Scheme 23, entry 2, turned out to be largely the result of the strongly solvent-dependent partial molar volume of the reactant — V(reactant) — whereas the partial molar volume of the transition state [$V^{\neq} = \Delta V^{\neq} + V$(reactant)] appears to be almost unaffected by the nature of the solvents. The activation volumes of the intramolecular Diels–Alder reactions in the pure hydrocarbon systems (Scheme 23: entries 6 and 7) were found to be $\Delta V^{\neq} = -24.8\ \mathrm{cm^3\,mol^{-1}}$ or $\Delta V^{\neq} = -37.6$ and $-35.0\ \mathrm{cm^3\,mol^{-1}}$, respectively. The absolute values here are approximately twice as large as, or even larger than, those observed for the Cope rearrangements or the electrocyclization of 1,3,5-hexatriene to 1,3-cyclohexadiene. From this it was extrapolated that each additional five- or six-membered ring formed in the rate-determining step of reactions contributes about -10 to $-15\ \mathrm{cm^3\,mol^{-1}}$ to the activation volume.

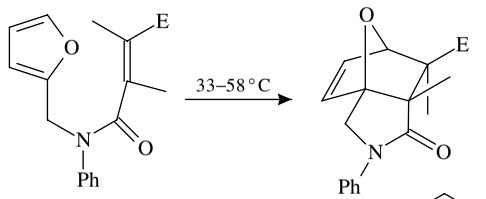
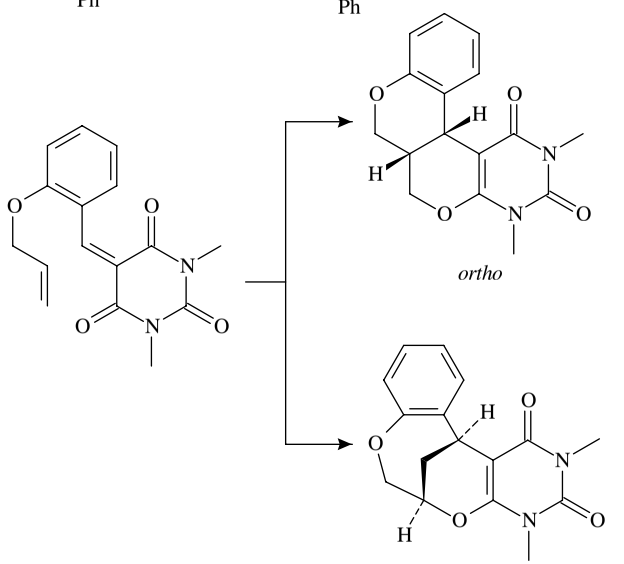
A particularly instructive example is the thermolysis of (*Z*)-1,3,8-nonatriene in which an intramolecular Diels–Alder reaction competes with a sigmatropic [1,5] hydrogen shift (Scheme 24). The use of high pressure here enables a reversal of the selectivity. At 150 °C and 1 bar the [1,5] hydrogen shift passing through a monocyclic transition state is preferred. At 7.7 kbar the intramolecular Diels–Alder reaction is preferred due to its bicyclic transition state.

E. The Relationship between Activation or Reaction Volume and Ring Size

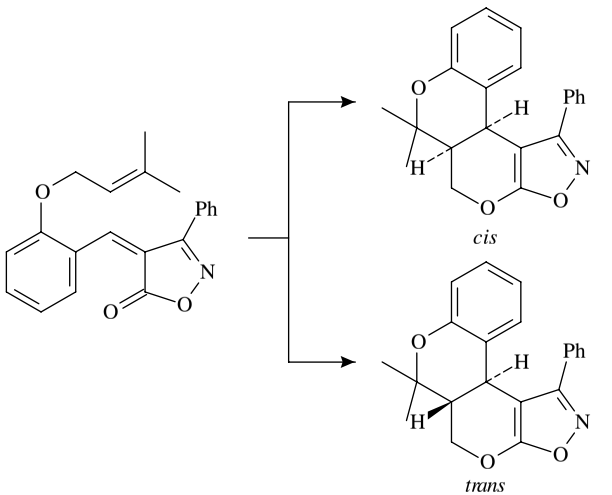
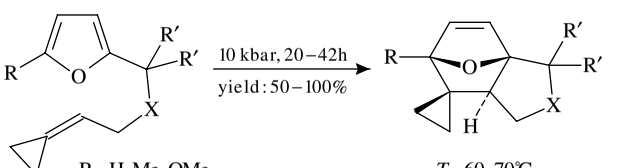
The investigation of the pressure effect on the rearrangement and cleavage of *trans*-1,2-divinylcyclobutane showed that the volume of reaction depends not only on the number but also on the size of the newly forming ring. In contrast to the Cope rearrangement of *cis*-1,2-divinylcyclobutane (Scheme 20: entry 4) the competitive reactions of *trans*-1,2-divinylcyclobutane leading to 4-vinylcyclohexene, 1,5-cyclooctadiene and 1,3-butadiene are slowed by pressure and the volumes of activation become positive, consistent with the hypothesis of the opening of the cyclobutane ring leading to an acyclic diradical intermediate (Scheme 25). Because the product ratio shows no significant pressure dependence, the activation volumes of the individual reactions are essentially equal. It was concluded here that in the diradical intermediate neither ring closure reactions nor cleavage are product-determining, contrary to the [2 + 2] cycloaddition shown in Scheme 16, entry 3. Probably pressure-independent rotations about C−C bonds in the diradical determine the distributions among the three products.

The volumes of reaction determined for the isomerization of *trans*-1,2-divinylcyclobutane to 4-vinylcyclohexene or 1,5-cyclooctadiene, in which a six- or eight-membered ring is formed, respectively, at the expense of a four-membered ring, were found to be highly negative. This observation of the decrease in volume from the four- to the six- or eight-membered ring indicates that the activation volumes of cyclizations also depend on the size of the newly forming ring. The van der Waals volumes of the cyclic structures do not differ from each other appreciably and cannot explain the observed differences between the reaction volumes.

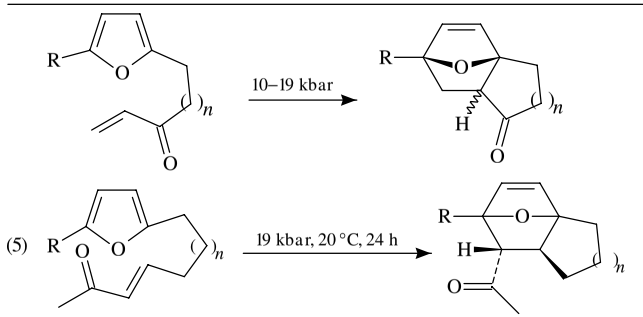
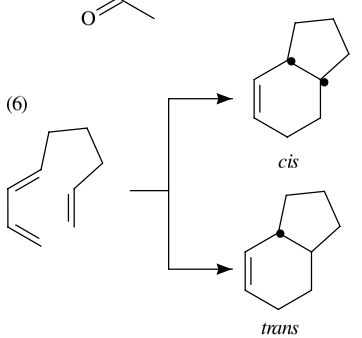
The volumes of reaction calculated for the hypothetical cyclizations of *n*-alkenes to the corresponding cycloalkanes by the use of experimentally observed partial molar volumes[190] confirm the trend derived from the ring enlargements shown in Scheme 25.

		Solvent	$\Delta V_T^{\neq a}$	$\Delta V_{20}^{\neq a}$	$\Delta V_{20}{}^a$	Reference
(1)			–25		–23	181
(2)	 *ortho*	CH_2Cl_2 THF PhMe MeCN	–33.1 –34.2 –17.0 –13.4	–23.6 –24.4 –9.5 –12.5	–30 –35 –18 –15	182
	meta	CH_2Cl_2 THF PhMe MeCN	–32.1 –32.7 –15.2 –12.1			
	$T = 110\,^{\circ}C$; *ortho* : *meta* = (3.8 – 6.8) : 1					

SCHEME 23. Intramolecular Diels–Alder reactions

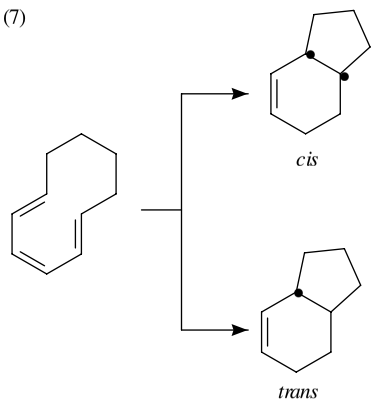
		Solvent	$\Delta V_T^{\neq a}$	$\Delta V_{20}^{\neq a}$	$\Delta V_{20}{}^a$	Reference
(3)	 *cis*	CH_2Cl_2	−19.4			183
	trans	CH_2Cl_2	−17.9			
	T=70°C; *cis* : *trans* = (5.5 − 6.8) : 1					
(4)	 R = H, Me, OMe R′ = H, Me, =O X = O, NMe	MeCN/ THF	−15.9			184
	T = 60–70°C for R = R′ = H, X = O:					

SCHEME 23. (*continued*)

		Solvent	$\Delta V_T^{\neq a}$	$\Delta V_{20}^{\neq a}$	$\Delta V_{20}{}^a$	Reference
(5)						185
(6)		n–C_6H_{14}	−24.8			186
		n–C_6H_{14}	−24.8			

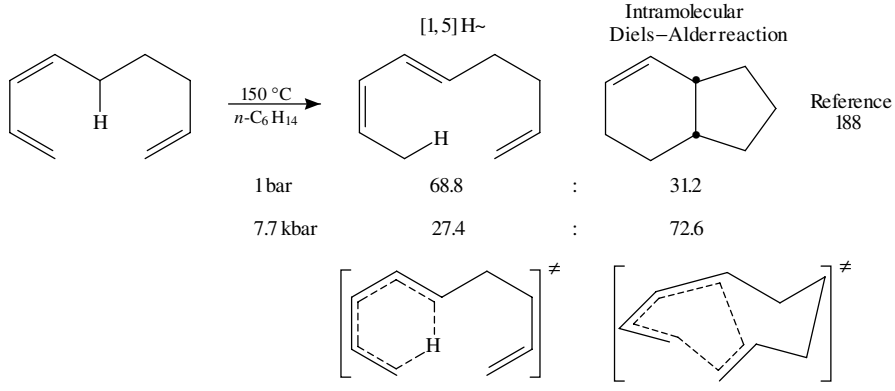
T = 153.2 °C; *cis* : *trans* = 3.0 : 1

SCHEME 23. (*continued*)

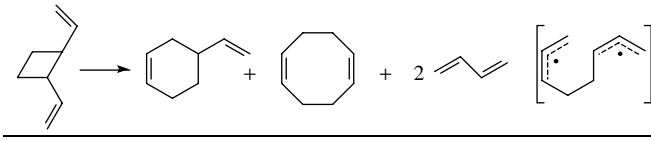
	Solvent	$\Delta V_T^{\neq a}$	$\Delta V_{20}^{\neq a}$	$\Delta V_{20}{}^a$	Reference
(7)  *cis* *trans* $T = 172.5\,^{\circ}C$; *cis* : *trans* = 1.2 : 1	n–C_7H_{16}	−37.6			187
	n–C_7H_{16}	−35.0			

[a] In $cm^3\,mol^{-1}$; the $\Delta V_{20}^{\neq}$ values were extrapolated from the $\Delta V_T^{\neq}$ values by using the El'yanov equation(equation I).

SCHEME 23. (*continued*)



SCHEME 24. The effect of pressure on the competitive rearrangements of *cis*-1,3,8-nonatriene



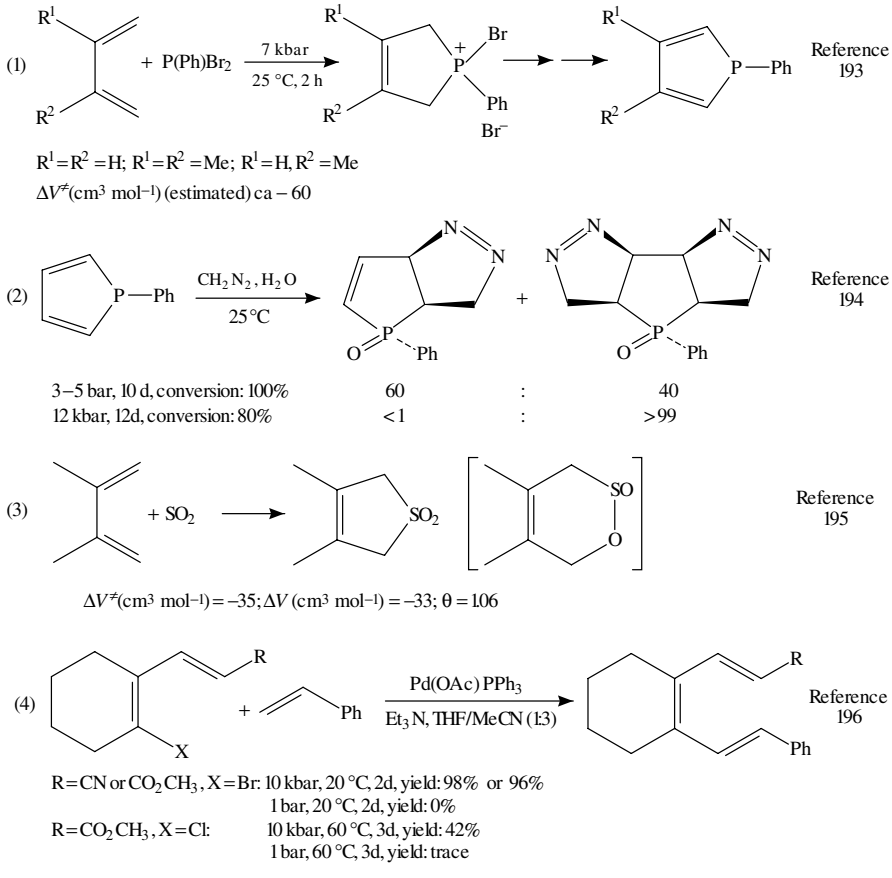
V_W ($cm^3\ mol^{-1}$):	79.3	77.5	76.6	$2 \times 44.8 = 89.6$	82.4
$\Delta V^{\neq}$ ($cm^3\ mol^{-1}$) (159.6 °C):		$+(4.2 \pm 0.7)$	$+(4.1 \pm 0.4)$	$+(5.0 \pm 9.5)$	
V ($cm^3\ mol^{-1}$) (159.6 °C):	162.0	149.0	135.2		
$\eta = V_W/V$	0.4895	0.5201	0.5666	0.4958	
V ($cm^3\ mol^{-1}$) (20.0 °C):	140.0	130.4	122.6	$2.83.2 = 166.4$	
ΔV ($cm^3\ mol^{-1}$):		$130.4 - 140.0 = -9.6$	$122.6 - 140.0 = -17.4$	$166.4 - 140.0 = +26.4$	

SCHEME 25. Activation and reaction volumes of the ring enlargment of *trans*-1,2-divinylcyclobutane

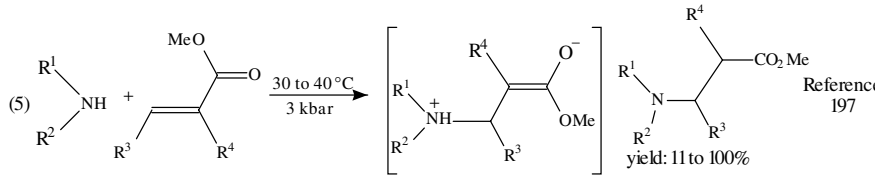
The volumes of reaction decrease continuously from formation of cyclopropane (from 1-propene: $\Delta V = -5.5\ cm^3\ mol^{-1}$) up to the formation of cyclodecane (from 1-decene: $\Delta V = -32.3\ cm^3\ mol^{-1}$) and then seem to be constant for the larger rings, whereas the van der Waals volumes of reaction are approximately equal ($\Delta V_W = -4.4$ to $-4.9\ cm^3\ mol^{-1}$) with the exception of the cyclopropane, cyclobutane and cyclopentane formation, and therefore independent of the ring size. Provided that the activation volumes depend similarly on the ring size, the formation of larger rings should be dramatically accelerated by pressure. The intramolecular Diels–Alder reactions of (*E*)-1,3,8-nonatriene and (*E*)-1,3,9-decatriene, in which either a new five- and six-membered ring or two new six-membered rings are formed, seems to be the first example for the validity of this assumption (Scheme 23: entries 6 and 7). Furthermore, this ring-size effect explains why the activation volume of the formation of three-membered rings in cheleotropic reactions of carbenes with alkenes[191] and of the five-membered rings in 1,3-dipolar cycloadditions[23,25,192] are substantially less negative than those of the formation of six-membered rings in the Diels–Alder reactions.

V. MISCELLANEOUS REACTIONS OF DIENES AND POLYENES

Other reactions than the pericyclic processes discussed in the previous sections can profit from high pressure. Scheme 26 shows a few recent examples which are related to the topic of this chapter. In the addition of dibromophenylphosphane to 1,3-dienes (Scheme 26: entry 1) charge separation and ring formation lead to a dramatic decrease in volume [$\Delta V^{\neq}$ (estimated) ≈ -60 cm^3 mol^{-1}] so that this reaction is strongly accelerated by pressure. The first step in the reaction of diazomethane with 1-phenylphosphole (Scheme 26: entry 2) is certainly the addition of diazomethane to the phosphorus ($R_3P + CH_2N_2 \rightarrow R_3P{=}N{-}N{=}CH_2$)[199] followed by hydrolysis leading to the highly reactive 1-phenylphosphole-1-oxide which reacts with diazomethane in the fashion of a 1,3-dipolar cycloaddition to form the monoadduct and subsequently the bisadduct. (In the absence of water none of the cycloadducts is formed[200].) Apparently, high pressure has a strongly rate-enhancing effect on the first addition of diazomethane and the 1,3-dipolar cycloaddition as well, so that the reaction is almost completed at 12 kbar within 12 hours compared to 10 days at 3–5 bars where the monoadduct is formed preferentially.



SCHEME 26. Miscellaneous reaction of dienes and polyenes



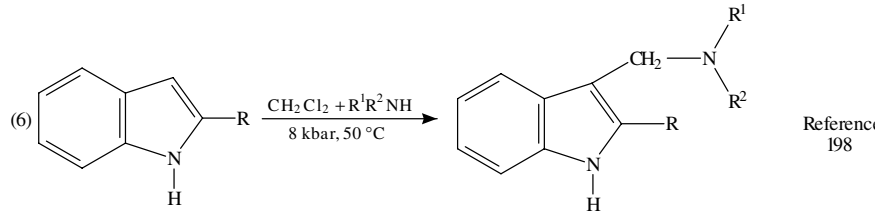
R^1 = *n*-Pr, *i*-Pr, *n*-Bu, *i*-Bu, *t*-Bu, R^2 = H, $R^3 = R^4 = H$

$R^1 = R^2$ = *n*-Pr R^3 = Me, R^4 = H

R^3 = H, R^4 = Me

$\Delta V^{\neq}$ ($cm^3\ mol^{-1}$) = − (42 to 53)

ΔV ($cm^3\ mol^{-1}$) = − (25 to 26)



SCHEME 26. (*continued*)

The addition of SO_2 to 1,3-dienes is considered to be an example of a linear cheleotropic reaction. The activation volume of the reaction between SO_2 and 2,3-dimethyl-1,3-butadiene was found by Isaacs and Laila to be more negative than the reaction volume ($\theta = \Delta V^{\neq}/\Delta V = 1.06$) (Scheme 26: entry 3). Comparable to several Diels–Alder reactions, the transition state volume is smaller than that of the product. Due to the large θ value one might speculate that in the rate-determining step the Diels–Alder adduct (the six-membered ring sulfinic ester)[201] is formed followed by a rearrangement to the observed five-membered ring sulfone.

The palladium-catalyzed Heck reaction of styrene with bromo- or chlorodienes leading to conjugated trienes (Scheme 26: entry 4) is also accelerated by pressure and the yields can be improved from 0% at 1 bar to 42–98% at 10 kbar. These findings indicate that the rate-determing steps of the Heck reaction are associative. The Heck coupling between aryl nonaflates (nonafluorobenzenesulfonate, ArONf) and 2,3-dihydrofuran in the presence of $Pd(OAc)_2$ and a chiral ligand [(R)-BINAP] shows a higher enantioselectivity at 10 kbar than at 1 bar[202]. The nucleophilic addition of primary and secondary amines to methyl acrylates (Scheme 26: entry 5) shows a powerful pressure-induced acceleration (with activation volumes smaller than the corresponding reaction volumes, $\theta = \Delta V^{\neq}/\Delta V > 1$). These findings are understandable on the assumption that in the rate-determing step a zwitterionic intermediate is formed. A pronounced effect is also observed for the Mannich reaction of indoles with dichloromethane and secondary amines (Scheme 26: entry 6) indicating that polar intermediates are involved in this reaction.

VI. CONCLUDING REMARKS

The packing coefficient, $\eta = V_W/V$, has been demonstrated to be a valuable tool with which to explain the effect of pressure on many pericyclic reactions. The finding, that η

of cyclic structures is larger than that of the corresponding acyclic structures, explains the preference of pericyclic cycloaddition over the corresponding stepwise reactions at high pressure and the negative activation volumes of many pericyclic rearrangements. The size of η depends on the number and size of the newly forming rings. This explains why, e.g., intramolecular Diels–Alder reactions involving bicyclic transition state are favored over rearrangements involving monocyclic transition states.

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    (b) Bernd Dieckers GmbH, Meß- und Prüfanlagen-Technik, Hagwinkel 46, D-47877 Willich-Neersen, Germany.
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    (d) Unipress Equipment, Division High Pressure Research Center, Polish Academy of Science, ul. Sokolowska 29/37, 04-142 Warszawa, Poland.
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CHAPTER **13**

Radical addition to polyenes

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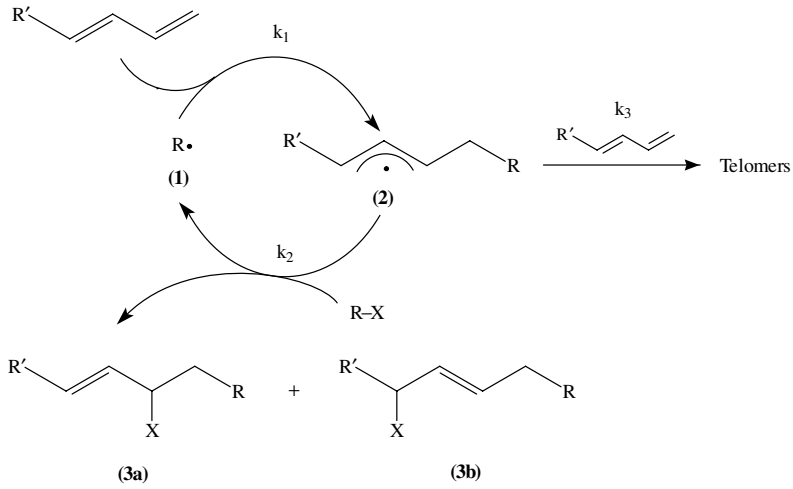
I. INTRODUCTION

Despite the enormous importance of dienes as monomers in the polymer field, the use of radical addition reactions to dienes for synthetic purposes has been rather limited. This is in contrast to the significant advances radical based synthetic methodology has witnessed in recent years. The major problems with the synthetic use of radical addition reactions to polyenes are a consequence of the nature of radical processes in general. Most synthetically useful radical reactions are chain reactions. In its most simple form, the radical chain consists of only two chain-carrying steps as shown in Scheme 1 for the addition of reagent R−X to a substituted polyene. In the first of these steps, addition of radical R• **(1)** to the polyene results in the formation of adduct polyenyl radical **2**, in which the unpaired spin density is delocalized over several centers. In the second step, reaction of **2** with reagent R−X leads to the regeneration of radical **1** and the formation of addition products **3a** and **3b**. Radical **2** can also react with a second molecule of diene which leads to the formation of polyene telomers.



SCHEME 1

Even though more complex schemes involving three or more chain-carrying steps are frequently observed, this most simple mechanism is sufficient to discuss the conditions under which radical chain processes will be synthetically successful. To begin with, the overall rate of product formation is proportional to the square root of the rate of initiation. Once initiated, both chain-carrying steps must occur at rates which are high enough to compete with typical chain-breaking processes such as recombination, disproportionation or reaction with the solvent. It is commonly assumed that successful radical chain reactions can only be achieved if the rate constants k_1 and k_2 are larger than 10^2 M^{-1} s^{-1}[1,2]. While this reactivity requirement is necessary to keep the chain process running at all, synthetically useful chain reactions also have to show sufficient selectivity in a twofold sense. First, reaction of adduct radical **2** with reagent R−X must be significantly faster than reaction with a second polyene molecule. Even though the branching ratio between these two reactions can be influenced to a certain extent by choosing suitable concentrations of R−X and polyene, the rate constant k_2 for reaction between radical **2** and R−X should be at least as large as the propagation rate constant (k_3) for polymerization. Second, the use of polyenes adds an additional selectivity requirement in that the regiochemistry in the initial addition step and in the final reaction of polyenyl radical **2** with reagent R−X should be high for the reaction to be synthetically useful. In the following, we will take a detailed look at each of these criteria to identify the suitability of polyenes in radical chain reactions and identify possible problem areas.

II. REACTIVITY OF POLYENES TOWARDS RADICALS

Absolute rates for the addition of the methyl radical and the trifluoromethyl radical to dienes and a number of smaller alkenes have been collected by Tedder (Table 1)[3]. Comparison of the rate data for the apolar[4] methyl radical and the electrophilic trifluoromethyl radical clearly show the electron-rich nature of butadiene in comparison to ethylene or propene. This is also borne out by several studies, in which relative rates have been determined for the reaction of small alkyl radicals with alkenes. An extensive list of relative rates for the reaction of the trifluoromethyl radical has been measured by Pearson and Szwarc[5,6]. Relative rates have been obtained in these studies by competition with hydrogen

TABLE 1. Absolute rate constants for the addition of methyl and trifluoromethyl radicals to simple alkenes at 164 °C[3]

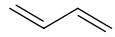
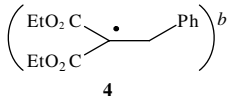
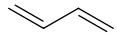
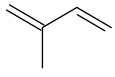
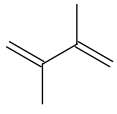
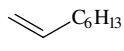
Alkene	k_{ADD} M^{-1} s^{-1}	
	$\bullet CH_3$	$\bullet CF_3$
	3.6×10^5	7.0×10^8
	3.2×10^4	8.1×10^6
	4.5×10^4	3.5×10^6

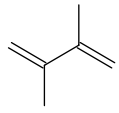
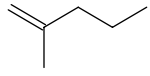
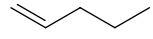
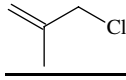
TABLE 2. Relative rate constants for the addition of the trifluoromethyl radical and the diethyl α-benzylmalonyl radical to simple alkenes and dienes

Alkene	$k_{REL}(\bullet CF_3)^a$	k_{REL}  **4** ^{b}
	1.0	—
	1.47	—
	2.10	70
	0.54	82
	0.13	—
	—	1.0

[a] References 5 and 6, in the gas phase at 65 °C.
[b] References 7 and 8, in CH_3CO_2H at 60 °C.

abstraction from 2,3-dimethylbutane (Table 2). Even though the analytical method has been a point of controversy[9], the relative rate data for pairs of alkenes leave little doubt about the high reactivity of dienes towards electrophilic radicals. The higher addition rate to dienes results in this case from lower activation barriers, while preexponential factors are rather similar in most cases. The electrophilic dicyanomethyl radical[10] has also been shown to add significantly faster to 2,3-dimethyl-1,3-butadiene than to other structurally similar alkenes (Table 3)[11]. Dicyanomethyl radicals have in this instance been generated by photochemical initiated addition of bromomalononitrile to alkenes. The diethyl α-benzylmalonyl radical **(4)** has been characterized as ambiphilic due to its bell-shaped reactivity profile in alkene addition reactions[7]. Addition of **4** to styrene and 2,3-dimethyl-1,3-butadiene occurs at comparable rates while addition to 1-octene or to acrylates is

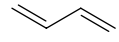
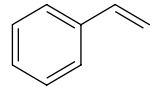
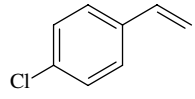
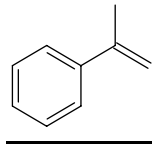
TABLE 3. Relative rate constants for the addition of the dicyanomethyl radical to simple alkenes and dienes in 1,2-dichloroethane at 28 °C[11]

Alkene	k_{REL} (•CH(CN)$_2$)
	100
	6.7
	0.44
	0.52

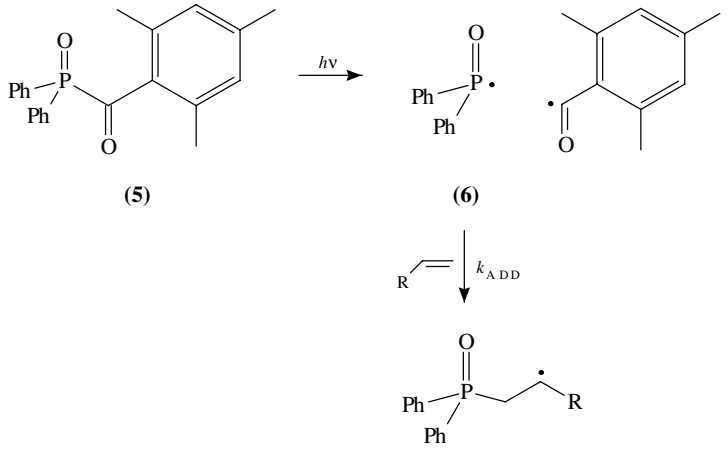
slower by almost two orders of magnitude (Table 2). From the absolute rate constant for addition of **4** to 1-octene of $k_{ADD} = 9.8 \times 10^4$ M^{-1} s^{-1} at 60 °C in acetic acid, the rate for addition to 2,3-dimethyl-1,3-butadiene can be calculated as $k_{ADD} = 6.9 \times 10^6$ M^{-1} s^{-1}[7,8]. Comparable rates for the addition to butadiene and substituted styrenes have also been found in the trichloromethyl radical addition to alkenes[12]. Again, the technique of competition kinetics has been used to obtain these values (Table 4).

Due to the significant importance of dienes as monomers, absolute as well as relative rate data have been determined for the addition of initiator derived radicals. Photolysis of (2,4,6-trimethylbenzoyl)diphenylphosphine oxide (TMDPO) **5** leads to the formation of

TABLE 4. Relative rate constants for the addition of the trichloromethyl radical to substituted styrenes and butadiene in $BrCCl_3$ at 80 °C[12]

Alkene	k_{REL}(•CCl_3)
	1.0
	0.5
	0.5
	2.1

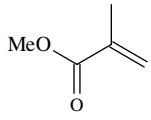
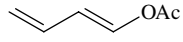
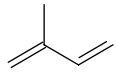
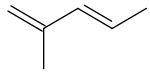
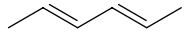
diphenylphosphonyl radical **6**. Subsequent addition of **6** to alkenes and dienes has been shown to proceed rapidly (equation 1) by time-resolved EPR spectroscopy (Table 5)[13,14].



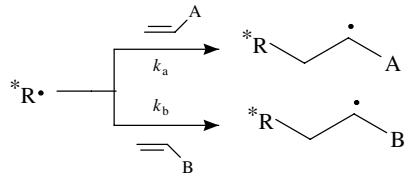
(5) **(6)** (1)

The phosphonyl radical **6** cannot easily be classified as nucleophilic or electrophilic, since the bimolecular rate constants for addition to a wide range of alkenes vary by no more than one order of magnitude. A similar observation can be made for relative addition rates of other initiator derived radicals, in which the radical centers are substituted by electron-donating as well as electron-withdrawing substituents. The end group analysis of diene polymers using isotopically labeled initiators has proven especially fruitful in this regard[15,16a]. In this method, isotopically labeled initiators are reacted with a mixture of alkenes. The ratio of the rate constants for addition of initiator derived radicals to both monomers can then be determined by end group analysis of the resulting copolymer. ^{13}C-NMR spectroscopy appears to be the method of choice if ^{13}C-enriched initiator is

TABLE 5. Absolute rate data for the addition of the diphenylphosphonyl radical to various alkenes in benzene at 20 °C[13,14]

Polyene	Bimolecular rate constant k_{ADD} ($M^{-1}\,s^{-1}$)	Reference
	$(1.6 \pm 0.4) \times 10^7$	13
	$(1.5 \pm 0.2) \times 10^7$	13
	$(1.4 \pm 0.2) \times 10^7$	14
	$(1.2 \pm 0.2) \times 10^7$	14
	$(2.9 \pm 0.2) \times 10^6$	14

available that carries the label sufficiently close to the alkene addition site (equation 2).



(2)

As a point of reference, relative rates for methyl methacrylate have also been included in Table 6. While addition to butadiene or isoprene is significantly faster as compared to methyl methacrylate for electrophilic or ambident radicals, little rate variation is found for the 1-phenylethyl radical.

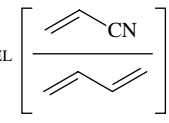
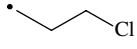
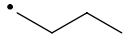
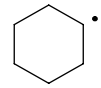
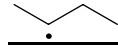
The dependence of relative rates in radical addition reactions on the nucleophilicity of the attacking radical has also been demonstrated by Minisci and coworkers (Table 7)[17]. The evaluation of relative rate constants was in this case based on the product analysis in reactions, in which substituted alkyl radicals were first generated by oxidative decomposition of diacyl peroxides, then added to a mixture of two alkenes, one of them the diene. The final products were obtained by oxidation of the intermediate allyl radicals to cations which were trapped with methanol. The data for the acrylonitrile–butadiene

TABLE 6. Relative bimolecular addition rates for the reaction of initiator derived radicals obtained by polymer end group analysis[15,16a]

Alkene	Relative addition rates k_{rel}			
	NC, H_3C^*, CH_3^*, •	MeO_2C, H_3C^*, CH_3^*, •	Ph, $*$, H, CH_3, •	O, Ph, O•
CO_2Me	1.0[a]	1.0[b]	1.0[c]	1.0
	7.0	3.0	1.3	6.4
	3.3	1.9	0.7	3.5
	6.5	4.2	1.2	8.3
Ph, Ph	1.4	1.1	0.7	13.0

[a] At 60 °C in benzene, Reference 16a
[b] At 60 °C in benzene, Reference 16b
[c] At 100 °C in toluene, Reference 16a.

TABLE 7. Relative rate constants for the addition of substituted alkyl radicals to the acrylonitrile/butadiene pair in methanol at 0 °C[17]

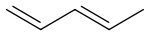
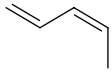
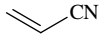
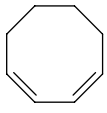
Radical	k_{REL} 
$ClCH_2\bullet$	1.2
$H_3C\bullet$	1.7
	1.7
	3.1
$CH_3CH_2\bullet$	6.2
	9.0
	9.3
	11.6
	15.8

pair collected in Table 7 is rather typical and shows how the relative addition rate mainly depends on two effects. First, the addition to the electron-deficient alkene becomes comparatively faster with an increasing number of alkyl substituents at the radical center. Second, substitution of the alkyl groups by electronegative chlorine atoms reduces the relative addition rate. Both effects can readily be explained with substituent effects on the nucleophilicity of the radicals. The relative addition rate does not, however, exceed a value of 20 even for the most nucleophilic alkyl radicals.

In many synthetically useful radical chain reactions, hydrogen donors are used to trap adduct radicals. Absolute rate constants for the reaction of the resulting hydrogen donor radicals with alkenes have been measured by laser flash photolysis techniques and time-resolved optical absorption spectroscopy for detection of reactant and adduct radicals[18a]. Addition rates to acrylonitrile and 1,3-pentadienes differ by no more than one order of magnitude, the difference being most sizable for the most nucleophilic radical (Table 8). The reaction is much slower, however, if substituents are present at the terminal diene carbon atoms. This is a general phenomenon known from addition reactions to alkenes, with rate reductions of *ca* 100 observed at ambient temperature for the introduction of methyl groups at the attacked alkene carbon atom[18b]. This steric retardation of the addition process either completely inhibits the chain reaction or leads to the formation of unwanted products.

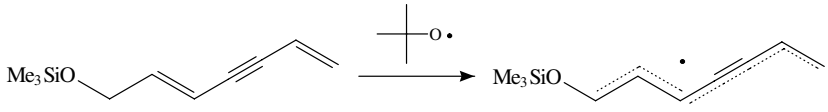
One side reaction commonly encountered in the reaction of alkyl-substituted polyenes with oxygen-centered radicals is hydrogen abstraction from the alkyl group in positions adjacent to the polyene π-system. For reactions of the *tert*-butyloxy radical, this reaction becomes so dominant that it can be used to form polyenyl radicals by hydrogen abstraction

TABLE 8. Absolute rate constants for the addition of triethylsilyl, tri-*n*-butylgermyl and tri-*n*-butylstannyl radicals to alkenes[18a]

Alkene	$Et_3Si\bullet$		*n*-$Bu_3Ge\bullet$		*n*-$Bu_3Sn\bullet$	
	T(K)	k_{ADD} ($M^{-1}\,s^{-1}$)[a]	T(K)	k_{ADD} ($M^{-1}\,s^{-1}$)[b]	T(K)	k_{ADD} ($M^{-1}\,s^{-1}$)[c]
	299	1.4×10^8	297	4.6×10^7	298	6.8×10^7
	—	—	298	4.0×10^7	298	6.8×10^7
	302	1.1×10^9	300	1.8×10^8	299	8.8×10^7
	299	3.8×10^6	299	6.4×10^5	297	$< 7 \times 10^4$

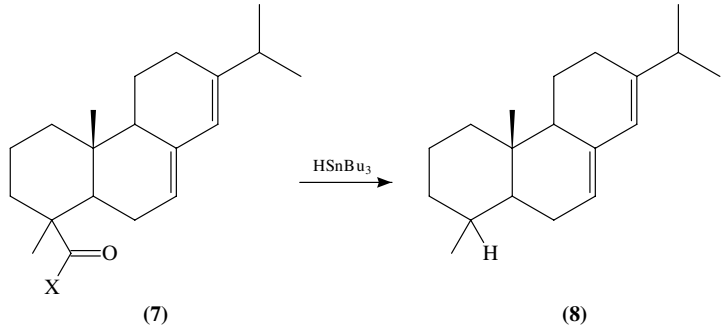
[a]Di-*tert*-butyl peroxide/Et_3SiH (1:1) as solvent.
[b]Di-*tert*-butyl peroxide + 15% (vol) *n*-Bu_3GeH as solvent.
[c]Di-*tert*-butyl peroxide + 10% (vol) *n*-Bu_3SnH as solvent.

from alkyl-substituted polyenes (equation 3)[19].



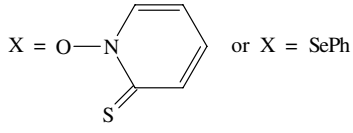
(3)

In most other cases, however, the diene system simply becomes too unreactive to participate in radical chain reactions. Thus, the reductive decarboxylation of ester **7** by Barton-POC ester methodology[20] or as the selenoester[21] gives the reduced product **8**, cleanly without any trace of product in which the diene system has participated in the reaction (equation 4)[20,21].



(7) **(8)**

(4)



or X = SePh

Based on the data collected in this section, one must conclude that the addition of radicals to dienes is certainly rapid enough to compete against the typical chain-breaking processes and that especially the addition of electrophilic radicals to polyenes appears to bear significant potential. Terminally substituted polyenes are likely to be unsuitable for radical addition reactions due to their lower addition rates and to undesirable side reactions.

III. REACTIVITY OF POLYENYL RADICALS

Little quantitative information is available for the kinetics of the reaction of polyenyl radicals. The propagation rate constants for polymerization reactions might be indicative, however, of the characteristics of free polyenyl radicals in solution[6,22,23]. From Table 9 it can be seen that the propagation rate constants for butadiene and isoprene are smaller by a factor of 10 to 20 as compared to those for acrylonitrile and typical acrylates. From Section 2, an increase in rate would have been expected on changing from acrylates to dienes. The lower rates actually observed must therefore be attributed to the lower reactivity of the allyl radicals formed during diene polymerization. The sluggish reactivity of polyenyl radicals is usually rationalized through the high resonance stabilization of these species[24–29]. The stabilization energy for the allyl radical obtained in various ways amounts to 13.2–14.6 kcal mol^{-1}. A limiting value for the stabilization energy of indefinitely long polyenyl radicals has been estimated to be between 24 and 33.3 kcal mol^{-1}. Even if reaction occurs at the terminal positions of the polyenyl radical system, partial loss of the stabilization energy and an increased activation barrier will result for this reaction.

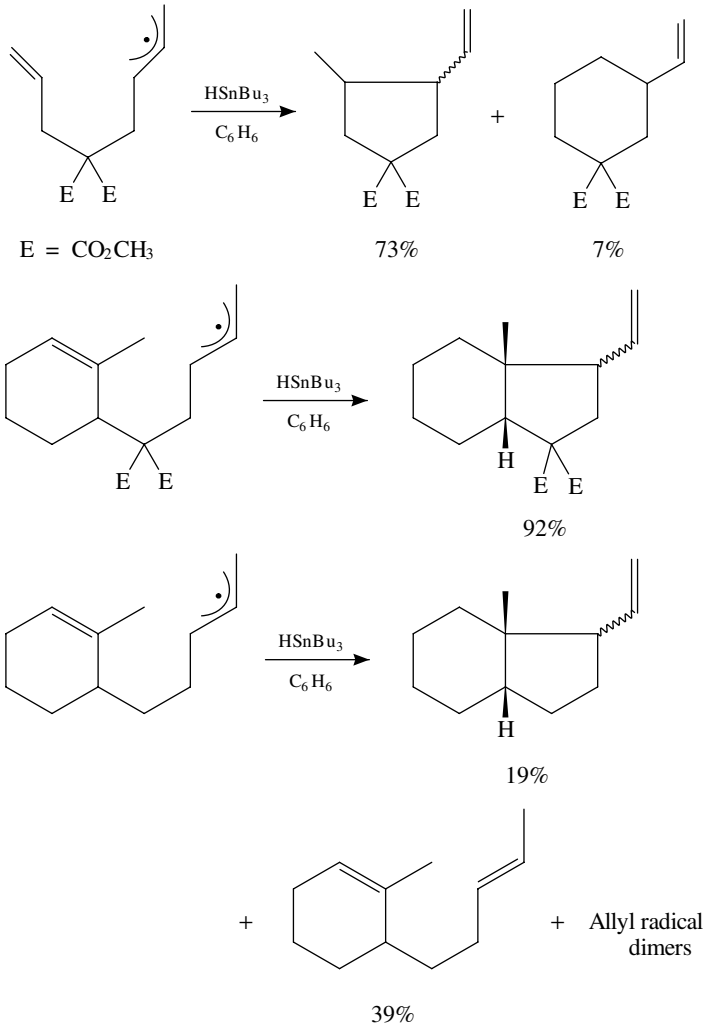
Cases in which allyl radicals display sufficient reactivity to participate successfully in radical chain reactions include the addition of bromotrichloromethane to butadiene[30,31], the reaction of cyclopentadiene with tosyl cyanide[32], the addition of thiols[33–36a], stannanes[35,37–39] and hydrogen halides[35,40]. All these reactions follow the simple two-step radical chain mechanism depicted in Scheme 1, and the low reactivity of the intermediate allyl radicals can be compensated by using the trapping agent in excess or even as the solvent. In chain reactions with three or more chain-carrying radicals, this compensation is not possible anymore, because the concentration of the reaction partners has to be chosen such that the selectivity requirements for all intermediate radicals are satisfied[1]. Complex radical chain reactions with polyenes as one of the reactants are therefore not known.

The reactivity of allyl radicals does, however, appear to be sufficient for intramolecular radical reactions. In a systematic study, Stork and Reynolds investigated the feasibility of allyl radical 5-*exo* cyclizations[41]. It was found that cyclization proceeds readily for a variety of systems, especially for those with geminal 3,3-diester substitution. Mixtures of *cis/trans*-cyclopentanes are formed as the major products, while 6-*endo* cyclization is hardly observed[42]. Allyl radicals behave in this respect much like alkyl radicals[43]. Cyclization is not even hindered by the presence of substituents at the attacked carbon

TABLE 9. Propagation rate constants (k_{prop}) for the polymerization of selected alkenes and dienes at 60 °C[6,22,23]

Alkene	k_{PROP} (M^{-1} s^{-1})	log A	E_a (kcal mol^{-1})
Butadiene	100	8.1	9.3
Isoprene	50	8.1	9.8
Methyl methacrylate	734	7.0	6.3
Acrylonitrile	1960	—	—

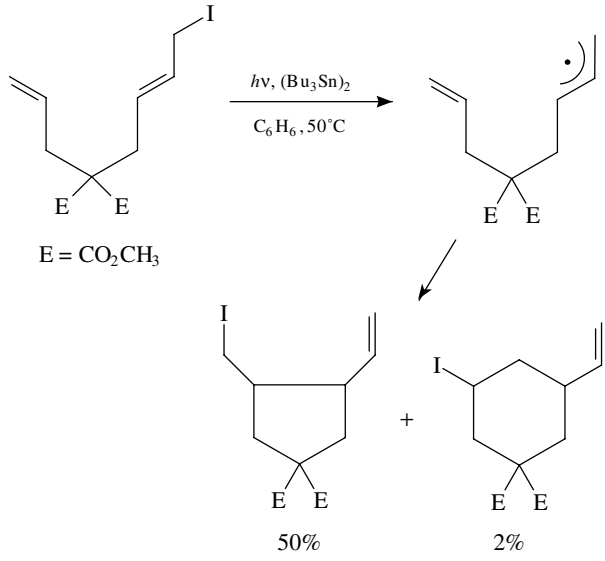
atom. Only in the absence of the accelerating[44] effect of the *gem*-diester substitution does cyclization become too slow to compete with either reduction of the allyl radical or, as a typical side reaction of allyl radicals, dimerization (equation 5). Experimental evidence was also collected to show that allyl radical cyclizations are mainly under kinetic control. The *cis/trans* selectivity in cyclopentane formation depends, however, on the nature of the hydrogen donor.



(5)

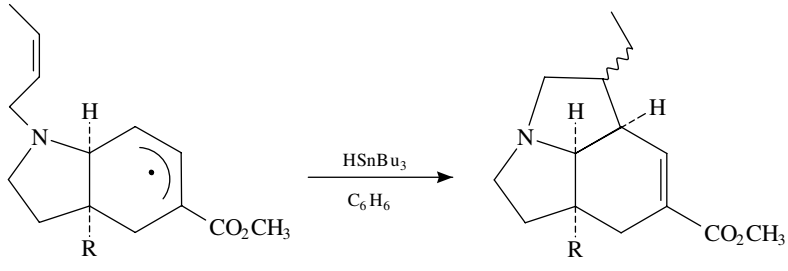
The strong prevalence for allyl radicals to cyclize in 5-*exo* fashion as well as the accelerating effect of geminal diester substitution was also observed in iodide atom transfer reactions of allylic iodides[44]. The ratio of 5-*exo* to 6-*endo* product is even higher than for hydrogen trapping, probably also due to the lower temperature in this photolytically initiated reaction (equation 6). Allylic dimers were again isolated as side products. No

cyclization was observed in the absence of ester groups.



(6)

Cyclization has also been observed for those cases in which allyl radicals are stabilized by additional substituents. Radicals **9**, which carry an ester group at one allyl terminus, cyclize readily in a 5-*exo* fashion to furnish products **10** in good yield. No 6-*exo* product was found in this instance (equation 7)[45].

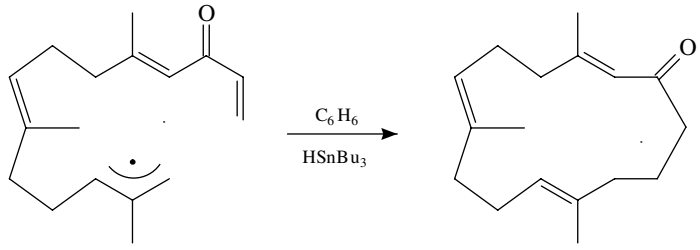


(7)

(9) **(10)**

R = Ph, SPh 60 – 85%

Finally, allyl radicals have successfully been employed in macrocyclization reactions, in which the slower rate of reaction of allyl radicals with hydrogen donors turned out to be advantageous[46]. Thus, radical **11** cyclizes in 14-*endo* mode to provide, after trapping with tin hydrogen, the product **12** as a *E/Z*-mixture of the C2/C3 double bond. No products derived from 6-*exo* or 10-*exo* cyclizations could be found (equation 8). This can be rationalized by assuming a faster rate of addition of the nucleophilic allyl radical to the electron-deficient terminal double bond than to the C6 or C10 double bonds.



(8)

(11) **(12)** 52%

In conclusion, it appears that allyl or polyenyl radicals are much less reactive than alkyl radicals, which restricts the use of polyenes in intermolecular radical chain reactions to simple two-step processes. Allyl radicals are, however, reactive enough to partake in a variety of intramolecular reactions.

IV. REGIOSELECTIVITY OF RADICAL ADDITION REACTIONS TO POLYENES

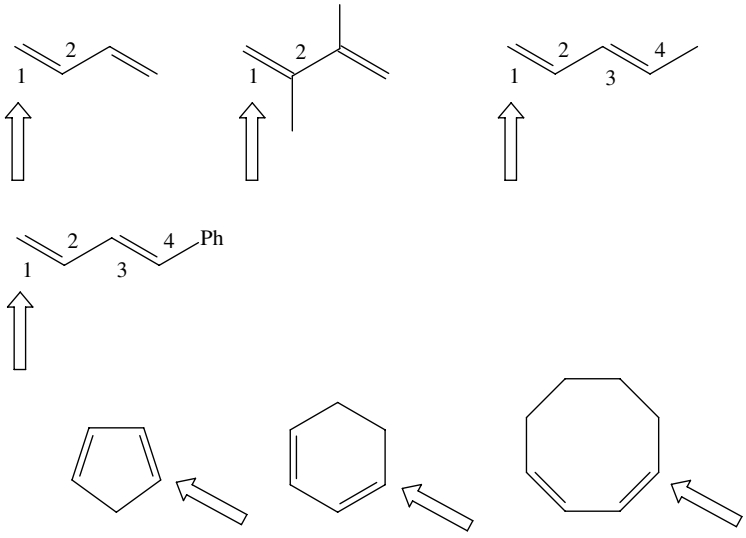
The regioselectivity in radical addition reactions to alkenes in general has successfully been interpreted by a combination of steric and electronic effects[18b,47]. In the absence of steric effects, regiochemical preferences can readily be explained with FMO theory. The most relevant polyene orbital for the addition of nucleophilic radicals to polyenes will be the LUMO; for the addition of electrophilic orbitals it will be the HOMO. Table 10 lists the HOMO and LUMO coefficients (without the phase sign) for the first three members of the polyene family together with those for ethylene as calculated from Hückel theory and with the AM1 semiempirical method[48].

The orbital coefficients obtained from Hückel calculations predict the terminal position to be the most reactive one, while the AM1 model predicts the C1 and C3 positions to be competitive. In polyenes, this is true for the addition of nucleophilic as well as electrophilic radicals, as HOMO and LUMO coefficients are basically identical. Both theoretical methods agree, however, in predicting the C1 position to be considerably more reactive as compared to the C2 position. It must be remembered in this context that FMO-based reactivity predictions are only relevant in kinetically controlled reactions. Under thermodynamic control, the most stable adduct will be formed which, for the case of polyenyl radicals, will most likely be the radical obtained by addition to the C1 position.

TABLE 10. HOMO and LUMO coefficients for ethylene and selected polyenes

Alkene		HMO				AM1			
		C1	C2	C3	C4	C1	C2	C3	C4
1	LUMO	0.71				0.71			
	HOMO	0.71				0.71			
1 2	LUMO	0.60	0.37			0.56	0.43		
	HOMO	0.60	0.37			0.56	0.43		
1 2 3	LUMO	0.52	0.23	0.42		0.45	0.28	0.47	
	HOMO	0.52	0.23	0.42		0.44	0.29	0.47	
1 2 3 4	LUMO	0.46	0.16	0.41	0.30	0.36	0.20	0.44	0.37
	HOMO	0.46	0.16	0.41	0.30	0.36	0.21	0.43	0.37

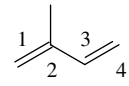
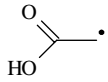
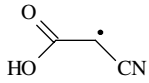
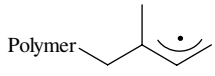
Most of the dienes investigated experimentally show high regioselectivity in radical addition reactions. The preferred position of attack is shown in Scheme 2.



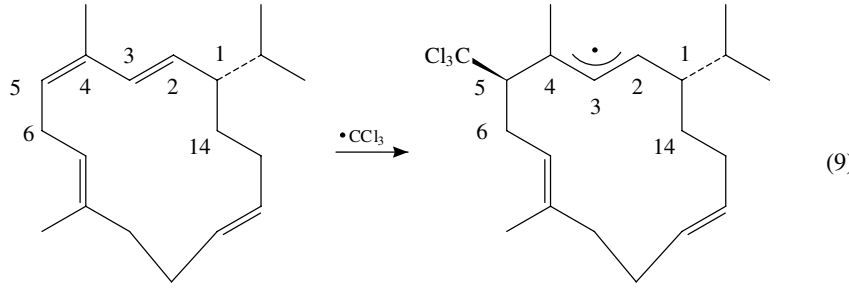
SCHEME 2

In one of the earliest investigations of regioselectivity in radical addition reactions to polyenes, the addition of hydrogen bromide to 1,3-butadiene was observed to yield mainly the 1,4-addition product in the presence of peroxides[40]. The preference for attack at the C1 position of 1,3-butadiene has subsequently been observed for a large number of radicals[3,14,17,30,34,37–39,49–56]. Only for the addition of the methyl radical has the ratio of addition to the C1 vs C2 actually been measured. A value of C1:C2 = 1.0:0.01 has been found[50]. For all other cases, products arising from attack at C2 have not been reported. This is also true for radical addition to 2,3-dimethyl-1,3-butadiene[9,10,32,34,37–39,57]. Additions to 1,3-pentadiene occur predominantly at the C1 position due to the steric effect exerted by the terminal methyl group[10,33,34,37,51,58]. This is a reflection of the reduced addition rate to C4 due to the steric effects of α-substituents[18b]. Rate retardation does not, however, go as far as redirecting addition to the C2/C3 centers, as ESR investigation of the propagating radical chain in the polymerization of 2,4-hexadiene has shown[14]. The early observation of exclusive C4-addition in the reaction of thiophenol with 1-phenyl-1,3-butadiene can also be explained by steric effects[59]. The hydrostannation of cyclic olefins proceeds with exclusive attack of the intermediate stannyl radicals on the terminal diene positions[37,38]. Addition of malonyl or tosyl radicals to cyclopentadiene and cyclohexadiene also takes place at the C1 position[10,32,57,60]. Isoprene represents an interesting case in that the two terminal positions are nonidentical due to their β-substituents. Again, no additions to the non-terminal carbon centers have been reported, but the C1:C4 addition ratio strongly depends on the attacking radical (Table 11). The selectivity pattern in the addition of thiols to chloroprene is almost identical to that observed for isoprene[33,34]. A somewhat more complex situation exists in the radical chain addition of CCl_4 to cembrene **13**[61]. Attack of the trichloromethyl radical occurs exclusively at the C5 center of **13** to form adduct radical **14** (equation 9). The high regio- and stereoselectivity appears

TABLE 11. Regioselectivity in the radical addition to isoprene

Radical	T (°C)	Solvent	 $C_1:C_2:C_3:C_4$	Reference
$Cl_3C\bullet$	80	CCl_4	C4 only	51
	20	C_6H_6	C1 only	13
	25	HOAc	1.0:0.0:0.0:2.8	53
	25	HOAc	1.0:0.0:0.0:7.8	53
	0	CH_3OH	3.4:0.0:0.0:1.0	54b
$Me_3Sn\bullet$	100	Me_3SnH	1.0:0.0:0.0:1.0	38
	20	Isoprene	C1 only	14
$CH_3S\bullet$	25	neat	3.5:0.0:0.0:1.0	33,34
$PhS\bullet$	25	neat	39:0.0:0.0:1.0	33,34
	25	neat	8.9:0.0:0.0:1.0	33,34

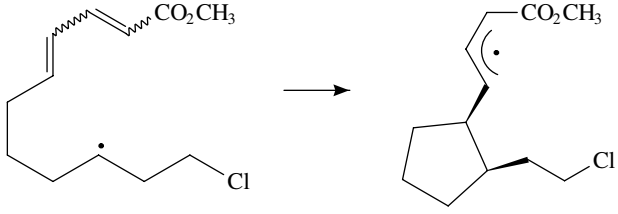
to be the consequence of steric effects as the X-ray structure of **13** shows the C2 position blocked by the isopropyl group from the top side, and by the ring C14 center from the bottom side, while addition can occur unhindered from the top side at C5.



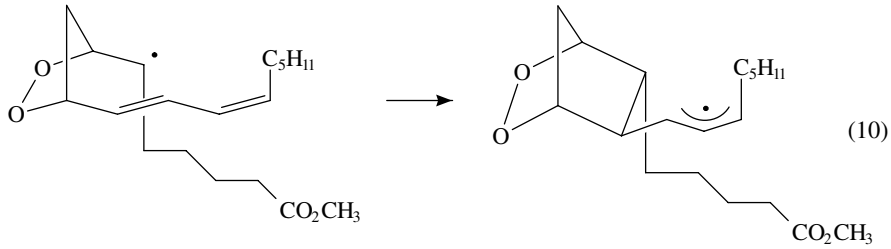
(9)

(13) **(14)**

The regioselectivity in diene addition reactions can also be influenced by ring strain effects in cyclization reactions. The regioselectivity is highly predictable in those cases, in which addition to the preferred diene center forms the preferred ring size. Thus, the cyclization of radical **15** proceeds readily to form the *cis*-disubstituted cyclopentylmethyl radical **16** with high selectivity[39]. Similarly, cyclization of **17** affords exclusively bicyclic radical **18**, in which the additional cyclopentane ring has been formed by addition to the terminal position of the butadiene subunit[62]. This preference for 5-*exo* cyclizations onto dienes is not even disrupted by substituents at the C1 or C4 positions of the diene system, as seen for radical **19**, which cyclizes to **20** (equation 10)[63]. This is in contrast to alkyl radical cyclizations to alkenes, in which major amounts of 6-*endo* cyclization is observed for 5-substituted systems[43].

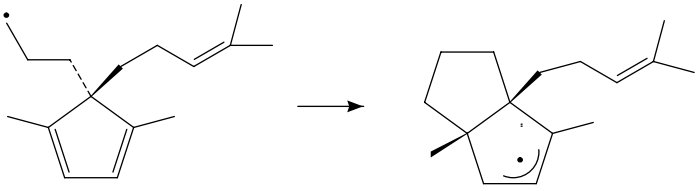


(15) **(16)**



(10)

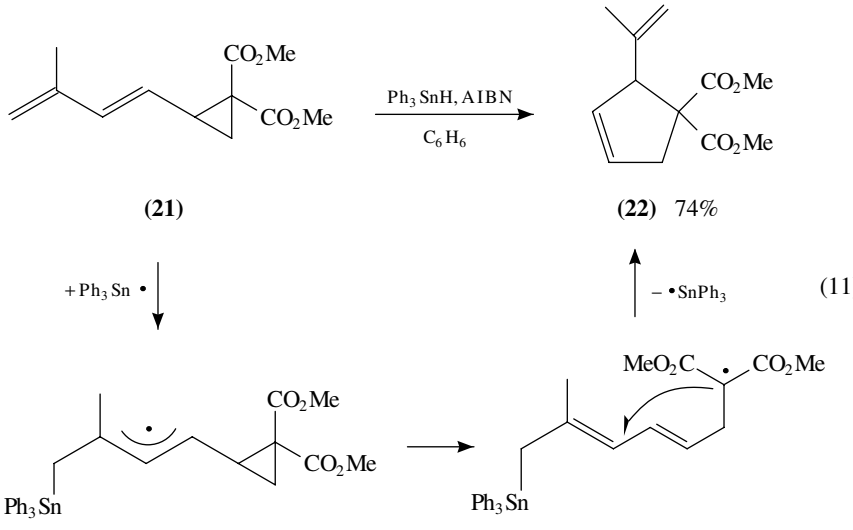
(17) **(18)**



(19) **(20)**

An interesting example of the situation in which the preferred addition site does not lead to the preferred ring size has been provided by Miura and coworkers with the extended vinylcyclopropane rearrangement of substrate **21**[64]. Formation of vinylcyclopentyl derivative **22** requires the addition of the triphenylstannyl radical to the unsubstituted terminus

of the diene moiety in **21** to form intermediate allyl radical **23**. Cyclopropane ring opening then gives acyclic radical **24**, which cyclizes in a 5-*exo*-trig fashion to yield, after elimination of triphenylstannyl radical, product **22** (equation 11). The attack at the C2 center of the diene system in the cyclization step is the only known example in which addition to the central carbon atoms of the diene unit occurs readily. In this particular case, the unusual regiochemistry is caused by the favorable cyclization geometry as well as by the presence of the triphenylstannyl leaving group in the γ-position.



(11)

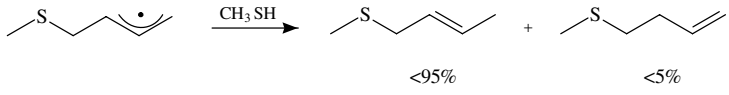
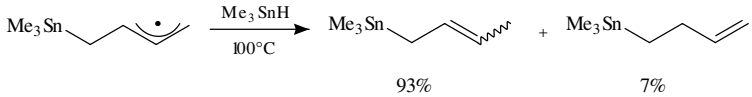
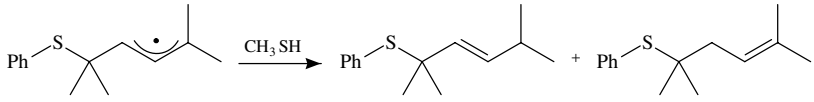
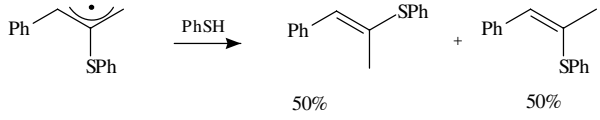
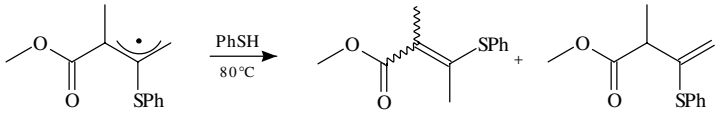
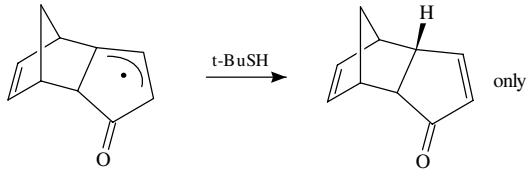
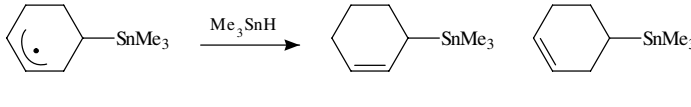
In conclusion, the regiochemistry of radical attack at dienes appears to be rather predictable by considering steric and electronic effects. Attack is almost always preferred at the terminal carbon atoms of the diene. α-Substituents retard the addition significantly in all known cases while the steric effects of β-substituents depend on the nature of the attacking radical.

V. REGIOSELECTIVITY IN REACTIONS OF POLYENYL RADICALS

A. Trapping with Closed-shell Molecules

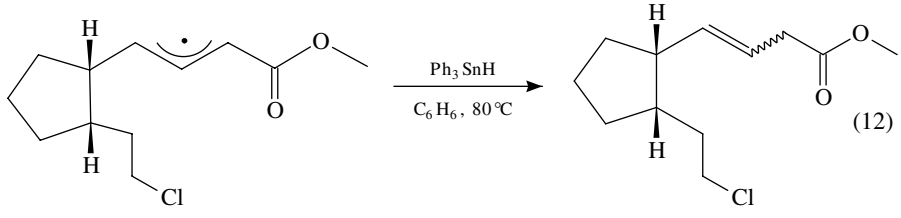
Allyl radicals substituted at only one of the terminal carbon centers usually react predominantly at the unsubstituted terminus in reactions with nonradicals. This has been shown in reactions of simple dienes such as butadiene, which react with hydrogen bromide, tetrachloromethane or bromotrichloromethane to yield overall 1,4-addition products[35,58]. The reaction of allyl radicals with hydrogen donors such as thiols[33,34,36a] or tin hydrides[37–39] has been investigated and reviewed repeatedly. In most cases, the thermodynamically more favorable product is formed predominantly. This accords with formation of either the higher substituted alkene or the formation of conjugated π-systems. Not in all cases, however, is the formation of the thermodynamically more favorable product identical to overall 1,4-addition to the diene. In those cases in which allyl radicals are formed through reaction of dienes with tin hydrides or thiols, the

TABLE 12. Examples for the trapping of allyl radicals with thiols and tin hydrides

	Reference
	33
	38
	33
	36a
	36b
	36c
	38

reaction with thiols appears to proceed with slightly higher regioselectivity. The rule of predominant formation of the thermodynamically more favorable product also pertains to the *E*:*Z* selectivity of the product alkenes[36]. Table 12 gives some representative examples.

The few cases in which thermodynamic control is not effective appear to be dominated by steric effects[39]. Thus, trapping of radical **25** with triphenyltin hydride regioselectively yields product **26**, in which the double bond is separated from the ester through a methylene bridge (equation 12).



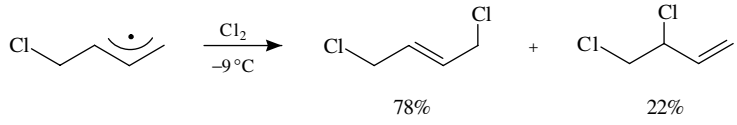
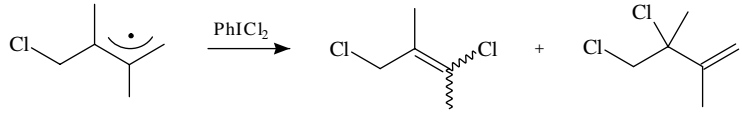
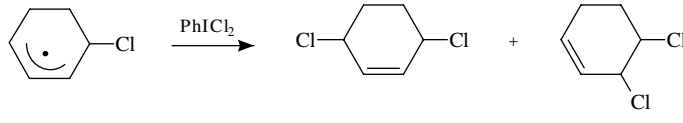
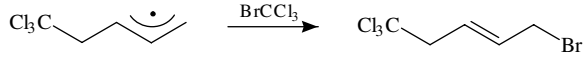
(12)

(25) **(26)** 60%

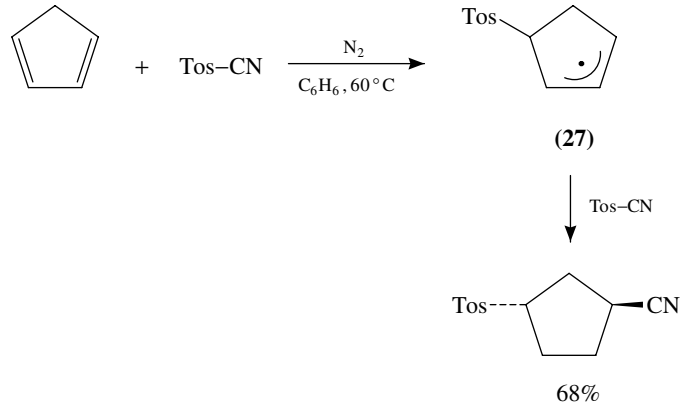
Allyl radicals are also formed during the radical halogenation of dienes[65,66]. The regioselectivities obtained in these reactions depend markedly on the reaction conditions, because formation of the reaction products is also possible through polar reaction pathways. In those cases in which proper care has been taken to ensure a radical mechanism, the halogenation of dienes proceeds with much lower regioselectivity in the halogen transfer step as compared to the hydrogen transfer reactions considered before (Table 13). The reagent used to deliver the halogen, in contrast, appears to have only a small influence. Many results for the trapping of allyl radicals with bromine exist from the allylic halogenation with *N*-bromosuccinimide. The regioselectivity of this reaction has been reviewed[67].

The addition of tosyl cyanide to cyclopentadiene leads to intermediate formation of radical **27**, which then is trapped by tosyl cyanide by cyano group transfer. The *trans*-

TABLE 13. Examples for the trapping of allyl radicals with halogen donors

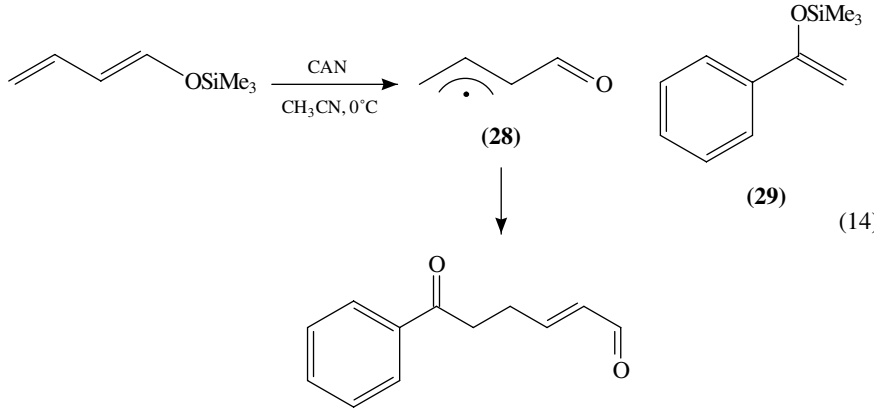
	Reference
 78% 22%	65
 52% 48%	66
 50% 50%	66
	30, 31, 35

1,4-addition product is formed exclusively (equation 13).



(13)

Only a few examples exist for the intermolecular trapping of allyl radicals with alkenes[68,69]. The reaction of α-carbonyl allyl radical **28** with silyl enol ether **29** occurs exclusively at the less substituted allylic terminus to form, after oxidation with ceric ammonium nitrate (CAN) and desilylation of the adduct radical, product **30** (equation 14). Formation of terminal addition products with *trans*-configuration has been observed for reaction of **28** with other enol ethers as well.



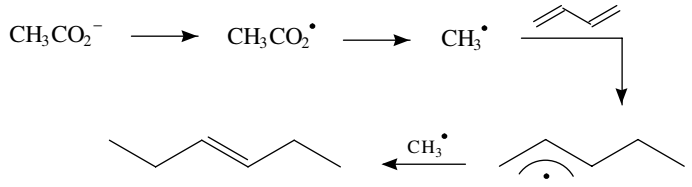
(14)

Intramolecular trapping of allyl radicals by carbon–carbon double bonds has, of course, been observed to occur readily and with high selectivity (see Sections III and IV).

B. Trapping with Radicals

The trapping of allyl radicals with other open-shell species can be studied in all reactions in which a sufficiently high concentration of radicals is created and in which the concentration of nonradical trapping agents is low. This prerequisite has been met in Kolbe electrolysis reactions, in which radicals are generated by one-electron oxidation of carboxylate anions. One of the simplest systems, the reaction of methyl radicals with

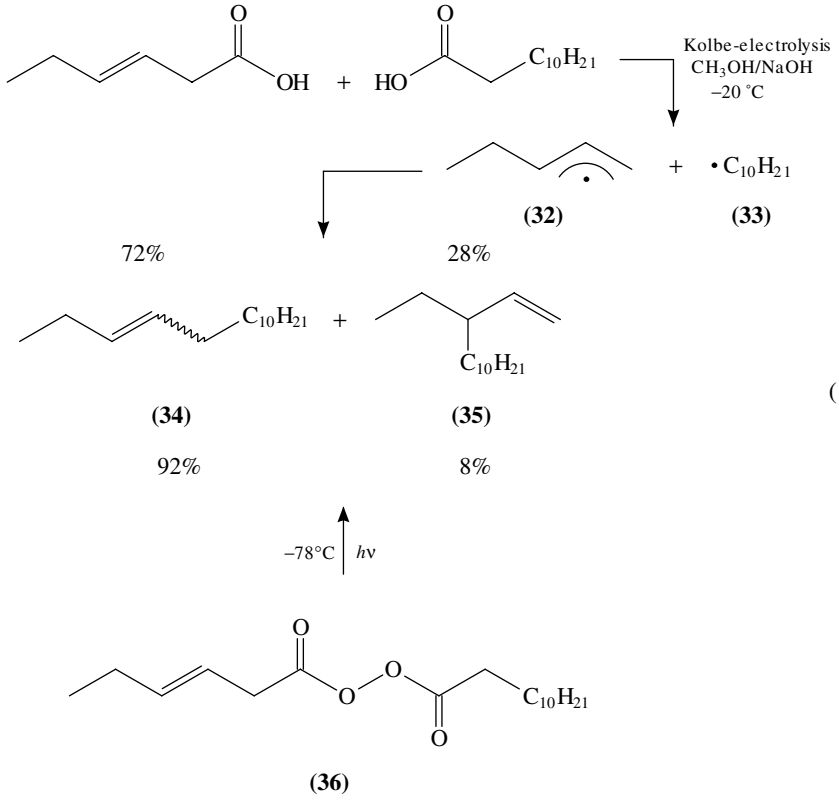
butadiene, has been studied in this way[52]. Methyl radicals are obtained by oxidation of acetate anions and subsequent decarboxylation of the resulting acetyloxy radicals. Addition to butadiene then leads to the adduct allyl radical **31**, which is trapped by a second methyl radical to form the overall 1,4-addition product *trans*-3-hexene exclusively (equation 15).



(15)

(31)

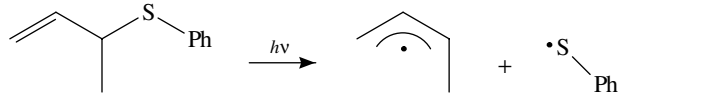
Allyl radicals can, of course, also be generated by electrolysis of the corresponding β,γ-unsaturated carboxylic acids together with a second carboxylic acid. This 'mixed Kolbe electrolysis' method has been used to study the recombination of allyl radical **32** with the undecyl radical **33**[70]. Recombination leads to the formation of adducts **34** and **35** in a ratio of 72:28, again preferring the product with the higher substituted double bond (equation 16).



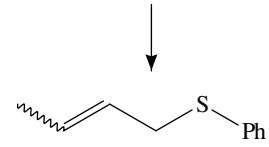
(16)

(36)

The same intermediate radicals can be formed by photolysis of the mixed diacyl peroxide **36**[70]. The resulting radical pair recombines, after decarboxylation, in a ratio of 92:8 (equation 16). The higher regioselectivity in this latter case appears to result from the limited mobility of the intermediate radicals in the solid state (at −78 °C). This experiment illustrates that a meaningful comparison of selectivities requires experimental data obtained under comparable reaction conditions. Photolytically generated radical pairs have also been used to investigate the regioselectivity in the recombination of allyl radical **38** with thiophenyl radical **39**. Terminal trapping is, as seen before for radical **32**, the preferred mode of action since photolysis of thiol ether **37** gives product **40** exclusively (equation 17)[71].



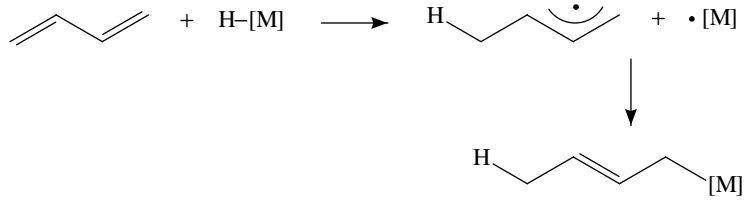
(37) **(38)** **(39)**



(40)

(17)

Many more examples have been collected for the reaction of transition metal hydride complexes with 1,3-dienes, which appear to proceed via radical pair mechanisms, even without photochemical activation[72–77]. The following general mechanism has been assumed to be operative for the reaction of $HMn(CO)_5$[72,73], $HFe(CO)_4SiCl_3$[74,75], $HFe(CO)_2Cp$[76] and $HCo(CO)_4$ (H-[M]) (equation 18)[77].

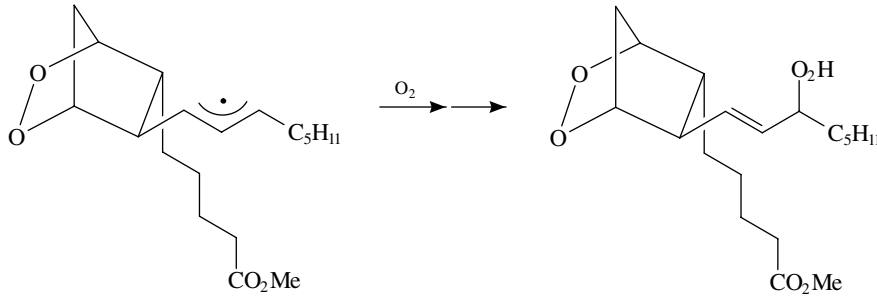


(18)

The mechanistic proposal of rate-limiting hydrogen atom transfer and radical recombination is based on the observed rate law, the lack of influence of CO pressure, kinetic isotope effects [studied with $DMn(CO)_5$] and CIDNP evidence. In all known cases, exclusive formation of the overall 1,4-addition product has been observed for reaction of butadiene, isoprene and 2,3-dimethyl-1,3-butadiene. The preferred trapping of allyl radicals at the less substituted side by other radicals has actually been so convincing that its observation has been taken as a mechanistic probe[78].

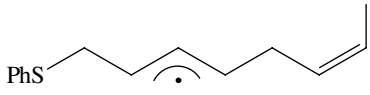
Oxygen can also be considered an open-shell trapping agent in its ground state triplet state. An example for the highly regioselective trapping of a sterically demanding allyl radical by oxygen has been provided in the study of the biomimetic synthesis

of prostaglandins[62]. As seen before in the tin hydride trapping of allyl radicals, the bicyclic substituent in **41** reduces the reactivity of one of the allylic radical centers dramatically and reaction occurs regioselectively only at one end of the allyl system to yield hydroperoxide **42** (equation 19)[79]. Trapping by oxygen proceeds much less selectively in more symmetrically substituted allyl radicals such as **43**, which yields peroxy radicals **44** and **45** in a ratio of 27:73 (equation 20)[79].

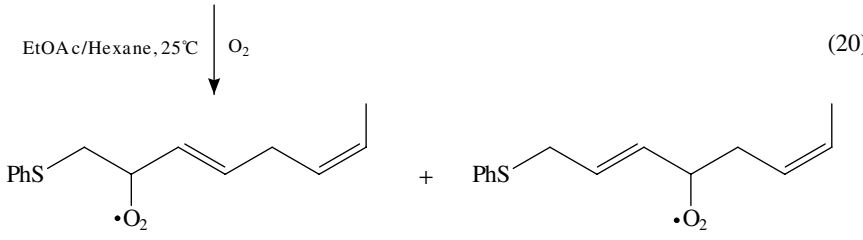


(41) **(42)**

(19)



(43)



(20)

(44) **(45)**

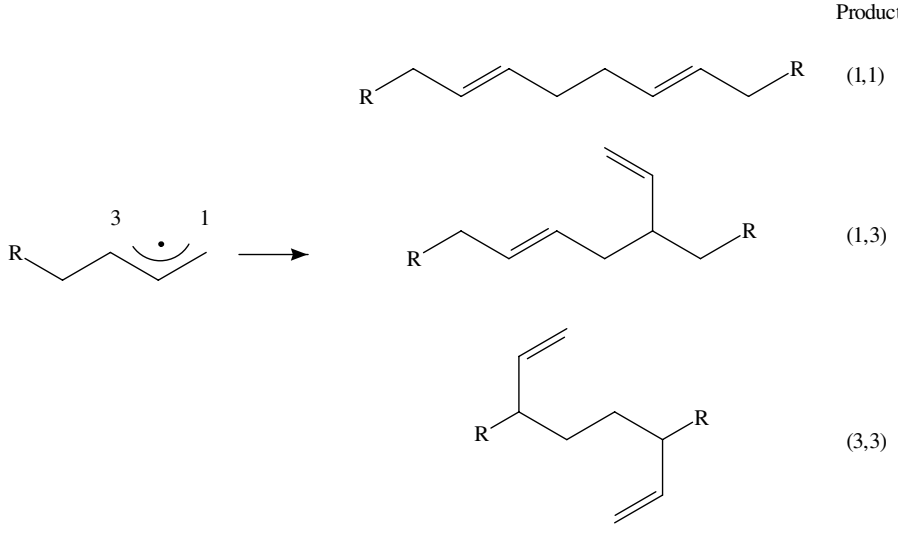
27 : 73

A number of earlier investigations of the regioselectivity in the reaction of allyl radicals with other radicals has been plagued by severe analytical problems[41,80].

C. Dimerization of Allyl Radicals

The regioselectivity in the dimerization of allyl radicals has been studied by a variety of methods. One of the earliest investigations into this field employed the Kolbe electrolysis

to generate carboxylate derived radicals in the presence of dienes[49]. The complex product mixture obtained could only be analyzed at that time to contain major amounts of product resulting from recombination at the least substituted allyl terminus. The same difficulty was encountered in the dimerization of allyl radicals, which result from the addition of alkoxy radicals to butadiene[81a]. Again, the major product appeared to result from recombination at the less substituted center of the intermediate allyl radical. Generally, the recombination of allyl radicals with an unsymmetrical substitution pattern can produce (1,1)-, (1,3)- or (3,3)-coupling products (Scheme 3). Products (1,1) and (1,3) frequently occur as mixtures of *Z*- and *E*-isomers.



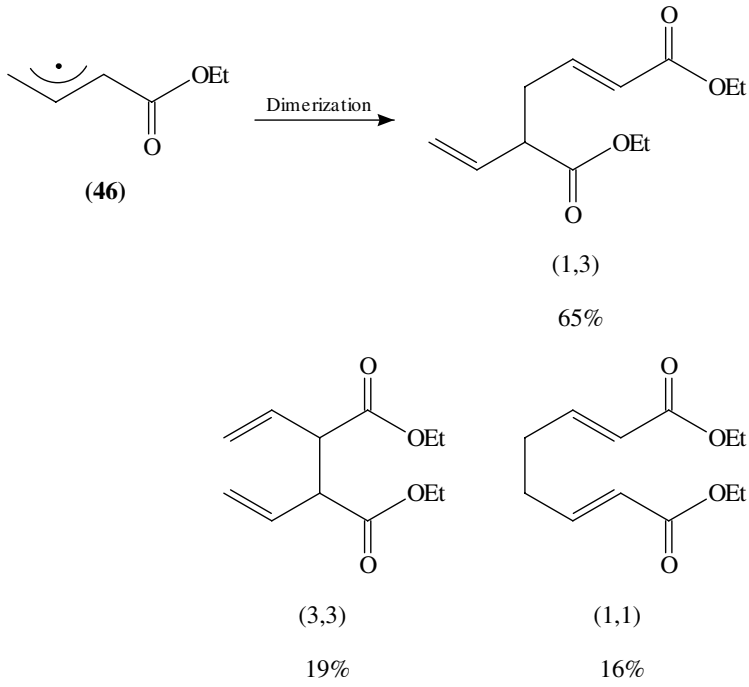
SCHEME 3

Assuming that the allyl C1 and C3 centers have an intrinsic reactivity, which is independent of the direct coupling partner (C1 or C3 of the second allyl radical), the results of a variety of different experimental investigations can be examined comparatively. If this assumption holds true, the relative product distribution for an allyl radical with intrinsic reactivity of **A** at C1 and of **B** at C3 should be given by equation 21.

$$(1,1):(1,3):(3,3) = \mathbf{A}^2 : 2\mathbf{AB} : \mathbf{B}^2 \tag{21}$$

Despite the fact that a quantitative product analysis is often difficult to achieve in these reactions, the product distribution expected from equation 21 is indeed found in many cases. Table 14 lists some representative examples.

In all cases, reaction at the less substituted allyl terminus is preferred by a factor of two or more, even though the actual degree of regioselectivity depends strongly on the substitution pattern. Those cases in which the product distribution deviates strongly from that predicted by equation 21 include allyl radicals connected to other π-systems. A point in case is the recombination of 1-ethyloxycarbonyl allyl radical **46**, which predominantly yields the (1,3)-recombination product (equation 22)[71].



(46)

(1,3)

65%

(3,3)

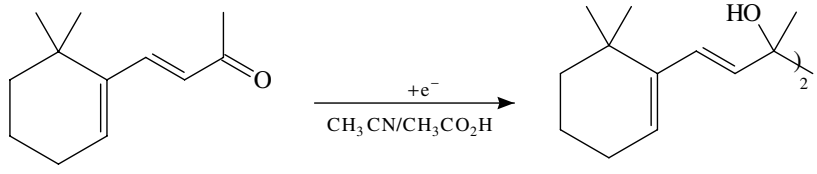
19%

(1,1)

16%

(22)

The product distribution observed in the dimerization of polyene-substituted ketyl radicals is also remarkable in that only products involving dimerization at the carbonyl carbon atom are observed (equation 23)[82,83]. This finding is quite independent of the reducing agent, since ketyl radicals formed by reduction with low-valent transition metal complexes behave analogously[84–86].

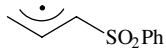
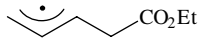
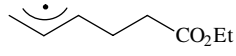
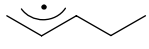
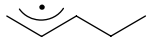
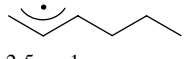
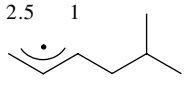
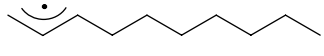
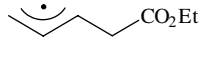


(23)

In summary, it appears that the trapping of allyl radicals with closed-shell trapping agents is quite selective, especially in those cases in which the allyl radical contains one substituted and one unsubstituted terminus. Trapping with radicals appears to produce mixtures of isomers, especially in the dimerization of allyl radicals. The observed regioselectivities do, however, depend on the reaction conditions, allowing for some control of the reaction outcome for a given substrate.

Reviewing now the last four sections, it is obvious that the major problem in radical chain reactions involving dienes or polyenes is the low reactivity of the diene (or polyene) adduct radicals. This allows for the occurrence of allyl radicals in intramolecular reactions but poses a major problem in intermolecular radical chain reactions. The obvious solution to this problem is to use methods in which radicals are produced stoichiometrically and not

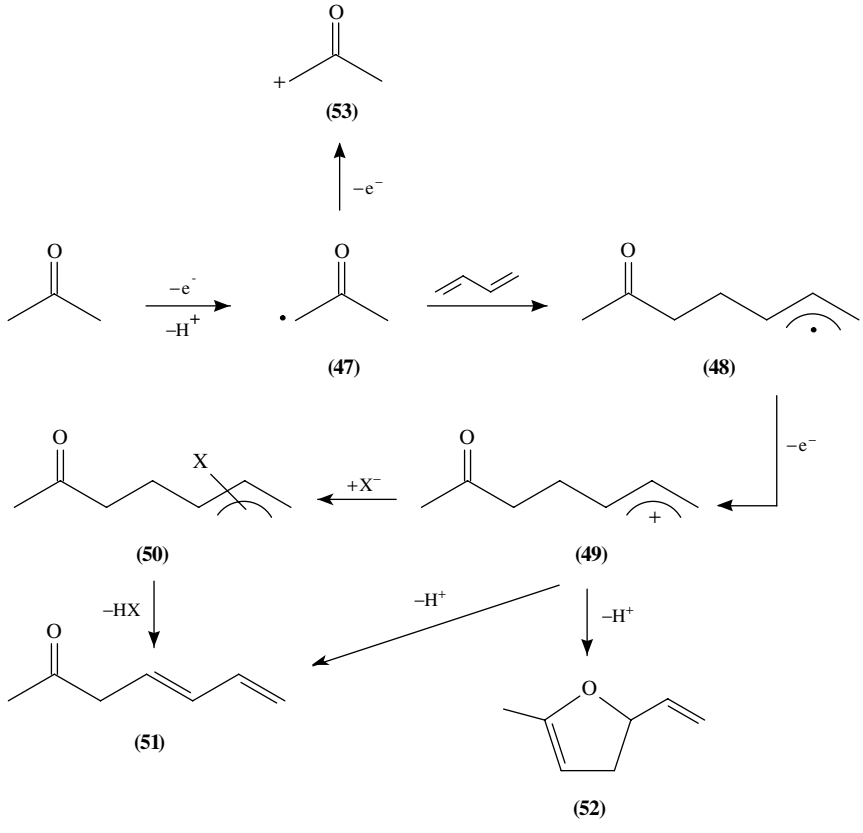
TABLE 14. Relative reactivities at allyl radical termini calculated from product distributions from allyl radical recombination

Relative reactivities	T (°C)	Method	Reference
>3.9 <1 	−78	Carbanion oxidation	81b
2.7 1 	0	Kolbe electrolysis	81c
2.9 1 	0	Kolbe electrolysis	81c
1.7 1 	35	Photolysis	71
1.9 1 	−10	Kolbe electrolysis	81d
1.9 1 	−10	Kolbe electrolysis	81d
2.5 1 	0	Kolbe electrolysis	54b
H>4.0 <1.6 	−20	Diene addition	54a
>6.9 <1 	0	Kolbe electrolysis	81d

in radical chain processes. Not surprisingly, most examples of the successful use of dienes in radical reactions are located in this area. Even though the use of non-chain methods does solve the problem of adduct radical reactivity, the problem of competing polymerization still persists. It is therefore mandatory also for nonchain methods to convert the adduct radicals to product faster than addition to a second polyene molecule. With the trapping of polyene radicals by closed-shell molecules being too slow, three further possibilities exist: (1) trapping with other radicals; (2) oxidation to polyene cations; or (3) reduction to polyene anions. Since option (1) has been shown before to proceed with low selectivity at times and not much is known about option (3), we have to restrict ourselves here to consideration of (2), which has been applied successfully in many cases.

VI. NON-CHAIN RADICAL REACTIONS—OXIDATION AS AN ALTERNATIVE TERMINATING STEP

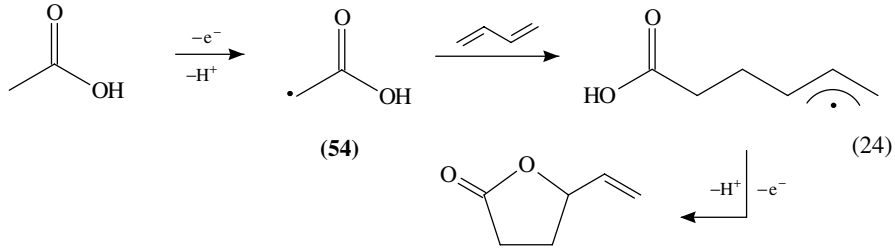
A general mechanistic scheme for the radical addition-adduct radical oxidation sequence is given in Scheme 4. Initial radicals are usually derived from easily enolizable compounds such as ketones, esters and, most frequently, 1,3-dicarbonyl compounds by oxidation with metal salts. The resulting α-carbonyl radical **47** is more difficult to oxidize and addition to dienes can occur. The resulting adduct radical **48** has a much lower oxidation potential as compared to **47.** Oxidation to cation **49** is therefore faster than repeated addition to diene molecules and polymerization can be prevented. Depending on oxidants and reaction conditions, a number of possibilities exist to convert cation **49** to stable products. Trapping of the cation by nucleophiles is frequently observed to produce products of type **50**, which can also be formed directly through inner-sphere electron transfer to radicals **48**. Cation **49** can also deprotonate to form **51**, which can alternatively be formed via **50** through elimination of HX. Finally, **49** is often trapped intramolecularily by the carbonyl functionality of the initial radical to form, after deprotonation, substituted di- and tetrahydrofurans such as **52**. If carboxylic acids or esters are used as enolizable compounds, γ-lactones are formed instead. For this mechanistic scheme to work, the oxidant must be strong enough to effect



SCHEME 4

rapid oxidation of the enolate and the adduct radical **48**. If the oxidant is too strong, however, oxidation of enol radical **47** to form cation **53** will be too rapid and no addition to diene will be observed.

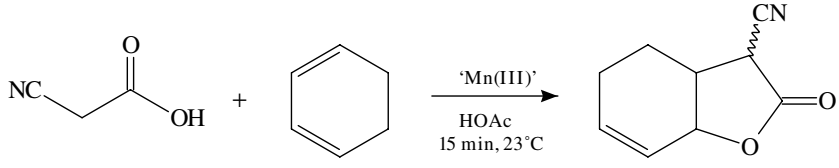
Among the preferred and also first oxidants to be used for this purpose was manganese(III) acetate in acetic acid, for which the formula $Mn_3O(OAc)_7$ might be appropriate[53,87]. Oxidation of acetic acid, for example, leads to radical **54** which, upon addition to butadiene and oxidation of the adduct radical, leads to γ-lactone **55** (equation 24).



(24)

(55) 30%

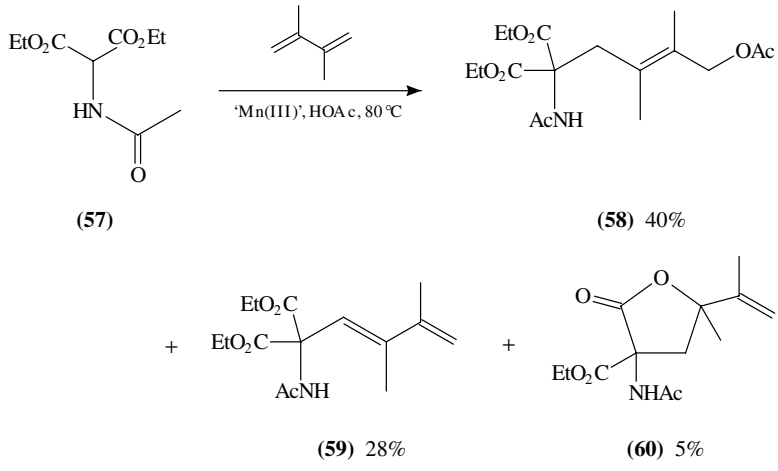
The low yield in this reaction might be caused by a number of reasons. First, the overall reaction is only rapid for readily enolizable compounds. 1,3-Dicarbonyl compounds will therefore be a better choice as compared to acetic acid. Second, to prevent oxidation of radical **54**, it is advantageous to work with excess diene and therefore speed up trapping of **54** through diene addition. Finally, lactone **55** can, as an enolizable compound itself, also be oxidized by manganese(III) acetate and form various oxidation products. Shorter reaction time and the use of understoichiometric amounts of oxidant might therefore benefit the overall result. All these factors have been taken into account in the synthesis of bicyclic γ-lactone **56**, which has been obtained from cyanoacetic acid and 1,3-cyclohexadiene in 78% yield within 15 min reaction time (equation 25)[60,88].



(56) 78%

(25)

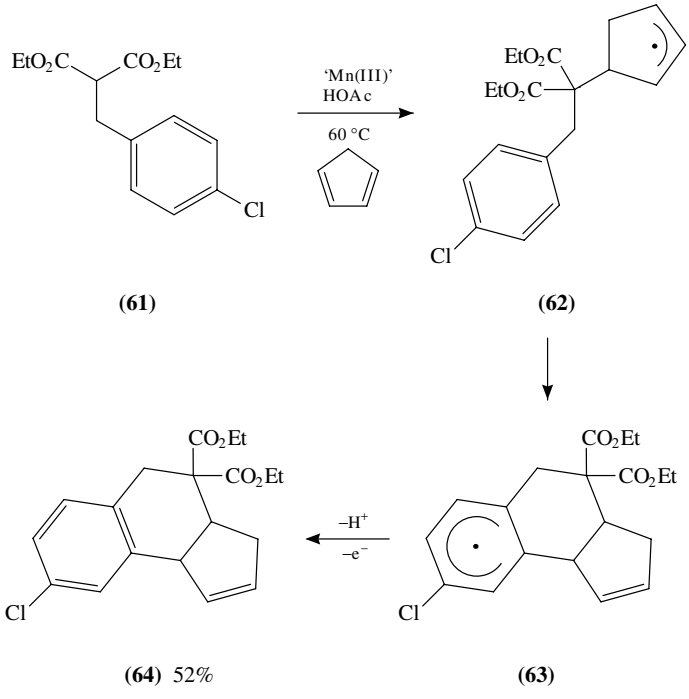
Using esters instead of acids reduces the rate of formation of lactones and gives rise to trapping by solvent as well as the formation of overall diene substitution products. Oxidation of amidomalonic ester **57**, for example, yields as major products the acetic acid trapping product **58** and the diene substitution product **59**, but only 5% of lactone **60** (equation 26). The oxidation of the initially formed amidomalonic ester radical, of increased importance in this case due to the amide substituent, could be largely reduced through addition of sodium acetate or trifluoroacetic acid, which are known to reduce the oxidation potential of the Mn(III) acetate.



(57) **(58)** 40% **(59)** 28% **(60)** 5%

(26)

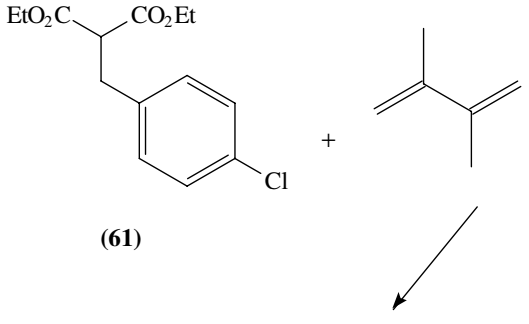
Further variations of the general scenario described in Scheme 4 consist in trapping adduct radical **48** before oxidation occurs[7]. This can be achieved if intramolecular radical additions are possible, as is the case in radical **62**. Oxidation of **62** to the corresponding allyl cation is slower than 6-*exo*-cyclization to the chlorobenzene ring to form radical **63**, which subsequently is oxidized to yield tetrahydronaphthalene **64** as the main product (equation 27). This sequence does not work well for other dienes such as 2,3-dimethyl-1,3-butadiene, for which oxidation of the intermediate allyl radical is too rapid to allow radical cyclization onto the aromatic π-system.



(61) **(62)** **(63)** **(64)** 52%

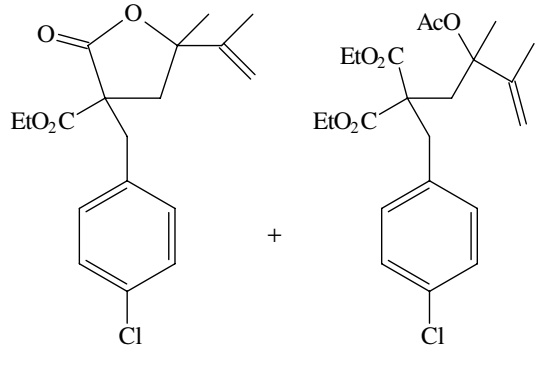
(27)

The competition between intramolecular and intermolecular trapping of the intermediate allyl cation **49** (Scheme 4) can be influenced to a large part by the ligands of the oxidizing metal salts. Intramolecular trapping by carbonyl groups becomes much more dominant when ligands of low nucleophilicity, such as perchlorate, are used in aprotic solvents. This is illustrated by reaction of α-benzylmalonate **61** with 2,3-dimethyl-1,3-butadiene, which yields a mixture of products **65** and **66** with manganese(III) acetate[7], but only intramolecular trapping product **65** when iron(III) perchlorate nonahydrate in acetonitrile is used as oxidant (equation 28)[89,90].



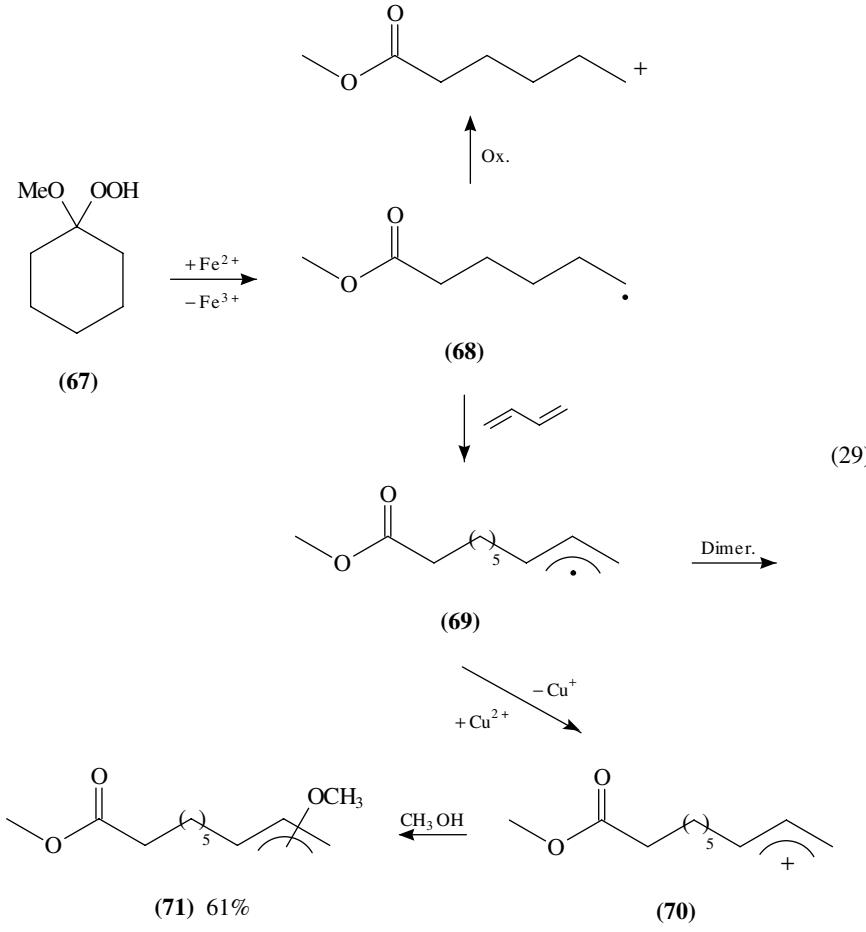
(61)

(28)



	(65)	**(66)**
$Mn_3O(OAc)_7$, HOAc, 60 °C	30%	55%
$Fe(ClO_4)_3 \cdot 9H_2O$, CH_3CN, 20 °C	89%	–

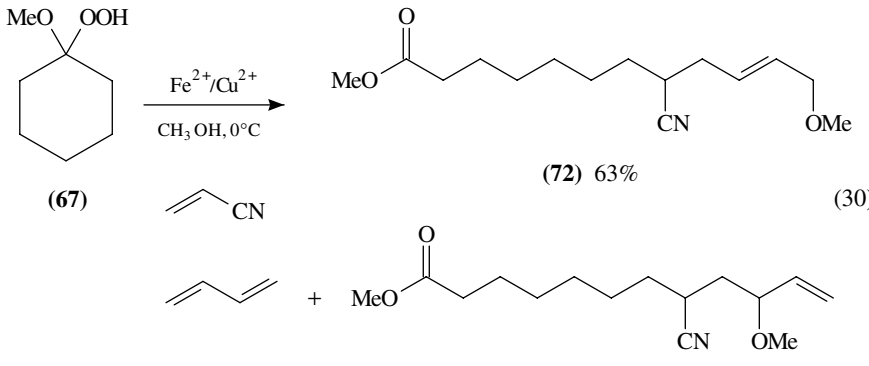
Iron(II) salts, usually in conjunction with catalytic amounts of copper(II) compounds, have also been used to mediate radical additions to dienes[91,92]. Radicals are initially generated in these cases by *reductive* cleavage of peroxyesters of hydroperoxides to yield, after rearrangement, alkyl radicals. Addition to dienes is then followed by oxidation of the allyl radical and trapping by solvent. Hydroperoxide **67**, for example, is reduced by ferrous sulfate to acyclic radical **68**, which adds to butadiene to form adduct radical **69**. Oxidation of **69** by copper(II) and reaction of the resulting allyl cation **70** with methanol yield product **71** in 61% yield (equation 29).



(29)

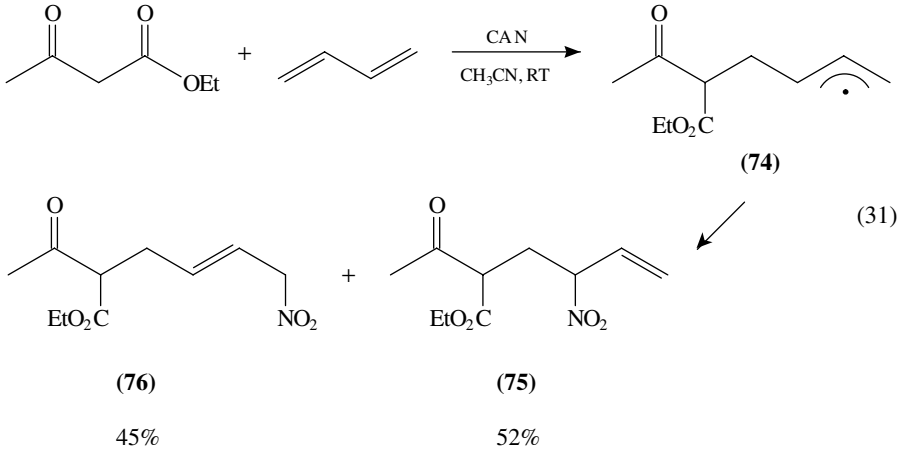
The concentration of copper(II) has a pronounced effect on the course of the reaction. In the presence of very low copper(II) concentrations, oxidation of allyl radical **69** is slow and major amounts of allyl radical dimer are formed. In the presence of very high concentrations of copper(II), radical **68** is oxidized rapidly before addition to diene can take place. An optimum yield of product **71** can therefore only be achieved at certain copper(II) concentrations. The metal-ion-promoted addition of chloramines to butadiene appears to follow the same mechanism[93].

This scheme can be extended by using mixtures of dienes with electron-deficient alkenes such as acrylonitrile. Due to its nucleophilic nature, addition of radical **68** to acrylonitrile is faster than addition to butadiene. The resulting ambiphilic adduct radical then adds to butadiene to form a relatively unreactive allyl radical. Oxidation and trapping of the allyl cation by methanol lead, as before, to products such as **72** and **73**, which are composed of four components: the radical precursor **67**, acrylonitrile, butadiene and methanol (equation 30)[17,94].



(30)

Reactions involving ceric ammonium nitrate (CAN) as oxidant give nitrates instead of acetates or methyl ethers as final trapping products[8,55,56]. Oxidation of the adduct allyl radicals **48** (Scheme 4) appears in this case to follow a ligand transfer mechanism rather than a stepwise electron transfer/nucleophilic addition sequence. The oxidation of ethyl acetoacetate in the presence of butadiene, for example, leads to adduct radical **74**, which is trapped by CAN to form the two possible products **75** and **76** in high yield but low selectivity (equation 31). A similar sequence has been used starting from silyloxycyclopropanes, which yield β-carbonylalkyl radicals after CAN oxidation. Addition to butadiene and trapping with CAN again forms a mixture of nitrates, which have in this case been used as substrates for the palladium(II) catalyzed coupling with carbon- and nitrogen-centered nucleophiles[56].



(31)

For completeness, it must also be noted that the oxidation of enolizable compounds and intermediate allyl radicals can be achieved electrochemically[54b]. The resulting product mixtures, however, proved much more complex as compared to oxidation by transition metal salts.

VII. ACKNOWLEDGEMENT

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CHAPTER **14**

Palladium-catalyzed oxidation of dienes

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I. INTRODUCTION

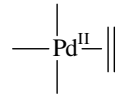
Palladium-catalyzed oxidation of hydrocarbons has been a matter of intense research for about four decades. The field was initiated by the development of the aerobic oxidation of ethylene to acetaldehyde catalyzed by palladium chloride and co-catalyzed by cupric chloride (the Wacker process, equation 1)[1].

$$CH_2{=}CH_2 + 1/2\,O_2 \xrightarrow[CuCl_2]{PdCl_2} CH_3CHO \qquad (1)$$

A number of reviews dealing with the palladium-catalyzed oxidation of unsaturated hydrocarbons have been written[2–8]. The present review will focus on the palladium-catalyzed oxidation of dienes including both conjugated and nonconjugated dienes. Since this topic has been thoroughly reviewed up to *ca* 1979 in the book by Henry[2] the present review will mainly cover the time period 1979–95. During this time several reviews[3–7] have been written which partly cover the present topic.

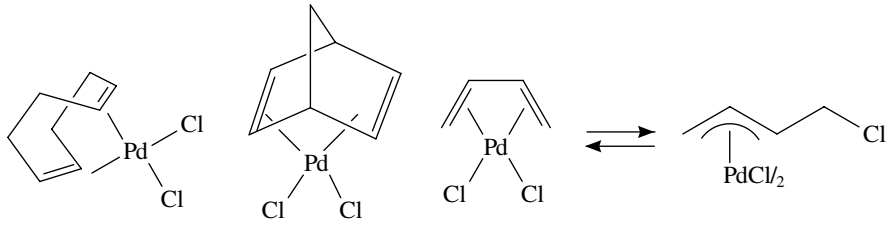
A. Principle for the Oxidation of Unsaturated Hydrocarbons

In most palladium-catalyzed oxidations of unsaturated hydrocarbons the reaction begins with a coordination of the double bond to palladium(II). In such palladium(II) olefin complexes **(1)**, which are square planar d^8 complexes, the double bond is activated towards further reactions, in particular towards nucleophilic attack. A fairly strong interaction between a vacant orbital on palladium and the filled π-orbital on the alkene, together with only a weak interaction between a filled metal d-orbital and the olefin π^*-orbital (back donation), leads to an electrophilic activation of the alkene[9].



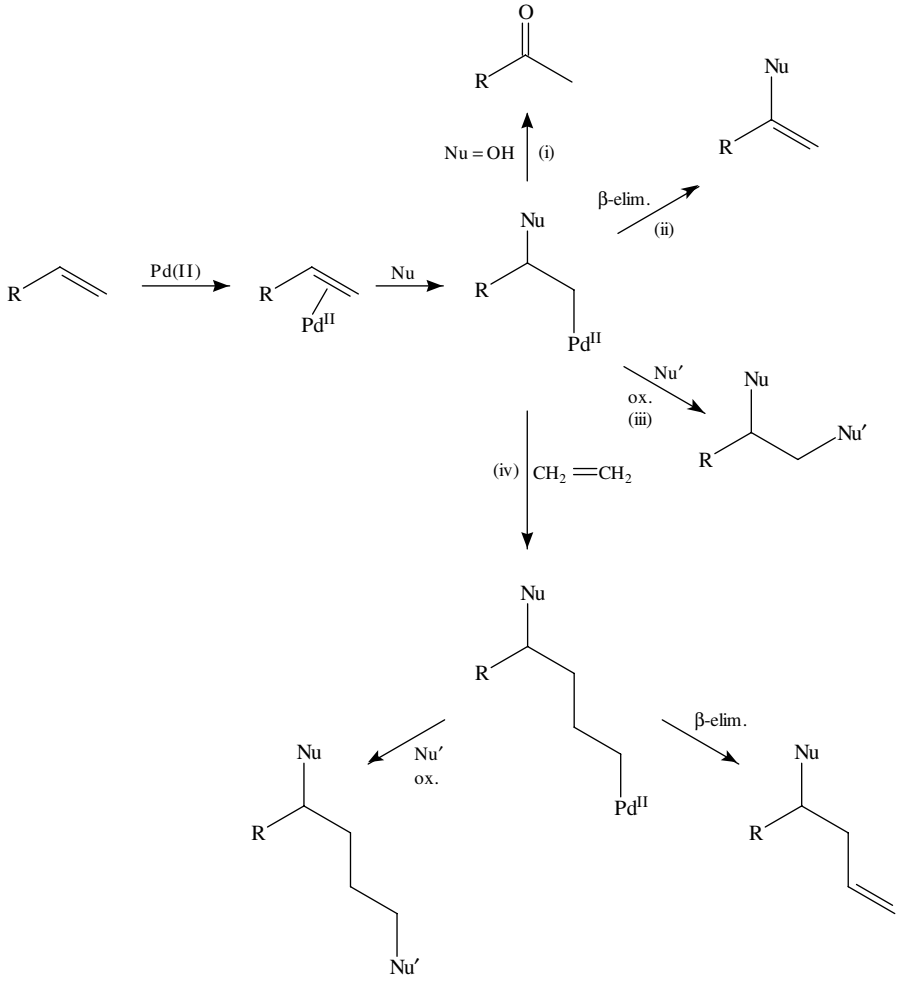
(1)

If the unsaturated hydrocarbon is a diene, both double bonds may coordinate to palladium(II). (Diene)palladium(II) complexes have been isolated and characterized. For example, **2** and **3** are stable complexes in which both double bonds are coordinated to the metal[10]. Conjugated dienes constitute a special case and although η^4-diene complexes, e.g. **4**, are postulated as intermediates, they have not yet been isolated. The butadiene complex **4** is in equilibrium with the π-allyl complex **5** in solution, and attempts to isolate the diene complex from this mixture lead to formation of a yellow crystalline complex **5**[11].



(2) **(3)** **(4)** **(5)**

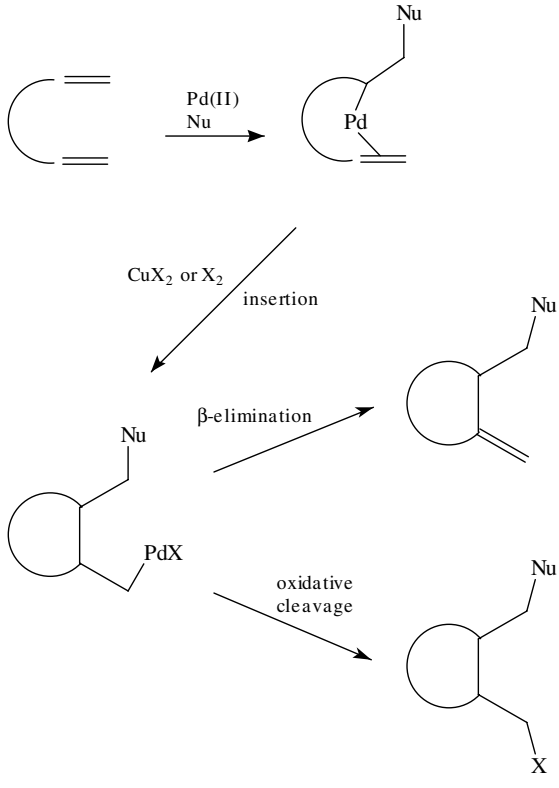
A common pathway in palladium-catalyzed oxidation reactions is that the π-olefin complex formed reacts with a nucleophile, either external or coordinated, and the new organometallic intermediate may then undergo a number of different reactions (Scheme 1): (i) an intramolecular hydride shift leads to ketone formation; (ii) a β-elimination results in the formation of a vinyl functionalized olefin; (iii) an oxidative cleavage of the palladium–carbon bond produces a 1,2-functionalized olefin[7]; and (iv) an insertion reaction, exemplified by insertion of an olefin, leads to formation of a new palladium–carbon bond, which may be cleaved according to one of the previous processes (β-elimination or oxidative cleavage). In all cases palladium has removed 2 electrons from the organic molecule, which becomes oxidized. These electrons, which end up on Pd(0), are in turn transferred to the oxidant and Pd(II) is regenerated. In this way a palladium(II)-catalyzed oxidation is realized.



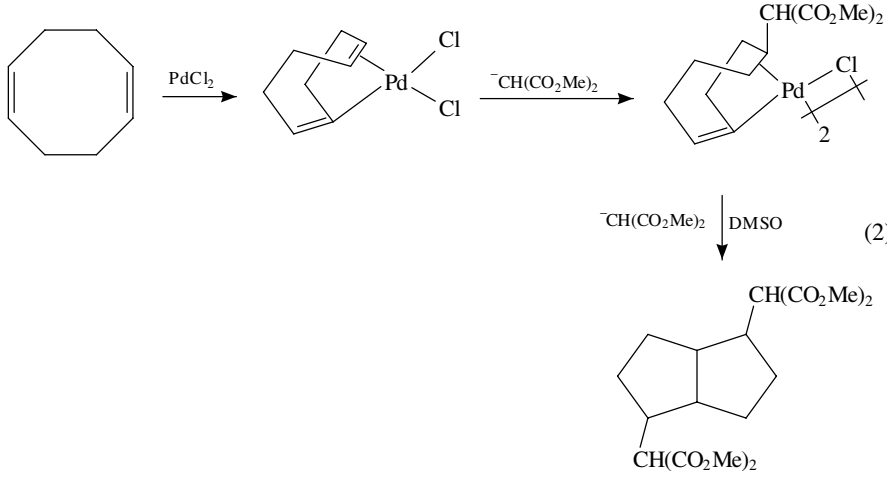
SCHEME 1

II. NONCONJUGATED DIENES

As mentioned above nonconjugated dienes give stable complexes where the two double bonds can form a chelate complex. A common pathway in palladium-catalyzed oxidation of nonconjugated dienes is that, after a first nucleophilic addition to one of the double bonds, the second double bond inserts into the palladium–carbon bond. The new (σ-alkyl)palladium complex produced can then undergo a β-elimination or an oxidative cleavage reaction (Scheme 2). An early example of this type of reaction, although not catalytic, was reported by Tsuji and Takahashi (equation 2)[12].

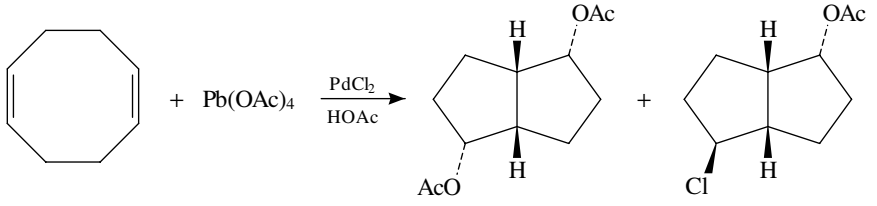

Nu
Pd(II)
Nu
Pd
CuX2 or X2
insertion
Nu
β-elimination
Nu
PdX
oxidative
cleavage
Nu
X

SCHEME 2


PdCl2
Cl
Pd
Cl
⁻CH(CO2Me)2
CH(CO2Me)2
Cl
Pd
2
⁻CH(CO2Me)2
DMSO
CH(CO2Me)2
CH(CO2Me)2

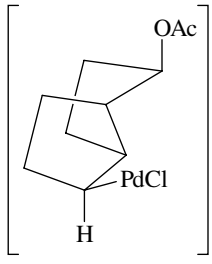
(2)

In this reaction the first addition product was isolated. In catalytic reactions this is not the case and in these reactions the first (σ-alkyl)palladium complex formed from the nucleophilic addition reacts further. For example, in the palladium-catalyzed oxidation of 1,5-cyclooctadiene with $Pb(OAc)_4$ in acetic acid the corresponding diacetate **6** was obtained in 76% yield together with some chloroacetate (equation 3)[13,14]. Adduct **7** is the suggested intermediate. An additional number of such palladium-catalyzed cyclizations of nonconjugated dienes have been reported[15–21]. In this system the two nucleophiles incorporated are either two acetates or one acetate and one chloride. For example, norbornadiene gives a mixture of three products, **8**, **9a** and **9b**, where the chloroacetate **8** is the main product (equation 4)[15]. Another example is the reaction of vinylnorbornene **10**, which gives a substituted brendane system **11** in good selectivity and yield[16,20]. The latter compound was transformed to the important synthetic intermediate **12** containing 5 stereogenic centers (equation 5). This transformation was done via hydrolysis, oxidation to ketone and subsequent Beyer-Villiger oxidation.

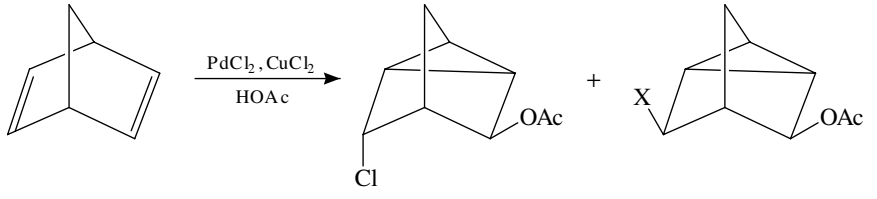


(6) 76% trace

(3)



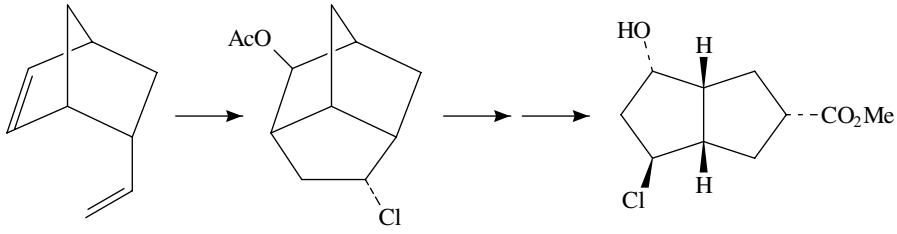
(7)



(8) 56%

(9a) X = Cl (13%)
(9b) X = OAc (13%)

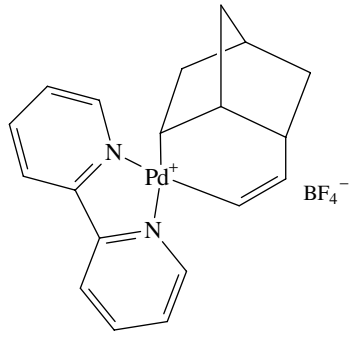
(4)



(10) **(11)** **(12)**

Isolated intermediate:

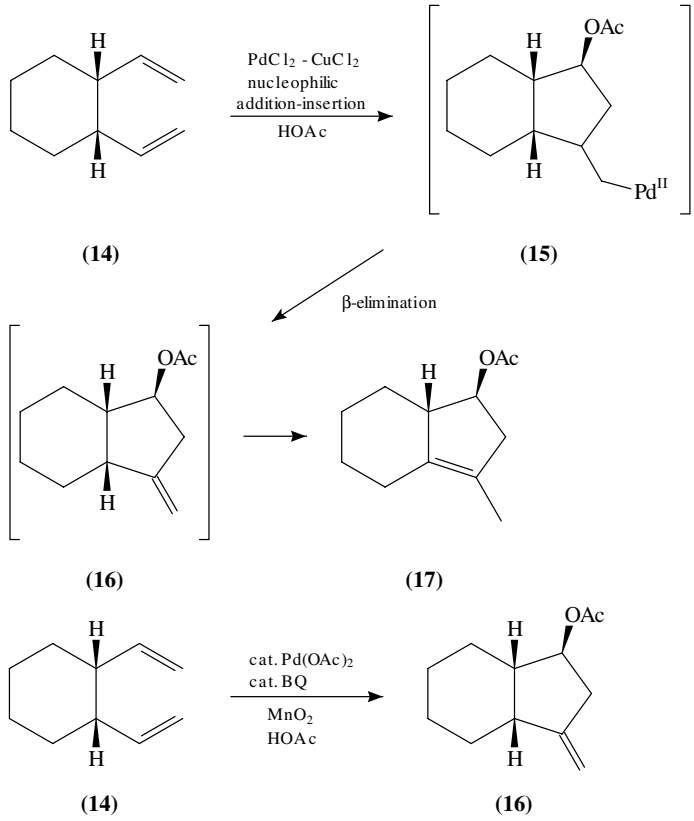
(5)



(13)

The palladium-catalyzed oxidations of the nonconjugated dienes to give products such as **6**, **8**, **9** and **11** involve three fundamental organometallic reactions: nucleophilic addition–insertion–oxidative cleavage of the Pd–C bond. It is interesting to note that in the formation of **6** and **11** all three reactions are highly stereoselective. It is generally assumed that the first two reactions are always stereospecific, while the oxidative cleavage may occur with either retention or inversion. The organopalladium intermediate was trapped by the addition of $AgBF_4$ and bipyridyl and in this way the cationic complex **13** was isolated.

When the $PdCl_2$–$CuCl_2$ system was applied to 1,2-divinylcyclohexane **14**, only one nucleophile is added to the diene system (equation 6)[16]. After nucleophilic addition and insertion the σ-palladium complex **15** formed undergoes a β-elimination. The primary product **16** generated undergoes a double bond isomerization to give **17**, which is the product observed. The latter reaction has been improved and developed into a synthetically useful reaction[3,4,22–25]. By changing the oxidation system to MnO_2/*p*-benzoquinone(BQ)[26] in acetic acid with $Pd(OAc)_2$ as catalyst, the product **16** with the *exo* methylene compound was obtained (equation 7)[22]. In the copper-catalyzed reaction the latter compound was postulated as the primary product, which under the reaction conditions undergoes an isomerization to the observed product. With MnO_2/BQ as the oxidation system, **16** does not isomerize.



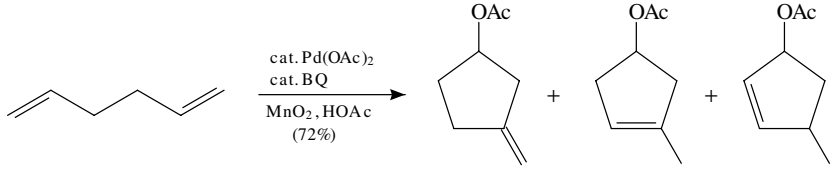
(14) **(15)** **(16)** **(17)**

(6)

(14) **(16)**

(7)

Acyclic dienes also undergo the palladium-catalyzed cyclization with the MnO_2/BQ oxidation system[22]. Thus, simple 1,5-hexadiene afforded a 72% isolated yield of cyclized products **18**, **19** and **20**, with an isomer distribution of 65:25:10, respectively (equation 8). In general, the selectivity and/or yield was lower for the acyclic dienes.

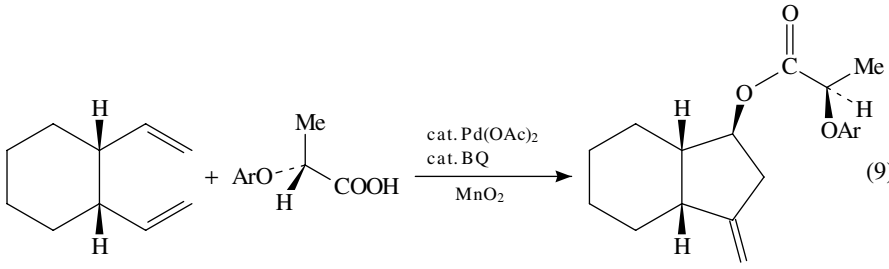


(18) **(19)** **(20)**

65 : 25 : 10

(8)

The palladium-catalyzed oxidation of the 1,2-divinylcyclohexane system was applied to diastereoselective reactions with the use of chiral acids as nucleophiles[25]. With this technique an asymmetric induction of up to 76% was obtained in the formation of **21** from **14** (equation 9). The use of molecular sieves was essential in order to obtain a good asymmetric induction.

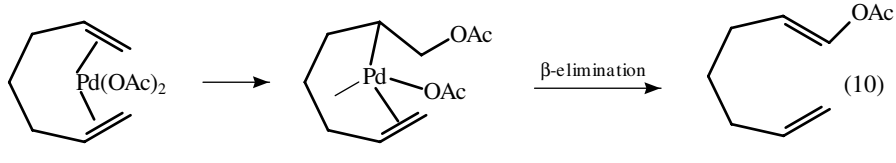


(9)

(14) **(21)**

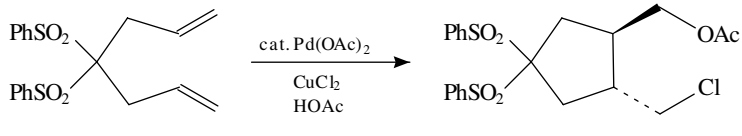
Ar = 2,4-$Cl_2C_6H_3$ 76% de

The use of 1,6-diene systems usually does not result in cyclization reactions with palladium(II) salts. For example, with 1,6-heptadiene a β-elimination takes place from the σ,π-intermediate to give diene **22** as the major product (equation 10)[27]. However, more recently Trost and Burgess[21] have shown that with a 4,4-bis(phenylsulfonyl) derivative of 1,6-heptadiene **(23)** an insertion takes place to give a 5-membered ring product (**24**, equation 11). The final step of the latter reaction is oxidative cleavage of the palladium–carbon bond by $CuCl_2$ to produce a carbon–chlorine bond.



(10)

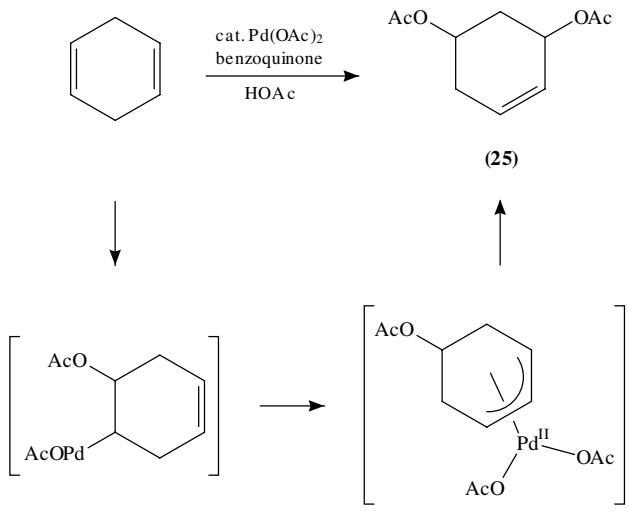
(22)



(11)

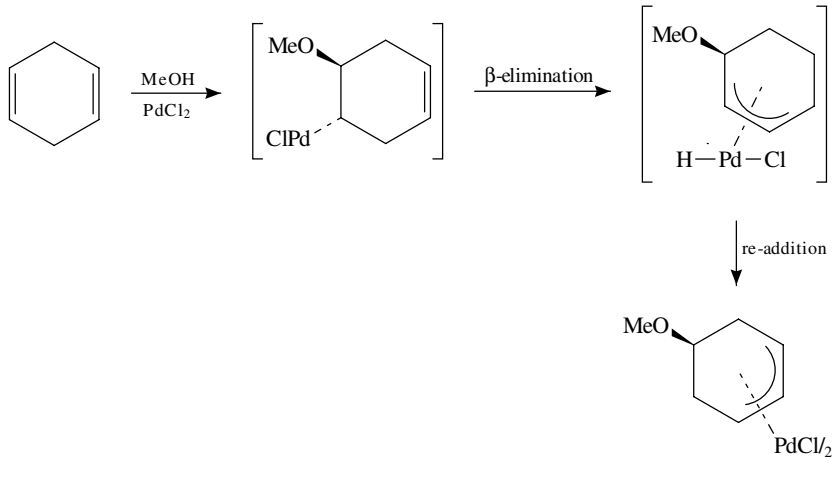
(23) **(24)**

Palladium-catalyzed oxidation of 1,4-dienes has also been reported. Thus, Brown and Davidson[28] obtained the 1,3-diacetate **25** from oxidation of 1,4-cyclohexadiene by benzoquinone in acetic acid with palladium acetate as the catalyst (Scheme 3). Presumably the reaction proceeds via acetoxypalladation–isomerization to give a π-allyl intermediate, which subsequently undergoes nucleophilic attack by acetate. This principle, i.e. rearrangement of a (σ,π-allyl)- to a (π-allyl)palladium complex, has been applied in nonoxidative palladium-catalyzed reactions of 1,4-dienes by Larock and coworkers[29]. Åkermark and coworkers have demonstrated the stereochemistry of this process by the transformation of 1,4-cyclohexadiene to the (π-allyl)palladium complex **26** by treatment



SCHEME 3

with palladium chloride in methanol (equation 12)[30]. The (π-allyl)palladium complex, in which the methoxy group is *trans* to palladium, was isolated and used for further organic reactions.



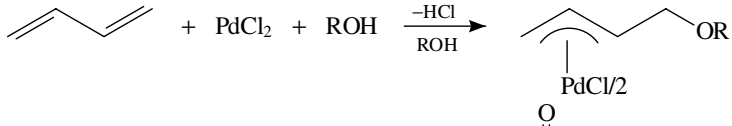
(12)

III. CONJUGATED DIENES

A. Intermolecular Reactions

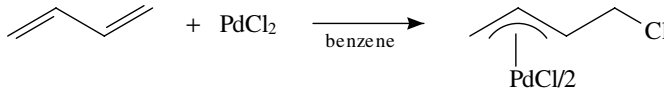
As mentioned in the introduction, π-complexes of conjugated dienes with palladium(II) are not stable enough to be isolated. However, reaction of a conjugated diene with $PdCl_2$ in alcoholic solvents or acetic acid gives a (π-allyl)palladium complex **27** in which the

alcohol or acetic acid has attacked the diene in the 4-position (equation 13)[31,32]. In a non-nucleophilic solvent a 4-chloro-η^3-(1,2,3)-alkenylpalladium complex **28** is formed (equation 14)[11,31].



(13)

R = OMe, OEt, RC(=O) **(27)**

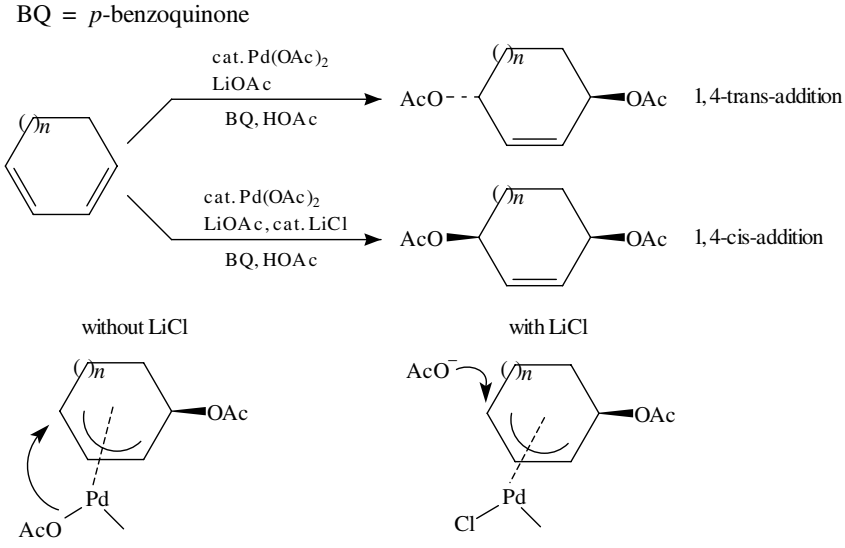


(14)

(28)

In 1971, Brown and Davidson reported that 1,3-cyclohexadiene undergoes a palladium-catalyzed 1,4-diacetoxylation of unspecified stereochemistry[28]. The oxidant employed was *p*-benzoquinone. They were uncertain about the mechanism at the time but later work has shown that the reaction proceeds via a (π-allyl)palladium intermediate and subsequent nucleophilic attack by acetate[6,7].

In 1981, a stereoselective palladium-catalyzed 1,4-diacetoxylation of 1,3-dienes with *p*-benzoquinone (BQ) as the oxidant was reported[33]. It was found that chloride ions can be used as a stereochemical switch. Thus, in the absence of chloride ions *trans* diacetoxylation takes place, whereas in the presence of a catalytic amount of chloride ion (as added LiCl) a *cis* diacetoxylation takes place (Scheme 4). In both cases the reaction is highly 1,4-regioselective. The explanation for



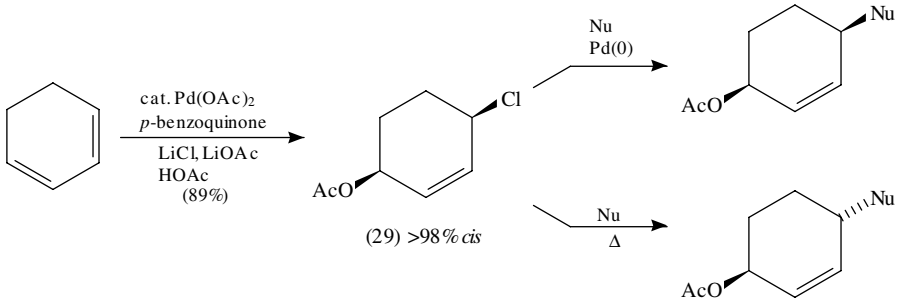
SCHEME 4. Ligand control in Pd-catalyzed 1,4-diacetoxylation

this remarkable ligand control of the stereochemistry is that in the absence of chloride ion, acetate ion will be the counterion on palladium and will undergo a *cis* migration. When chloride ions are present they will displace the acetate on palladium since the Pd−Cl bond is much stronger than the Pd−OAc bond. In this way the chloride blocks the coordination of acetate and, as a result, only external attack by acetate occurs.

The diacetoxylation works well with a number of cyclic and acyclic conjugated dienes and has been applied to the synthesis of natural products[33,34]. For example, the *meso* diacetate from 2,4-hexadiene was used for the enantiodivergent synthesis of the carpenter bee pheromone[34a].

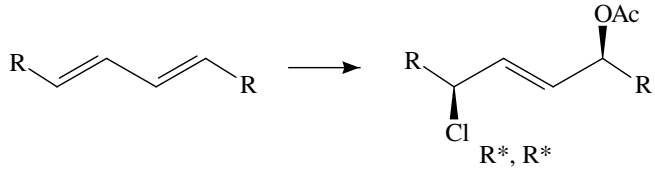
The 1,4-diacetoxylation was also extended to the use of other acyl groups than acetyl. Thus, an unsymmetrical 1,4-acetoxy-trifluoroacetoxylation of 1,3-dienes was developed by the use of added trifluoroacetic acid to the acetic acid used as the solvent[33c]. With the use of acetone as the solvent with an added carboxylic acid a general diacyloxylation was obtained and, for example, the 1,4-dibenzoates of 2-cycloalkene-1,4-diols were prepared directly from the corresponding 1,3-cycloalkadienes[33d].

An increased chloride ion concentration in the palladium-catalyzed oxidation of 1,3-cyclohexadiene resulted in a highly stereo- and regioselective 1,4-chloroacetoxylation[35]. The product selectivity was also high. Thus, palladium-catalyzed chloroacetoxylation afforded an 89% isolated yield of chloroacetate **29** which was >98% *cis* (Scheme 5). Only 1–2% of diacetate was observed in the crude product.

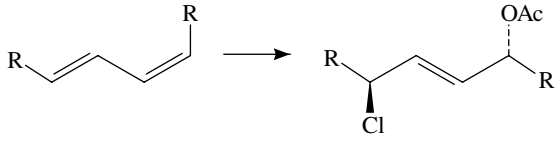


SCHEME 5

The chloroacetoxylation is a quite general reaction and works well with a number of conjugated dienes. Some additional examples are given in Scheme 6 and in equations 15 and 16. The reaction is highly *syn* stereoselective for a number of cyclic dienes tried. Also, for acyclic dienes the reaction leads to a 1,4 *syn* addition and the reaction takes place with good stereospecificity (94–96% *syn*). Thus (*E*,*E*)-dienes give the R*R* isomer whereas (*E*,*Z*)-dienes produce the R*S* isomer (equations 15 and 16). The reaction has also been extended to include other carboxylic acids than acetic acid (chloroacyloxylation)[33d].

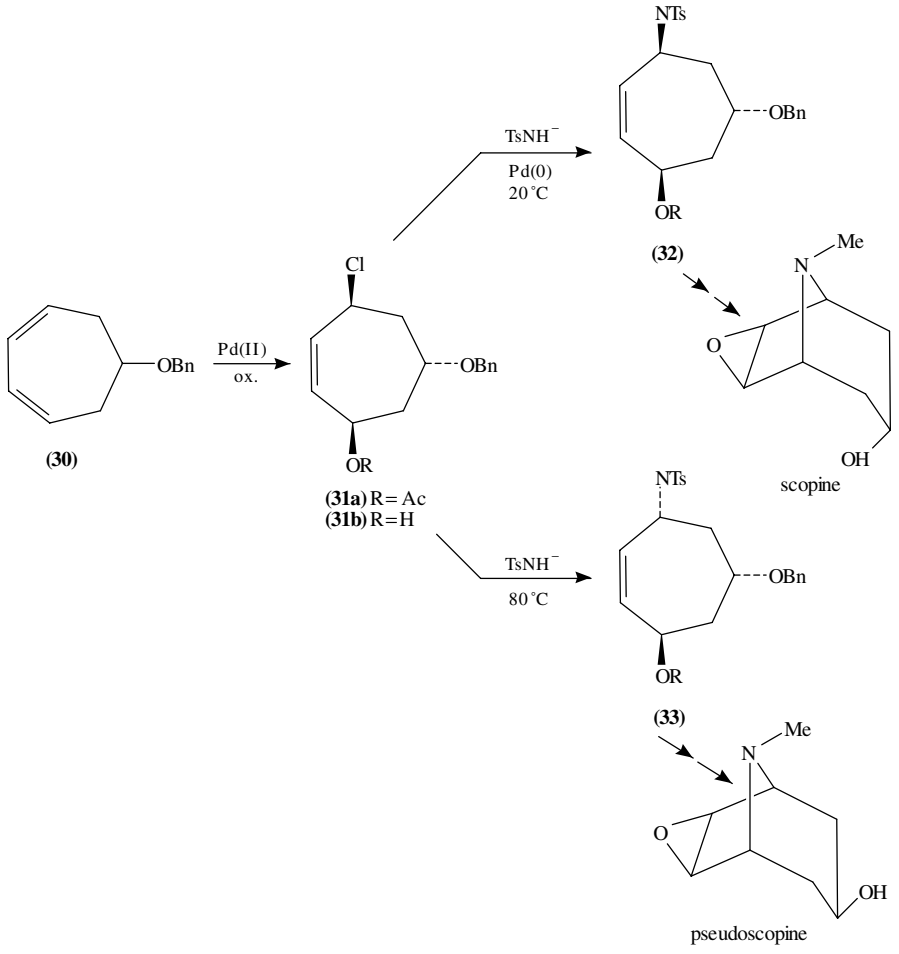


(15)



(16)

R*, S*

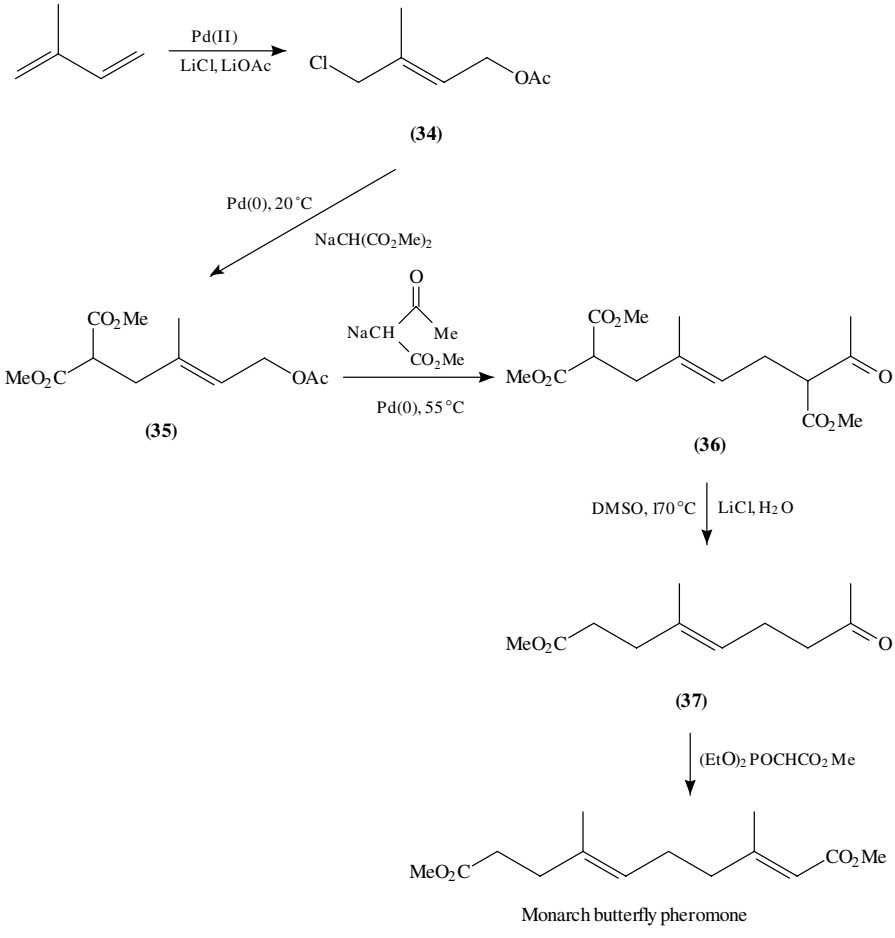


SCHEME 6

The chloroacetoxylation reaction is synthetically useful since the chloride can be substituted with either retention [Pd(0)-catalyzed reaction] or inversion (S_N2 reaction) by a number of nucleophiles. In this way both the *cis* and *trans* isomers are accessible and have been prepared from a number of allylic acetates (Schemes 5 and 6). In a subsequent reaction the allylic acetate can be substituted by employing a copper- or palladium-catalyzed reaction. The latter reactions are stereospecific.

An example of the use of the dual stereoselectivity offered by the chloroacetates is given in Scheme 6 for the synthesis of scopine and pseudoscopine[36]. Palladium-catalyzed chloroacetoxylation of diene **30** gave chloroacetate **31a** in 63% yield with high diastereoselectivity (>95% 1β,4β,6α) with the benzyloxy group *trans* to the chloro and acetoxy groups. Subsequent palladium(0)-catalyzed reaction of the allylic chloride **31** with $TsNH^-$ afforded **32**. The corresponding S_N2 reaction between **31** and the tosylamide anion at elevated temperature afforded the isomeric *trans* product **33**. The amido alcohol derivatives **32** and **33** were subsequently transformed to scopine and pseudoscopine, respectively, via stereoselective epoxidation and cyclization.

This sequential substitution of the chloro and acetoxy groups makes the chloroacetates useful as building blocks. An example of the use of the chloroacetate **34** from isoprene for the synthesis of the Monarch butterfly pheromone is given in Scheme 7[37]. Two different nucleophiles, sodium dimethyl malonate and sodium methyl acetoacetate, were employed in Pd(0)-catalyzed allylic substitutions. The transformation of **34** to **36** was also made

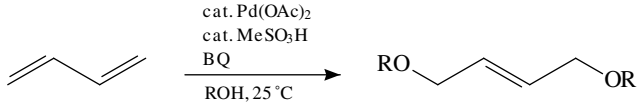


SCHEME 7

in one pot. Double decarboxylation of **36** afforded **37**, which was transformed to the pheromone via a Wittig–Horner reaction.

The principle of this stereoselective functionalization of 1,3-dienes has been applied in organic synthesis of several other natural products[38–44].

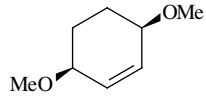
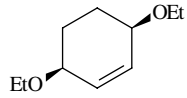
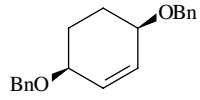
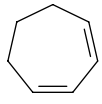
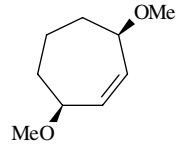
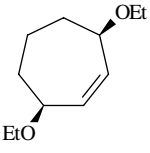
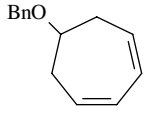
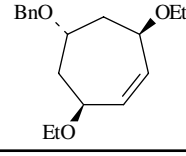
The 1,4-oxidation has also been extended to the use of alcohols as nucleophiles[45]. By performing the reaction in an alcohol as the solvent with $Pd(OAc)_2$ as catalyst and *p*-benzoquinone as the oxidant, a 1,4-dialkoxylation was obtained (equation 17). It was essential to add a catalytic amount of acid to get a reaction. The reaction is highly regio- and stereoselective and 1,3-cyclohexadiene and 1,3-cycloheptadiene afforded exclusively 1,4-*syn* addition products (Table 1).



(17)

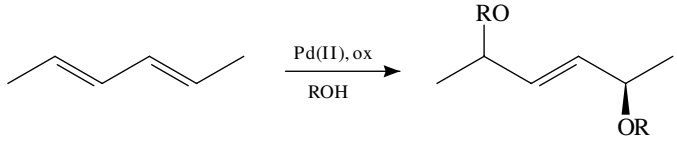
R = Me, Et, Bn

TABLE 1. Pd-catalyzed 1,4-dialkoxylations of 1,3-dienes

1,3-Diene	Alcohol	Product	% Yield	Stereochemistry
	MeOH		63	>98.8% *cis*
	EtOH		72	>98% *cis*
	BnOH		53	>98% *cis*
	MeOH		69	>98% *cis*
	EtOH		82	>98% *cis*
	EtOH		69	>95% 1β, 4β, 6α

The stereochemistry of the dialkoxylation arises from two external attacks by the alcohol, one on the π-diene complex and the second on the intermediate π-allyl complex. This is in accordance with the other palladium-catalyzed 1,4-*syn* additions discussed above.

Also, the 1,4-dialkoxylation of acyclic 1,3-dienes was stereoselective. For example, the reaction of (*E*,*E*)-2,4-hexadiene gave the *d*,*l* products **38** by a 1,4-*syn* addition. The double bond was exclusively of *E* configuration (equation 18).

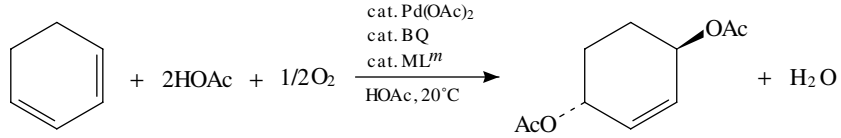


(18)

(38a) R = Me, 45%, >97% *dl*, >98% *E*

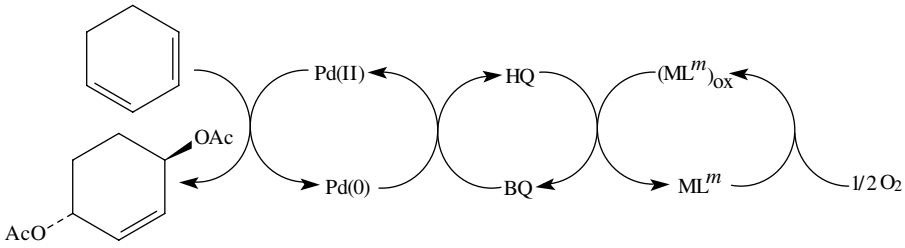
(38b) R = Et, 45%, >96% *dl*, >98% *E*

A mild aerobic palladium-catalyzed 1,4-diacetoxylation of conjugated dienes has been developed and is based on a multistep electron transfer[46]. The hydroquinone produced in each cycle of the palladium-catalyzed oxidation is reoxidized by air or molecular oxygen. The latter reoxidation requires a metal macrocycle as catalyst. In the aerobic process there are no side products formed except water, and the stoichiometry of the reaction is given in equation 19. Thus 1,3-cyclohexadiene is oxidized by molecular oxygen to diacetate **39** with the aid of the triple catalytic system Pd(II)−BQ−ML^m where ML^m is a metal macrocyclic complex such as cobalt tetraphenylporphyrin (Co(TPP)), cobalt salophen (Co(Salophen) or iron phthalocyanine (Fe(Pc)). The principle of this biomimetic aerobic oxidation is outlined in Scheme 8.



(39)

(19)



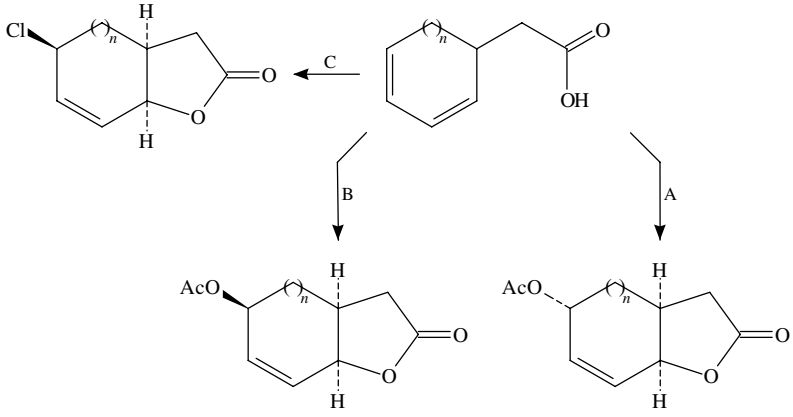
SCHEME 8

Further development of this aerobic oxidation was done by utilizing a quinone containing cobalt tetraphenyl porphyrin[47]. This gives a more efficient electron transfer between quinone and porphyrin and results in a faster aerobic 1,4-diacetoxylation of the diene. The

use of a zeolite encapsulated metal macrocycle (iron phthalocyanine or cobalt salophene) gave a more stable metal macrocyclic catalyst that was filtered off and reused many times in the aerobic 1,4-diacetoxylation[48].

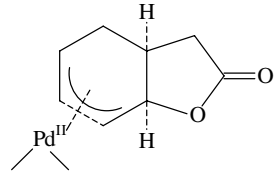
B. Intramolecular Reactions

If one of the nucleophiles is situated in the side chain of the diene an intramolecular palladium-catalyzed 1,4-oxidation takes place. The first example of this type of reaction was the 1,4-oxylactonization (Scheme 9)[49].



SCHEME 9. Pd-catalyzed oxylactonization: cat.$Pd(OAc)_2$, *p*-benzoquinone (BQ), acetone–HOAc (4 : 1); A: no LiCl, B: cat LiCl, C: excess LiCl

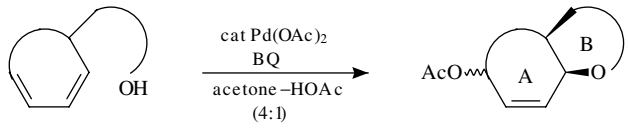
In this reaction a useful stereocontrol was obtained by the use of LiCl as a catalytic additive. Without added LiCl a 1,4-*trans* acetoxylactonization took place, while in the presence of a catalytic amount of LiCl a 1,4-*cis* acetoxylactonization occurred. This is in analogy with the diacetoxylation of conjugated dienes discussed above where chloride ions block the coordination of acetate to palladium[34]. At an increased chloride ion concentration (as added LiCl) a highly regio- and stereoselective 1,4-*cis* chlorolactonization took place. The presence of the π-allylpalladium intermediate **40** was demonstrated by its isolation and stereochemical assignment. The *trans* stereochemistry between palladium and oxygen in the π-allylpalladium complex **40** was established by the use of reporter ligands and NOE measurements[49b].



(40)

The analogous reaction of alcohol derivatives **41** gave fused tetrahydrofurans and fused tetrahydropyrans **42**[50]. As in the lactonization reaction the stereochemistry can be tuned

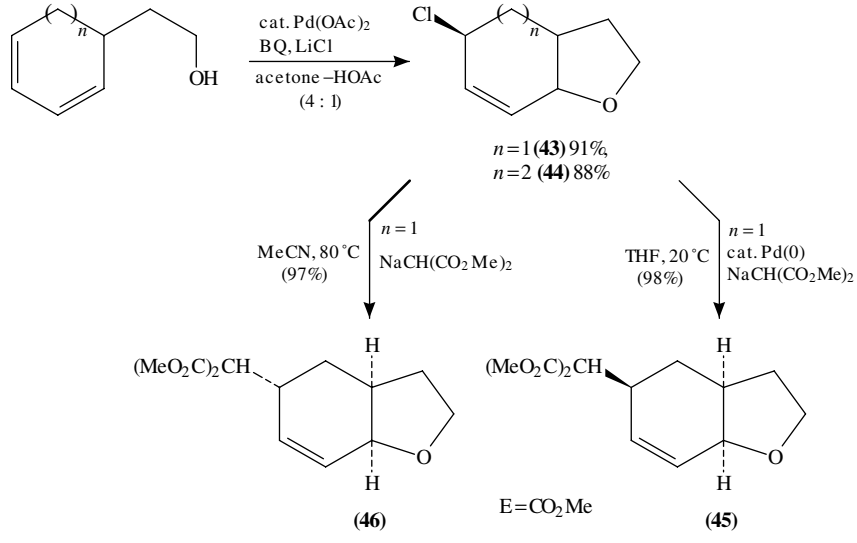
TABLE 2. Pd-catalyzed 1,4-oxylactonization



(41) **(42)**

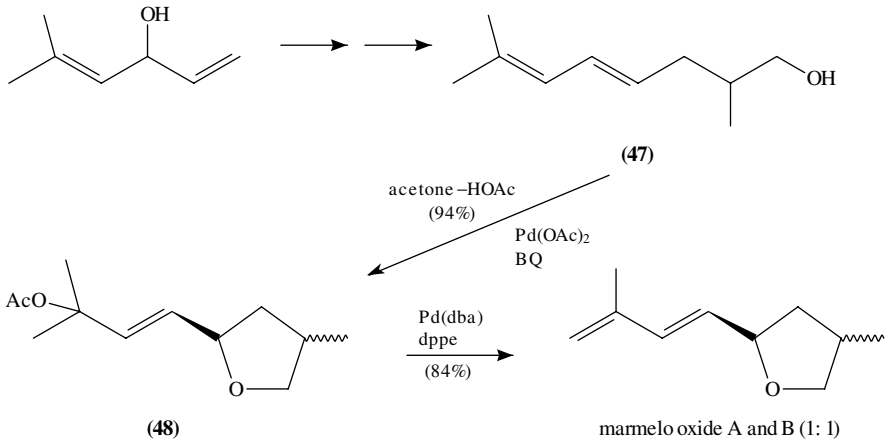
Ring size A	B	Cl^-	% Yield	*cis/trans* (of addition)
6	5	—	87	<2/98
6	5	cat.	82	91/9
6	6	—	87	<2/98
6	6	cat.	78	91/9
7	5	—	90	<2/98
7	5	cat.	81	>98/2

by the ligand control with addition of LiCl. In this way stereoselective 1,4-*trans* and 1,4-*cis* additions were obtained (Table 2). At a higher chloride concentration a 1,4-*cis* oxychlorination took place in high regio- and stereoselectivity to give **43** and **44**. This reaction opens up an entry into stereodefined heterocycles and a stereodivergent transformation of **43** with Pd(0) catalysis or classical S_N2 substitution afforded **45** and **46**, respectively (Scheme 10).



SCHEME 10. E = CO_2Me

The reaction was applied to an acyclic system for the synthesis of furanoid terpenes (Scheme 11)[51]. The palladium-catalyzed intramolecular reaction of **47** afforded **48** which was transformed to the target molecule. The latter product was obtained as a 1:1 mixture of marmelo oxide A and B, which is the isomeric mixture found in nature.

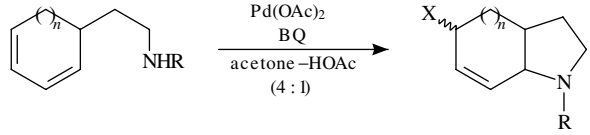


SCHEME 11

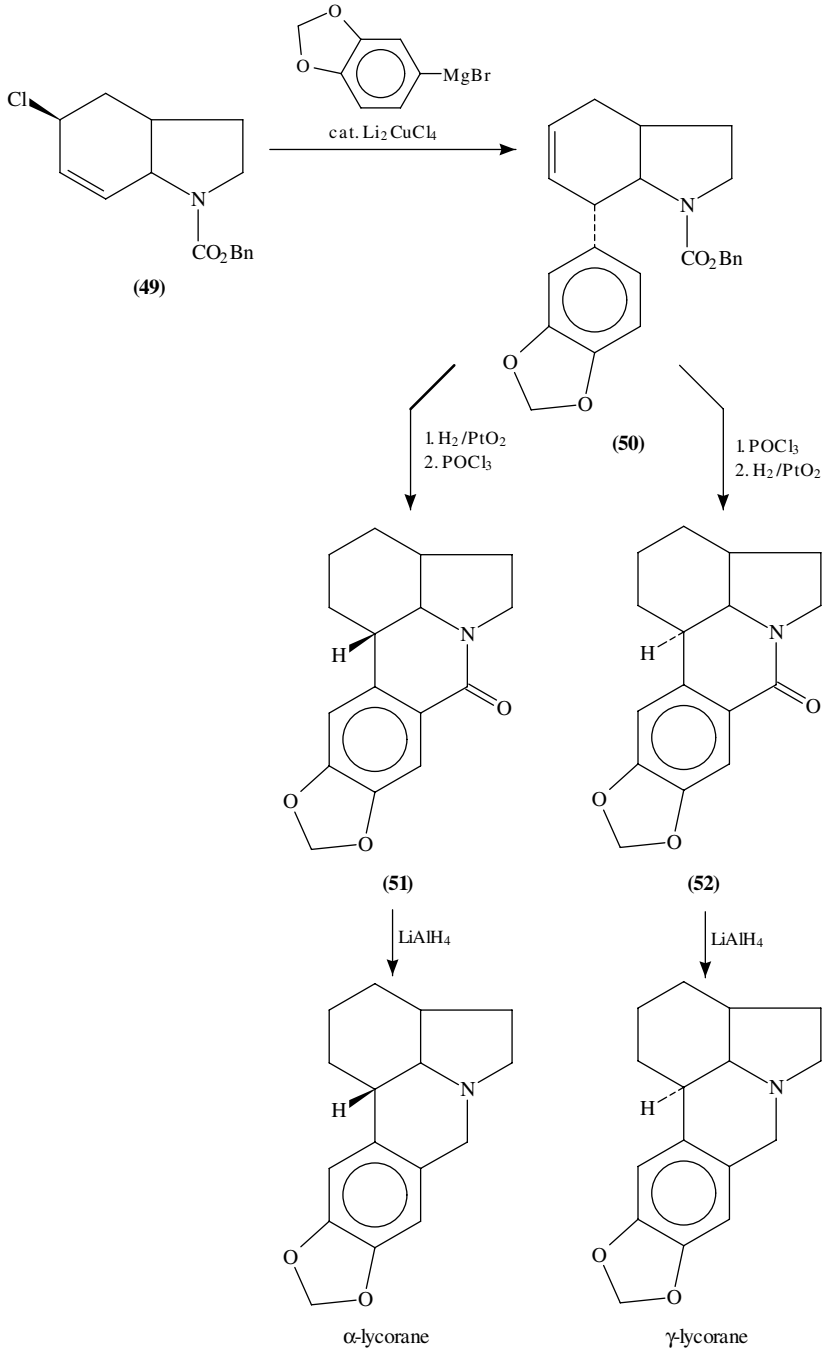
The use of a nitrogen nucleophile in the side chain (as an amide) also leads to an intramolecular 1,4-addition under the standard conditions for the palladium-catalyzed 1,4-oxidation reactions[52]. Nitrogen nucleophiles employed for this reaction comprise tosylamides, carboxamides, carbamates and ureas. The reactions are run in acetone-acetic acid with *p*-benzoquinone (BQ) as the oxidant. In most cases highly stereo- and regioselective reactions were obtained and some examples are given in Table 3.

One of these products **(49)** was used as a key intermediate for the synthesis of the *Amaryllidaceae* alkaloids α- and γ-lycorane (Scheme 12)[53]. A copper-catalyzed Grignard reaction with **49** afforded **50** via a selective γ-*anti* displacement of the chloride. Hydrogenation followed by Bischler–Napieralski cyclization gave **51**. Interestingly, reversal of the latter two steps gave the isomer **52** where an epimerization at the benzylic carbon had occurred in the cyclization step (>99% selectivity). Subsequent reduction of the amide in each case afforded the target molecules α- and γ-lycorane, respectively. The purity of the final product was very high with respect to the opposite stereoisomer. Thus <0.2% of γ-lycorane was present in α-lycorane and vice versa.

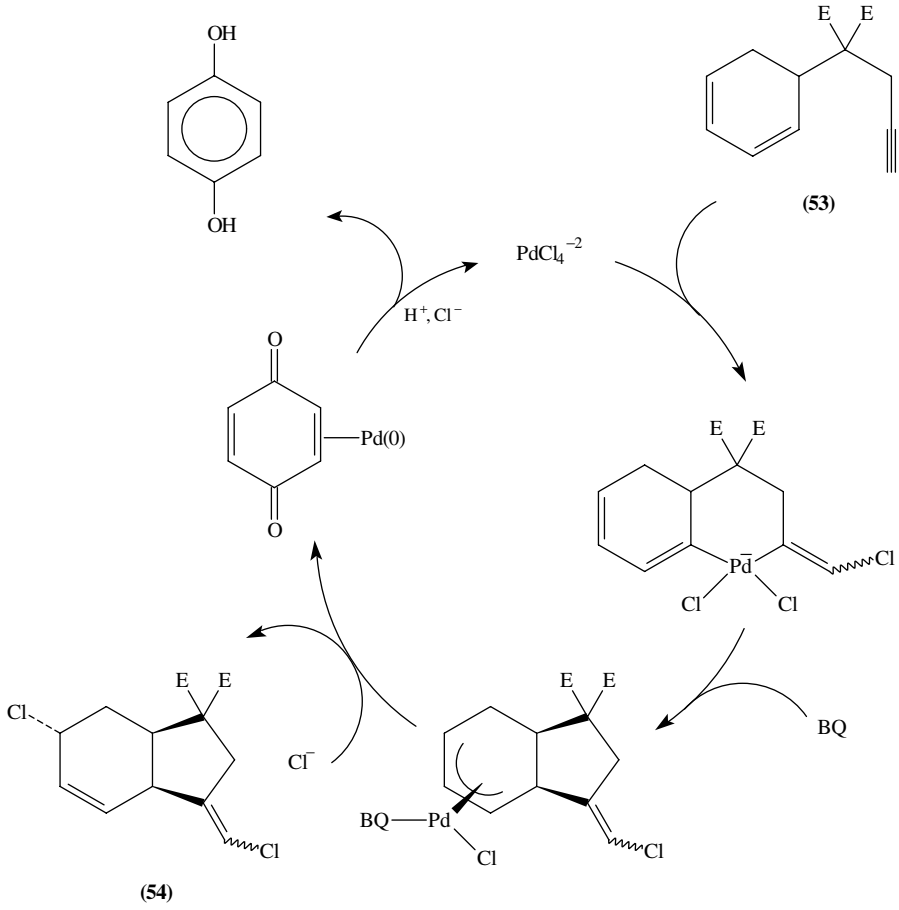
TABLE 3. Pd-catalyzed 1,4-oxyamination



Ring size,	R	Additive	X	% Yield	Stereochemistry of addition
6 ($n = 1$)	Ts	LiOAc	AcO	82	>93% *trans*
6 ($n = 1$)	Ts	LiCl(cat.)	AcO	65	>98% *cis*
6 ($n = 1$)	Ts	LiCl	Cl	90	>98% *cis*
6 ($n = 1$)	CO_2Bn	LiCl	Cl	97	>98% *cis*
7 ($n = 2$)	Ts	LiCl	Cl	86	>98% *cis*

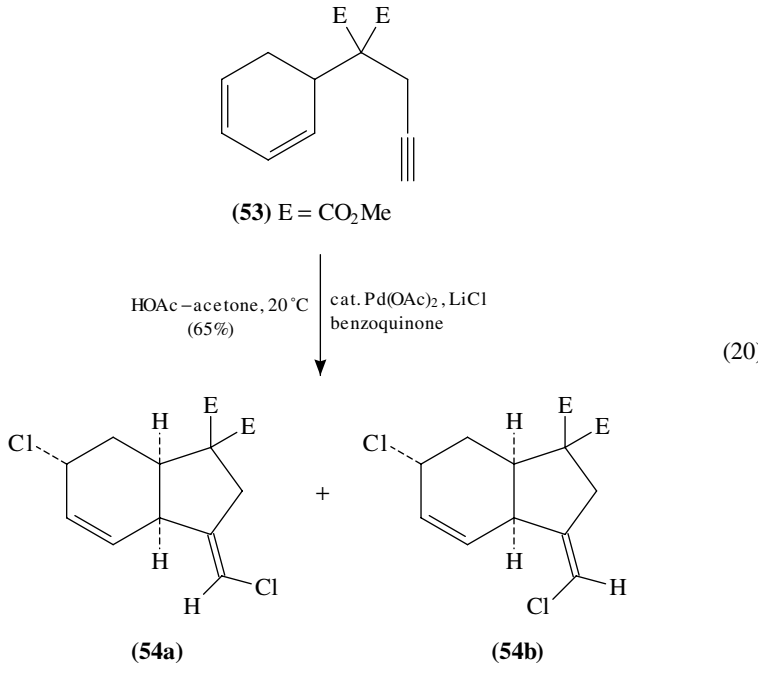

Cl
N
CO2Bn
(49)
O
O
MgBr
cat. Li2CuCl4
N
CO2Bn
O
O
(50)
1. H2/PtO2
2. POCl3
1. POCl3
2. H2/PtO2
H
N
O
O
O
(51)
(52)
LiAlH4
LiAlH4
α-lycorane
γ-lycorane

SCHEME 12



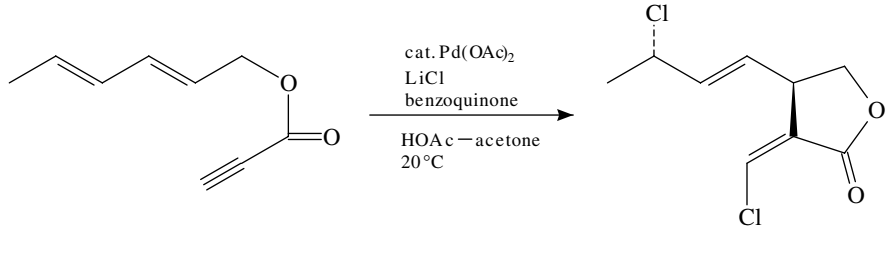
SCHEME 13. E = CO_2Me

The intramolecular palladium-catalyzed 1,4-oxidation has been extended to include carbon nucleophiles. There is an apparent problem with the use of carbon nucleophiles in an oxidation reaction due to the ease of oxidation of the carbanion to a radical. To overcome these problems, masked carbanions such as vinylpalladium and allylsilanes were employed in intramolecular palladium-catalyzed reaction of conjugated dienes[54,55]. In the first approach a vinylpalladium species is generated from an acetylene in the side chain. Subsequent vinylpalladation of the diene produces a (π-allyl)palladium complex. A benzoquinone-induced chloride attack on the π-allyl complex gives the product. The reaction works well with the use of either $Pd(OAc)_2$ or $PdCl_2(MeCN)_2$ as catalyst. The addition across the diene is highly regio- and stereoselective and takes place in a 1,4-*anti* fashion in agreement with the mechanism (Scheme 13). Reaction of dieneyne **53** gave a 65% yield of carbocyclization product as a 1:1.5 mixture of the chlorovinylic isomers **54a** and **54b** (equation 20)[54]. The *E* and *Z* isomerism at the chlorovinyl function originates from a nonstereoselective chloropalladation of the triple bond[56].



(20)

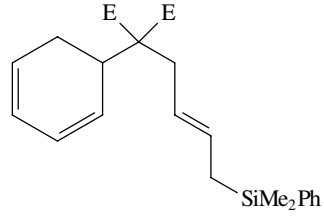
An example of this reaction in an acyclic case is given in equation 21. Dienyne **55** afforded compound **56** in a highly selective 1,4-addition. In this case the relative amount of the trans chloropalladation adduct was higher than in the reaction of **53** and the chlorovinyl group was 90% *E*[54].



(21)

In the second approach[55] an allylsilane was employed as carbon nucleophile in the side chain. Allylsilanes have been frequently used as masked allyl carbanions, usually in reactions with a keto function[57]. Palladium-catalyzed reaction of allylsilane **57** with LiCl under similar conditions as used for the other intramolecular 1,4-oxidations afforded **58** (equation 22). Interestingly, the carbochlorination over the diene was highly 1,4-*syn*

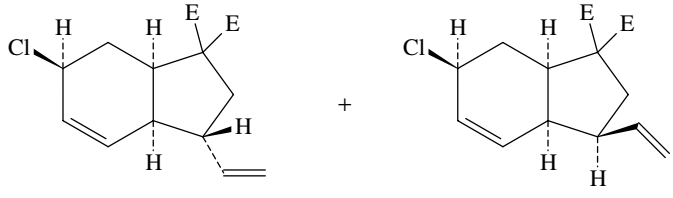
selective. The stereoselectivity is opposite to that obtained from dienyne **53** in equation 20 (*vide supra*).



(57) E = CO_2Me

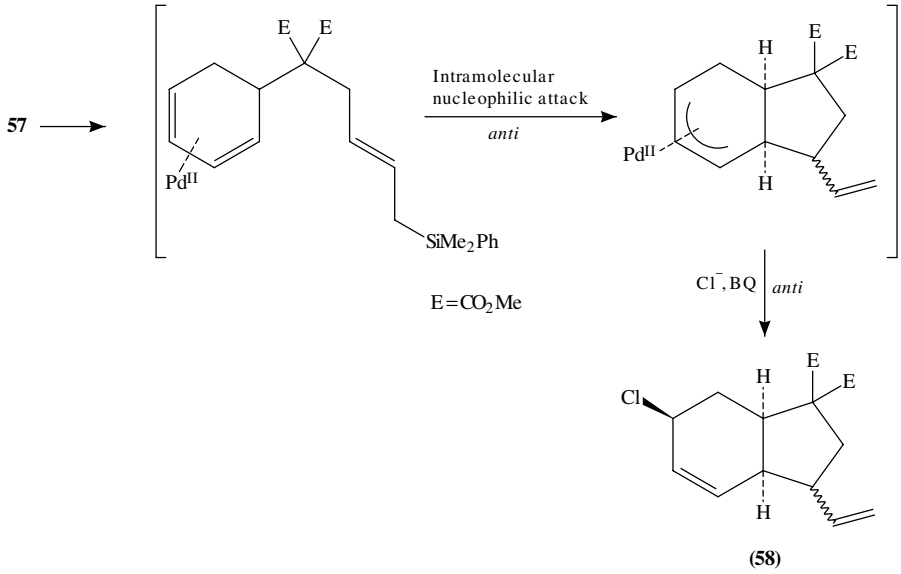
benzoquinone, LiCl
acetone–HOAc (2:1) (68%)
cat. Li_2PdCl_4

(22)



(58α) : **(58β)**

3 : 1

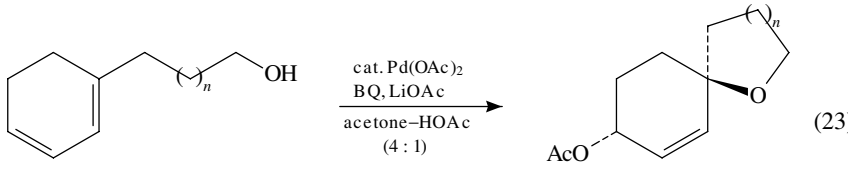


(58)

SCHEME 14

The mechanism of this new reaction is shown in Scheme 14. Coordination of the diene to palladium(II) makes the diene double bond electrophilic enough to be attacked by the allylsilane. The attack by the allylsilane takes place on the face of the diene opposite to that of the palladium (*anti*). This is the first example of an anti attack by an allylsilane on a π-(olefin)metal complex. Benzoquinone (BQ)-induced *anti* attack by chloride ion produces the product **58**.

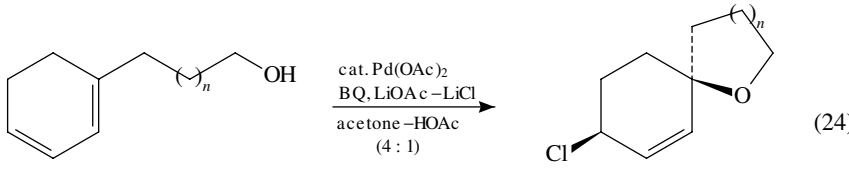
If the side chain with the nucleophile is situated in the 1-position of the conjugated diene, a palladium-catalyzed spirocyclization occurs. In this case stereoselective oxaspirocyclizations were obtained from the diene alcohols **59** and **60** (equation 23–25)[58]. The reaction worked well for the formation of a tetrahydrofuran and tetrahydropyran in the spirocyclization. In the absence of chloride ions **59** gave high yields of the acetoxy oxaspirocyclic compound **61** via a 1,4-*anti* addition across the diene (equation 23). In the presence of stoichiometric amounts of LiCl a 1,4-*syn* oxychlorination took place and allylic chloride **62** was obtained (equation 24). Under chloride-free conditions, cycloheptadiene alcohol **60** afforded oxaspirocyclic acetate **63** (equation 25).



(23)

(59a) $n = 1$
(59b) $n = 2$

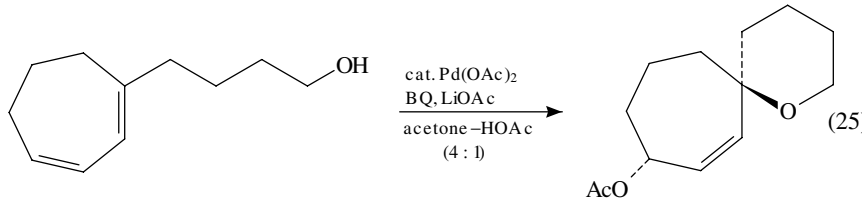
(61a) 86% (>98% *trans*)
(61b) 82% (>98% *trans*)



(24)

(59a) $n = 1$
(59b) $n = 2$

(62a) 70% (>98% *cis*)
(62b) 73% (>98% *cis*)

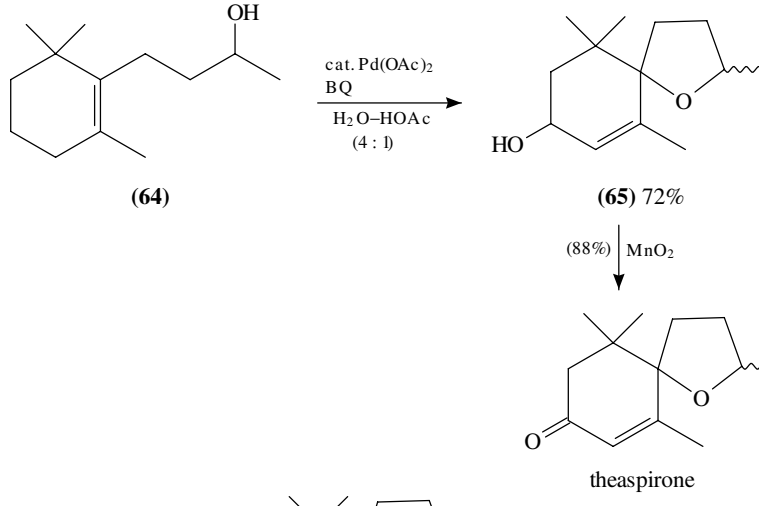


(25)

(60)

(63) 82% (>94% *trans*)

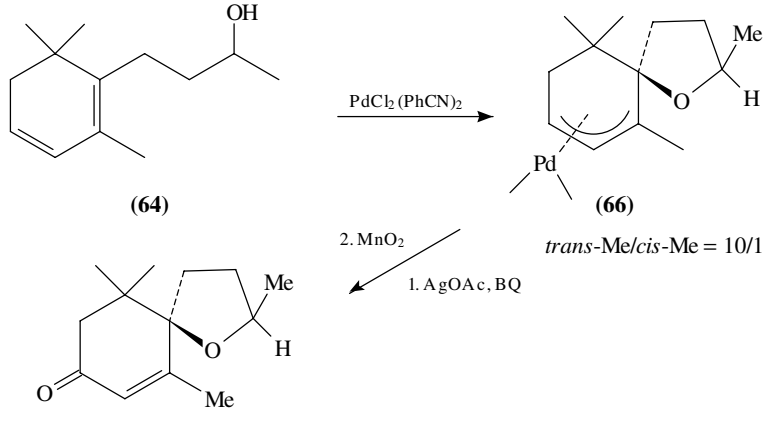
The oxaspirocyclization was applied to the synthesis of theaspirone and vitispirane (equations 26 and 27)[59]. Under slightly modified reaction conditions where water is employed as the major solvent, palladium-catalyzed 1,4-oxidation of **64** afforded **65**. Alcohol **65** was oxidized to theaspirone, which was obtained as a 1:1 isomeric mixture of *cis* and *trans* isomers. When the analogous reaction was performed at a lower pH by the use of trifluoroacetic acid, vitispirane was formed in high yield, again as a 1:1 isomeric mixture of stereoisomers.



(26)

(27)

In a stoichiometric reaction the (π-allyl)palladium complex **66** was isolated and characterized[58b]. In a subsequent reaction the π-allyl complex was reacted with benzoquinone in acetic acid to give an allylic acetate, which was hydrolyzed and oxidized to theaspirone. Interestingly, a quite high diastereoselectivity for the *trans* methyl isomer was obtained in the palladium-mediated spirocyclization (equation 28).

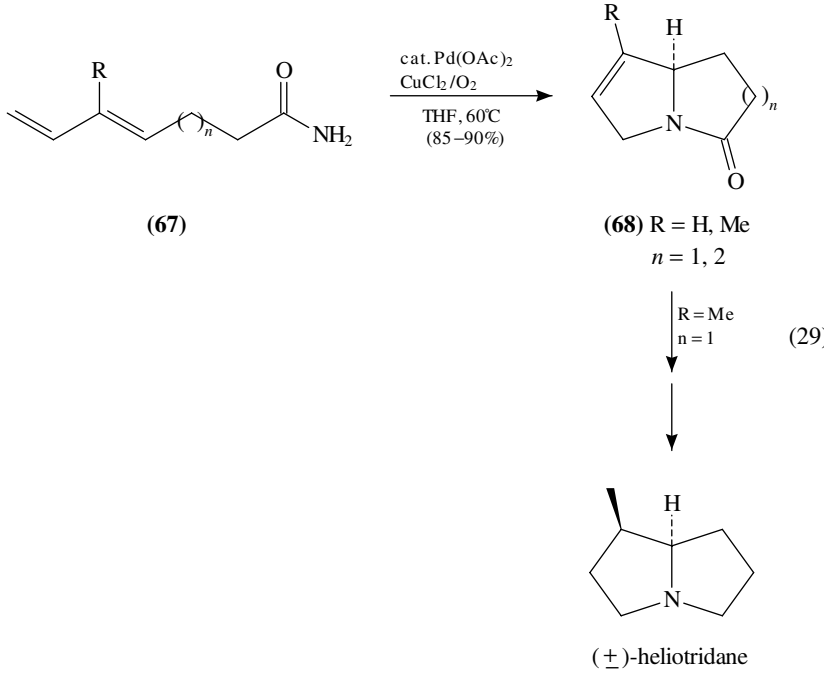


(28)

In the catalytic reaction this diastereoselectivity drops, and it was demonstrated that the π-allyl complex with the *cis* tetrahydrofuran is kinetically favored and is trapped by the

oxidant to give the product. In the stoichiometric reaction the thermodynamically favored π-allyl complex **66** with the *trans* tetrahydrofuran is formed.

An intramolecular palladium-catalyzed tandem cyclization of dienamides **67** in which the amide nucleophile adds twice has been developed (equation 29)[60]. This reaction constitutes a formal [4 + 1] cycloaddition and provides a new route to pyrrolizidine and indolizidine alkaloids. Reaction of dienamides **67** in the presence of catalytic amounts of $Pd(OAc)_2$ and $CuCl_2/O_2$ as the oxidant afforded bicyclic compounds **68** in good yields. The pyrrolizidine derivative **68** (R = Me, n = 1) was transformed to the alkaloid (±)-heliotridane.



(67)

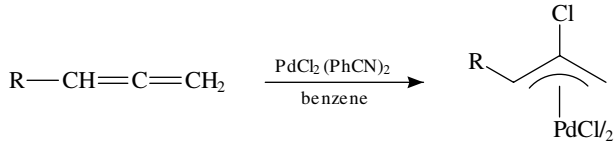
(68) R = H, Me
n = 1, 2

(±)-heliotridane

(29)

IV. ALLENES

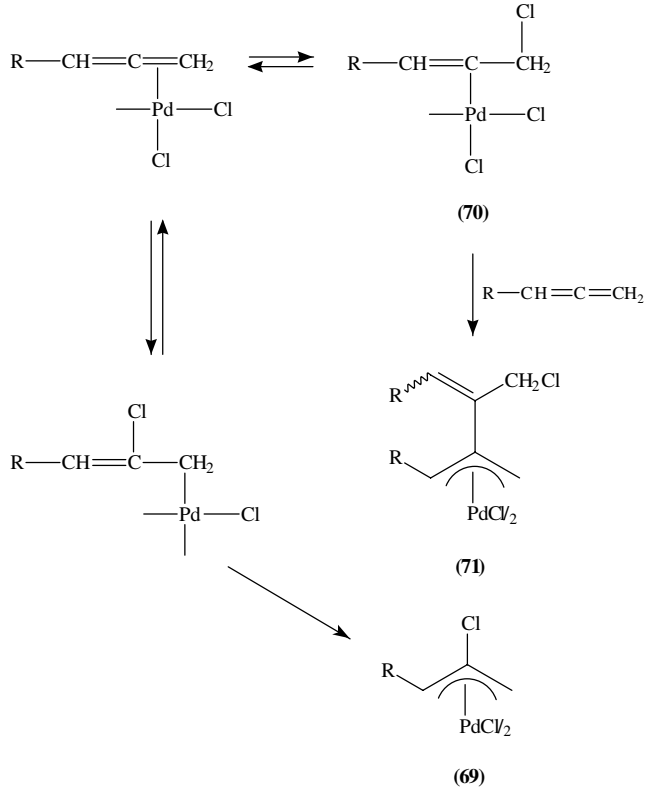
Reaction of allenes with $PdCl_2(PhCN)_2$ in benzene leads to the formation of 2-chloro π-allyl complexes **69** (equation 30)[61].



(30)

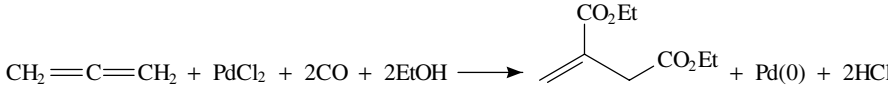
(69) R = H, R = alkyl

If an excess of allene is used, two allenes are incorporated in the π-allyl complex formed. The latter complex, **71**, is formed via a trapping of a vinyl complex **70** (Scheme 15).



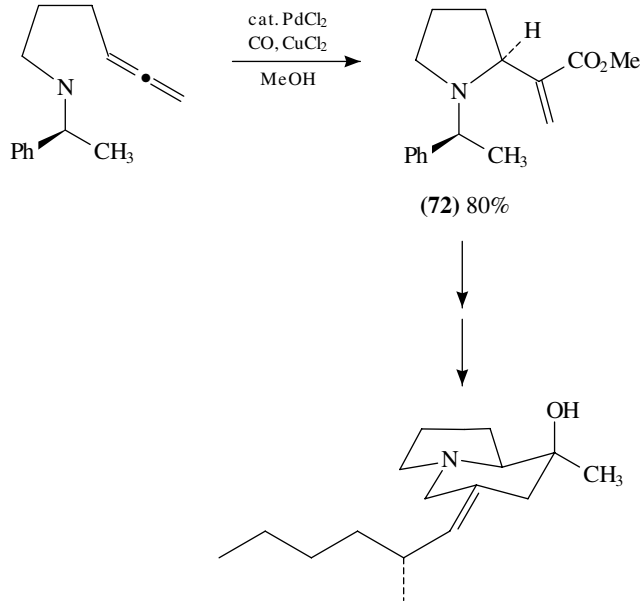
SCHEME 15

Attempts to employ allenes in palladium-catalyzed oxidations have so far given dimeric products via π-allyl complexes of type **71**[62,63]. The fact that only very little 1,2-addition product is formed via nucleophilic attack on π-allyl complex **69** indicates that the kinetic chloropalladation intermediate is **70**. Although formation of **70** is reversible, it is trapped by the excess of allene present in the catalytic reaction to give dimeric products. The only reported example of a selective intermolecular 1,2-addition to allenes is the carbonylation given in equation 31, which is a stoichiometric oxidation[64].



(31)

An example of an intramolecular palladium-catalyzed oxidation of an allene involving carbonylation was used in the synthesis of pumilotoxin 251 D (equation 32)[65]. Intramolecular aminopalladation of the allene followed by carbonylation of the palladium–carbon bond and subsequent oxidative cleavage of the acylpalladium intermediate by $CuCl_2$ afforded pyrrolidine **72** in which the chirality at the carbon at the 2-position was established.



(32)

pumilotoxin 251 D

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The Chemistry of Dienes and Polyenes. Volume 1
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CHAPTER **15**

Structural effects on dienes and polyenes

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I. DIENES AND POLYENES

A. Introduction

Polyenes are hydrocarbons with multiple double bonds. Dienes are simply special cases of polyenes. There are three types of polyenes:

1. Alternating polyenes in which single and double bonds alternate. There are two subtypes of alternating polyenes: conjugated alternating polyenes, of which 1,3,5-hexatriene and cycloheptatriene are examples; and cross-conjugated polyenes such as 2-vinyl-1,3-butadiene. The most important of the cross-conjugated dienes are the fulvenes[1].

2. Adjacent polyenes are hydrocarbons with double bonds between each pair of atoms in the polyene system; they are called cumulenes[2]. Two types of cumulenes exist: those with an even number of adjacent double bonds and those with an odd number. The former can exhibit chirality, the latter geometric isomerism. Allenes (propadienes) are the simplest members of the even-numbered type of cumulenes.

3. Isolated polyenes are those in which the double bonds are separated by one or more sp^3 hybridized carbon atoms. As their behavior is essentially that of ordinary molecules containing a double bond, they will not be considered further.

In this work we present a description of the quantification of structural effects on reactivities and properties of polyene systems.

II. THE NATURE OF STRUCTURAL EFFECTS

A. Introduction

Models for the quantitative description of the structural effects of substituents bonded to dienes or polyenes are described in this work. Also described are substituent effects of dienyl and polyenyl substituents.

In the second half of the nineteenth century the structural theory of organic chemistry was developed. It led to the concept that chemical, physical and biological properties of all kinds must vary with structural change. The earliest structure–property relationships (SPR) were qualitative. With the development of methods of quantitative measurement of these properties data accumulated. Attempts were then made to develop quantitative models of the structural dependence of these properties. These methods for the quantitative description of structural effects will now be described.

B. Structure–Property Quantitative Relationships (SPQR)

Quantitative descriptions of the structural dependence of properties are called structure–property quantitative relationships (SPQR). The four types of these relationships are:

1. Quantitative structure–chemical reactivity relationships (QSRR). Chemical reactivities involve the formation and/or cleavage of chemical bonds. Examples of chemical reactivity data are equilibrium constants, rate constants, polarographic half wave potentials and oxidation–reduction potentials.

2. Quantitative structure–chemical property relationships (QSCR). Chemical properties involve a difference in intermolecular forces between an initial and a final state. Examples of chemical property data are equilibrium constants for hydrogen bonding; charge transfer complex formation, conformational equilibria, partition coefficients; chromatographic properties such as capacity factors in high performance liquid chromatography, retention times in gas chromatography, and R_F values in thin layer and paper chromatography; melting and boiling points; solvent effects on equilibrium or rate constants; and solubilities.

3. Quantitative structure–physical property relationships (QSPR). Physical properties are either ground state properties or properties which depend on the difference in energy between the ground state and an excited state. Bond lengths, bond angles and dipole moments are ground state properties; infrared, ultraviolet, nuclear magnetic resonance and other types of spectra, ionization potentials and electron affinities are properties which depend on the energy difference between states.

4. Quantitative structure–activity relationships (QSAR). Any property associated directly or indirectly with a living organism is a biological activity. The bioactive substrates studied include pure enzymes, tissue homogenates, single celled organisms, whole tissues and large multicellular organisms. The data may be obtained in vitro or in vivo. They include rate and equilibrium constants for enzyme reactivity and for binding to receptor sites, various kinds of toxicity determinations such as lethal dose and lethal concentration, and minimum effective concentrations.

1. The nature of SPQR

There are several different types of chemical species (molecules, ions, radicals, carbenes; nitrenes, benzynes, etc.) for which SPQR can be determined. Three kinds of structure are possible:

1. Species with the structure XGY where X is a variable substituent, Y is a constant active site (an atom or group of atoms at which a measurable phenomenon takes place) and G is a constant skeletal group to which X and Y are bonded.

2. Species with the structure XY in which the variable substituent X is directly attached to the constant active site Y.

3. Species in which substituent and active site are the same, the entire species is the active site and it varies. These species are designated X_Y.

The purpose of SPQR is to provide a quantitative description of the change in some measurable quantity Q that occurs when a change is made in the structure of the species by varying the substituent X. All of the other pertinent variables such as the conditions of the measurement are held constant. Thus:

$$(\partial Q/\partial \mathrm{X})_{\mathrm{G,Y},T,P,\mathrm{Sv,I},\ldots} = Q_{\mathrm{X}} \tag{1}$$

where Q_X is the measured quantity when the substituent is X, G is the skeletal group, Y the active site, T the temperature, P the pressure, Sv the solvent, I the ionic strength, all of which are constant throughout the data set.

We assume that Q_X will be a linear function of some number of parameters which represent the effects of the structural variation of X. Then:

$$Q_{\mathrm{X}} = a_1 p_{1\mathrm{X}} + a_2 p_{2\mathrm{X}} + a_3 p_{3\mathrm{X}} + \cdots + a_0 \tag{2a}$$

$$= \sum_{i=1}^{n} a_i p_{i\mathrm{X}} + a_0 \tag{2b}$$

where the p_i are the parameters which account for the structural effect of X on Q. These parameters have been obtained in various ways:

1. From quantum chemical calculations[3]. This method is most suitable for electrical effect parameters.

2. From molecular mechanics calculations[4] for steric effect parameters.

3. From a reference set by definition (primary values). This method assumes that structural effects on the data set to be studied are a linear function of those which occur in the reference set. Secondary values of these parameters can be estimated by various methods.

4. From comparative molecular field analysis (COMFA)[5]. This method can be used for electrical, steric and polarizability parameters.

5. From molecular geometry for steric parameters.

6. From topological methods. This method is best restricted to steric effect and polarizability parameters.

Once suitable parameters are available the values of Q can be correlated with them by means of either simple linear regression analysis if the model requires only a single variable, or multiple linear regression analysis if it requires two or more variables. Such a correlation results in a SPQR. In this work we consider only those parameters that are defined directly or indirectly from suitable reference sets or, in the case of steric parameters, calculated from molecular geometries.

2. The uses of SPQR

SPQR have three major uses:

1. Mechanistic. QSRR and those QSAR which involve enzyme reactivity can provide information about the sensitivity of a reaction to electrical effects, its electronic demand, the composition of the electrical effect and the sensitivity to steric effects. QSAR which involve binding to receptor sites can provide information about the nature of the receptor site. Other QSAR can shed light on the bioactivity-determining step.

2. Predictive. All SPQR can be used to predict reactivities, chemical and physical properties and bioactivities. There are manifold practical applications of such predictions. Particular examples include the design of bioactive molecules such as medicinal drugs and

pesticides. In addition to the maximization of activity and minimization of side effects, desirable pharmaceutical properties such as improved solubility, longer shelf life and controlled release can be developed. They are also a major method in environmental science where they can be used to predict toxicities, biodegradabilities and other properties of environmental interest.

3. Archival. SPQR provide a concise, efficient and convenient method for storing the results of experimental studies on the effect of structural changes upon properties.

C. The Types of Structural Effects

Structural effects are conveniently divided into three categories:

1. Electrical effects. These effects cause a variation in the electron density at the active site. They account for the ability of a substituent to stabilize or destabilize a cation, anion, radical, carbene or other chemical species.

2. Steric effects. These effects result from the repulsion between valence electrons in orbitals on atoms which are in close proximity but not bonded to each other.

3. Inter- and intramolecular force effects. These effects result either from the interactions between the substituent and its immediate surroundings such as the medium, a surface or a receptor site, or from the effect of the substituent on the interactions of the skeletal group G and the active site Y with their surroundings.

Electrical effects are the major factor in chemical reactivities and physical properties. Intermolecular forces are usually the major factor in bioactivities. Either electrical effects or intermolecular forces may be the predominant factor in chemical properties. Steric effects only occur when the substituent and the active site are in close proximity to each other and even then rarely account for more than twenty-five percent of the overall substituent effect.

III. ELECTRICAL EFFECTS

A. Introduction

The earliest successful parameterization of electrical effects is that of Hammett[6–8]. Burkhardt reported the existence of QSRR two years before Hammett but did not develop a general relationship[9]. Hammett defined the σ_m and σ_p constants using the ionization constants (K_X) of 3- and 4-substituted benzoic acids in water at 25 °C as the reference set and hydrogen as the reference substituent (i.e. K_H) to which all others are compared. For hydrogen the values of the σ_m and σ_p constants were defined as zero.

$$\sigma_X \equiv \log \frac{K_X}{K_H} \tag{3}$$

These parameters were intended to apply to XGY systems in which the skeletal group is phenylene. Hammett found it necessary to define an additional set of parameters, σ_p^-, in order to account for substituent effects in 4-substituted benzene systems with an active site that has a lone pair on the atom adjacent to the benzene ring. The reference set was the ionization constants of 4-substituted phenols in water at 25 °C. Brown and his coworkers[10,11] later defined another set of constants, σ_p^+, to account for substituent effects in benzene derivatives with electronically deficient active sites. The reference set was the rate constants for the solvolysis of 4-substituted cumyl chlorides in 90% aqueous acetone at 25 °C. Finally, Wepster and coworkers[12] and Taft[13] both independently proposed constants intended to represent substituent effects in benzene derivatives with minimal delocalized effect. Using the Taft notation these constants are written as σ_p^0. The reference systems had a methylene group inserted between the benzene ring and the active

site ($XGCH_2Y$, where Y is 1,4-phenylene) as it was argued that the methylene group acted as an insulator preventing conjugation between X and Y. These parameters all differ in electronic demand. They are used in the Hammett equation (equation 3) which may be written in the form:

$$Q_X = \rho\sigma_X + h \tag{4}$$

where Q_X is the value of the quantity of interest when the substituent is X, and σ_X is either σ_{mX}, σ_{pX}, σ^0_{pX}, $\sigma_{pX}{}^+$, or $\sigma_{pX}{}^-$; ρ and h are the slope and intercept of the line. In using the Hammett equation it is necessary to make an *a priori* choice of parameters based on the location of the substituent and a knowledge of the electronic demand in the data set which is to be modelled. If such knowledge is unavailable, as is often the case, it is necessary to correlate the data set with each different parameter. The parameter which gives the best fit is then assumed to be the proper choice and the electronic demand associated with it is that of the data set.

Taft and his coworkers[14–16] developed a diparametric model which separated the electrical effect into contributions from the 'inductive' (actually the field) and resonance effects. This separation depends on the difference in the extent of electron delocalization when a substituent is bonded to an sp^3-hybridized carbon atom in one reference system and to an sp^2-hybridized carbon atom in another. As the first case represents minimal delocalization and the second extensive delocalization, we have referred to the two effects as the localized and delocalized electrical effects. This diparametric electrical effect model can be written in the form:

$$Q_X = L\sigma_{lX} + D\sigma_{DX} + h \tag{5}$$

where σ_l and σ_D are the localized and delocalized electrical effect parameters respectively, L and D are their coefficients while h is the intercept. Taft and coworkers[16] stated that four σ_D constants are required in order to account for all types of electronic demand: σ_{RX}, σ^0_{RX}, $\sigma_{RX}{}^+$, and $\sigma_{RX}{}^-$. They correspond to the σ_p constants described above. Charton noted that in cases of very large electron demand two additional σ_D constants were required: $\sigma_R{}^{\oplus}$ for highly electron-deficient (positive) active sites[17] and $\sigma_R{}^{\ominus}$ for active sites that have a large electron excess (negative)[18].

An alternative diparametric model was proposed by Yukawa and Tsuno[19] for use with electron-deficient active sites. The equation was originally written as:

$$Q_X = \rho\sigma_X + \rho r(\sigma_X{}^+ - \sigma_X) \tag{6}$$

A later version has the form[20]:

$$Q_X = \rho\sigma_X + \rho r(\sigma_X{}^+ - \sigma^0_X) \tag{7}$$

A similar relationship:

$$Q_X = \rho\sigma_X + \rho r(\sigma_X{}^- - \sigma_X) \tag{8}$$

has been proposed for active sites with an electron excess[21]. These relationships are termed the YT equations. They resemble the Hammett equation in being able to include both *meta*- and *para*-substituted compounds in the same data set. To do this it must be assumed that ρ_m is equal to ρ_p. This assumption is a reasonable approximation but in some cases the difference between ρ_m and ρ_p ($\Delta\rho$) is significant. If the molecular geometry of the system of interest does not differ much from that of the benzoic acids, then $\Delta\rho$ is likely to be negligible.

Like the case of the Hammett equation, the use of the LD equation (equation 5) for the description of chemical reactivities required either an *a priori* knowledge of the type

of σ_D substituent constant required, or a comparison of the results obtained using each of the available σ_D constants. The use of the YT equation has generally been restricted to electronically deficient active sites. Clearly there was a need for a more general model of electrical effects that would avoid the *a priori* parameter choice. A triparametric model of the electrical effect has been introduced[22] that can account for the complete range of electrical effects on chemical reactivities of closed-shell species (carbenium and carbanions), that is, reactions which do not involve radical intermediates. The basis of this model was the observation that the σ_D constants differ in their electronic demand. On the assumption that they are generally separated by an order of magnitude in this variable, it is possible to assign to each σ_D type a corresponding value of the electronic demand, η. Thus, the equation:

$$\sigma_{DX} = a_1\eta + a_0 = \sigma_{ex}\eta + \sigma_{dx} \tag{9}$$

is obeyed. The intercept of this linear relationship represents the intrinsic delocalized (resonance) effect, σ_{dX}. This is the delocalized effect observed when the electronic demand of the data set studied is zero. The slope represents the sensitivity of the X group to the electronic demand of the active site. On substituting equation 9 into the LD equation we obtain the triparametric LDR equation:

$$Q_X = L\sigma_{lX} + D\sigma_{dX} + R\sigma_{eX} + h \tag{10}$$

The σ_l values are identical to σ_I. The symbol was changed in order to be consistent with the other symbols used in the equation.

When the composition of the electrical effect, P_D, is held constant the LDR equation simplifies to the CR equation:

$$Q_X = C\sigma_{ldX} + R\sigma_{eX} + h \tag{11}$$

where σ_{ld} is a composite parameter. It is defined by the relationship:

$$\sigma_{ldX} = l\sigma_{lX} + d\sigma_{dX} \tag{12}$$

Lower-case letters are used for the coefficients in equations that represent a substituent constant as a function of other substituent constants. The difference between pure and composite parameters is that the former represent a single effect while the latter represent a mixture of two or more. The percent composition of these parameters is given by:

$$P_D = \frac{100d}{l + d} \tag{13}$$

If the constant value of P_D is written as k', then the σ_{ldX} parameter for a given value of k' is:

$$\sigma_{ldXk'} = \sigma_{lX} + [k'/100 - k']\sigma_{DX} \tag{14}$$

Writing:

$$k^* = k'/(100 - k') \tag{15}$$

gives:

$$\sigma_{ldXk'} = \sigma_{lX} + k^*\sigma_{dX} \tag{16}$$

The Yukawa–Tsuno (YT) equation for 4-substituted benzene derivatives is approximately equivalent to the CR equation[23,24]. This observation has led to the development of a modified Yukawa–Tsuno (MYT) equation which has the form:

$$Q_X = \rho\sigma_X + R\sigma_{eX} + h \tag{17}$$

with σ taking the value σ_m for 3-substituted benzene derivatives and σ_{50} for 4-substituted benzene derivatives, while σ_{eX} for 3-substituted benzene derivatives is 0. The σ_{50} constants have k' equal to 50 and η equal to zero; they are therefore equal to the sum of the σ_l and σ_d values.

If the sensitivity to electronic demand is held constant, the LDR equation reverts to the LD equation (equation 5). By means of an equation analogous to the MYT equation, the modified LD (MLD) equation is:

$$Q_X = \rho'\sigma_X + D\sigma_{DX} + h \tag{18}$$

where σ is σ_m for 3-substituted and σ_l for 4-substituted while σ_D is 0 for 3-substituents; 3- and 4-substituted benzene derivatives can be combined into a single data set. Again, the use of the MLD equation is restricted to systems for which $\Delta\rho$ is not significant.

When both the electronic demand and the composition of the electrical effect are held constant, a set of composite parameters having the form:

$$\sigma_{k'/kX} = l\sigma_{lX} + d\sigma_{dX} + r\sigma_{eX} \tag{19}$$

is obtained, where k' and k are given by equations 20a and 20b:

$$k' = P_D = \frac{100d}{(l+d)} \tag{20a}$$

$$k = \eta = r/d \tag{20b}$$

The Hammett substituent constants are special cases of these parameters.

The $\sigma_{k'/k}$ values describe the overall electrical effect of the X group. They are obtained from the expression:

$$\sigma_{k'/kX} = \sigma_{lX} + [P_D/(100 - P_D)](\sigma_{dX} + \eta\sigma_{eX}) \tag{21a}$$

$$= \sigma_{lX} + k^*(\sigma_{dX} + k\sigma_{eX}) \tag{21b}$$

A plot of the $\sigma_{k'/kX}$ values for a group with P_D on the x axis, η on the y axis and $\sigma_{k'/k}$ on the z axis produces a surface that characterizes the electrical effect of the X group.

B. Electrical Effects of Dienyl and Polyenyl Substituents

Values of electrical effect substituent constants for a few dienyl and polyenal groups have been reported[25]. They are set forth in Table 1 together with values of diynyl and phenyl groups for comparison. Also reported in Table 1 are values for some other types of substituents[22,25] for purposes of comparison.

1. Classification of substituent electrical effects

It is traditional to classify substituents as either electron acceptors (electron withdrawing, electron sink), EA; or electron donors (electron releasing, electron source), ED. There is a third category as well, however, that consists of groups whose electrical effect is not significantly different from zero (NS groups). Groups vary in the nature of their electrical effect to a greater or lesser extent depending on the electronic demand of the phenomenon being studied, the skeletal group, if any, to which they are bonded, and the experimental conditions. Very few groups are in the same category throughout the entire range of P_D and η normally encountered. We have observed earlier that a plot of the $\sigma_{k'/k,X}$ values for a group with $X = P_D$, $Y = \eta$ and $Z = \sigma_{k'/k}$, produces a surface that characterizes the

TABLE 1. Values of σ_l, σ_d, and σ_e[a]

X	σ_l	Ref.	σ_d	Ref.	σ_e	Ref.
Alternating Dienes and Polyenes						
Conjugated						
CH=CH−CH=CH_2	0.12	25	−0.37	25	−0.12	25
H_2C=C−CH=CH_2	0.14	*24a*	−0.24	*26a*	−0.086	*27a*
CH=CH−CH=CHPh	0.13	25	−0.48	25	−0.12	25
$(CH=CH)_2$CH=CH_2	0.12	25	−0.51	25	−0.12	25
H_2C=C−CH=CH−CH=CH_2	0.09	*24a*	−0.28	*26a*	−0.085	*27a*
$(CH=CH)_2$CH=CHPh	0.07	*24a*	−0.45	*26a*	−0.15	*27a*
$(CH=CH)_3$CH=CH_2	0.06	*24a*	−0.46	*26a*	−0.15	*27a*
Cross-conjugated						
CH=C$(CH=CH_2)_2$	0.15	*24a*	−0.58	*26a*	−0.17	*27a*
Adjacent						
CH=C=CH_2	0.12	25	−0.02	25	−0.11	25
Vinyl						
CH=CH_2	0.11	25	−0.08	25	−0.12	25
CH=CHPh	0.13	25	−0.33	25	−0.12	25
Ethynyl						
C≡CH	0.29	25	−0.02	25	−0.10	25
C≡C−C≡CH	0.39	25	0.04	25	−0.10	25
C≡CPh	0.33	25	−0.25	25	−0.14	25
Aryl						
Ph	0.12	22	−0.12	22	−0.12	22
C_6H_4Ph-4	0.13	25	−0.17	25	−0.12	25
1-Naph	0.14	*b*	−0.23	*b*	−0.12	*b*
2-Naph	0.13	22	−0.16	22	−0.12	22
Other groups						
Me	−0.01	22	−0.14	22	−0.030	22
Et	−0.01	22	−0.12	22	−0.036	22
i-Pr	0.01	22	−0.15	22	−0.040	22
t-Bu	−0.01	22	−0.15	22	−0.036	22
c-Pr	0.01	22	−0.17	22	−0.069	22
CF_3	0.40	22	0.13	22	−0.026	22
CHO	0.30	22	0.27	22	−0.10	22
Ac	0.30	22	0.25	22	−0.095	22
$CONH_2$	0.28	22	0.12	22	−0.055	22
CO_2Me	0.32	22	0.16	22	−0.070	22
CO_2Et	0.30	22	0.18	22	−0.064	22
CN	0.57	22	0.12	22	−0.055	22
NH_2	0.17	22	−0.68	22	−0.13	22
NHAc	0.28	22	−0.35	22	−0.088	22
NMe_2	0.17	22	−0.66	22	−0.24	22
NO_2	0.67	22	0.18	22	−0.077	22
N_3	0.43	25	−0.27	25	−0.12	22
PMe_2	0.10	22	−0.50	22	−0.27	22
$POMe_2$	0.30	22	0.14	22	−0.036	22
$PO(OMe)_2$	0.36	22	0.24	22	−0.033	22
OH	0.35	22	−0.57	22	−0.044	22
OMe	0.30	22	−0.55	22	−0.064	22
OEt	0.28	22	−0.55	22	−0.070	22
OAc	0.38	22	−0.24	22	−0.005	22
OPh	0.40	22	−0.51	22	−0.083	22

(*continued overleaf*)

TABLE 1. (*continued*)

X	σ_l	Ref.	σ_d	Ref.	σ_e	Ref.
SH	0.27	22	−0.40	22	−0.098	22
SMe	0.30	22	−0.38	22	−0.13	22
SAc	0.39	22	−0.08	22	−0.057	22
SEt	0.26	22	−0.39	22	−0.12	22
SPh	0.31	22	−0.34	22	−0.17	22
SOMe	0.54	27	−0.01	27	−0.037	*b*
SOPh	0.51	27	−0.02	27	−0.052	*b*
SO_2Me	0.59	22	0.13	22	−0.052	22
SO_2Ph	0.56	22	0.08	22	−0.082	22
SeMe	0.28	22	−0.40	22	−0.14	22
F	0.54	22	−0.48	22	0.041	22
Cl	0.47	22	−0.28	22	−0.011	22
Br	0.47	22	−0.27	22	−0.018	22
I	0.40	22	−0.20	22	−0.057	22
H	0	22	0	22	0	22

[a]Numbers in italics in the columns headed Ref. refer to equations in the text used to estimate the values reported; numbers in ordinary typeface refer to references to the source from which the values were taken.
[b]M. Charton, unpublished results

electrical effect of the X group. A matrix of these values can be obtained by calculating them for values of P_D in the range 10 to 90 in increments of 10 and values of η in the range −6 to 6 in increments of 1. The resulting 9 by 13 matrix has 117 values. We define $\sigma_{k'/k,X}$ values greater than 0.05 as EA, $\sigma_{k'/k,X}$ values less than −0.05 as ED and $\sigma_{k'/k,X}$ values between 0.05 and −0.05 as NS. The variability of the electrical effect of a group can be quantitatively described by the percent of the matrix area in the P_D–η plane in which the group is in each category (P_{EA}, P_{ED} and P_0). Approximate measures of these quantities are given by the relationships:

$$P_{EA} = \frac{n_{EA}}{n_T},\ P_0 = \frac{n_{NS}}{n_T},\ P_{ED} = \frac{n_{ED}}{n_T} \tag{22}$$

where n_{EA}, n_{NS}, n_{ED} and n_T are the number of EA, the number of NS, the number of ED and the total number of values in the matrix. Matrices for a number of substituents are given in Table 2, values of P_{EA}, P_0 and P_{ED}, for many substituents are reported in Table 3. We may now classify groups into seven types:

1. Entirely electron acceptor (EA) ($P_{EA} = 100$). Examples: CF_3, $PO(OMe)_2$, $POPh_2$.
2. Predominantly electron acceptor (PA) ($100 > P_{EA} \geqslant 75$). Examples: NO_2, HCO, CN.
3. Largely electron acceptor (LA) ($75 > P_{EA} \geqslant 50$). Examples: Cl, C≡CPh, OCN.
4. Ambielectronic (AM) ($50 > P_{EA}$ or P_{ED}). Examples: SH, CH_2Ph, $SiMe_3$.
5. Largely electron donor (LD) ($75 > P_{ED} \geqslant 50$). Examples: Me, OH, NH_2.
6. Predominantly electron donor (PD) ($100 > P_{ED} \geqslant 75$). Examples: *P=PMe*, *P=POMe*.
7. Entirely electron donor (ED) ($P_{ED} = 100$). Example: *P=PNMe*$_2$.

The values in italics are based on estimated substituent constants.

2. The nature of substituent electrical effects

The overall electrical effect of a substituent as was noted above is a function of its σ_l, σ_d and σ_e values. It depends on the nature of the skeletal group G, the active site Y, the

TABLE 2. Substituent matrices[a]

	P_D								
η	10	20	30	40	50	60	70	80	90
CH=CH−CH=CH_2									
6	0.00	*−0.15*	*−0.35*	*−0.61*	*−0.97*	*−1.51*	*−2.42*	*−4.24*	*−9.69*
5	0.01	*−0.12*	*−0.30*	*−0.53*	*−0.85*	*−1.33*	*−2.14*	*−3.76*	*−8.61*
4	0.03	*−0.09*	*−0.24*	*−0.45*	*−0.73*	*−1.16*	*−1.86*	*−3.28*	*−7.53*
3	0.04	*−0.06*	*−0.19*	*−0.37*	*−0.61*	*−0.98*	*−1.58*	*−2.80*	*−6.45*
2	0.05	−0.03	*−0.14*	*−0.29*	*−0.49*	*−0.80*	*−1.30*	*−2.32*	*−5.37*
1	**0.07**	0.00	*−0.09*	*−0.21*	*−0.37*	*−0.62*	*−1.02*	*−1.84*	*−4.29*
0	**0.08**	0.03	−0.04	*−0.13*	*−0.25*	*−0.44*	*−0.74*	*−1.36*	*−3.21*
−1	**0.09**	**0.06**	0.01	−0.05	*−0.13*	*−0.26*	*−0.46*	*−0.88*	*−2.13*
−2	**0.11**	**0.09**	**0.06**	0.03	−0.01	*−0.08*	*−0.18*	*−0.40*	*−1.05*
−3	**0.12**	**0.12**	**0.12**	**0.11**	**0.11**	**0.10**	**0.10**	**0.08**	**0.03**
−4	**0.13**	**0.15**	**0.17**	**0.19**	**0.23**	**0.28**	**0.38**	**0.56**	**1.11**
−5	**0.15**	**0.18**	**0.22**	**0.27**	**0.35**	**0.46**	**0.66**	**1.04**	**2.19**
−6	**0.16**	**0.21**	**0.27**	**0.35**	**0.47**	**0.65**	**0.94**	**1.52**	**3.27**
H_2C=C−CH=CH_2									
6	**0.06**	−0.05	*−0.18*	*−0.36*	*−0.62*	*−0.99*	*−1.62*	*−2.88*	*−6.66*
5	**0.07**	−0.03	*−0.15*	*−0.31*	*−0.53*	*−0.87*	*−1.42*	*−2.54*	*−5.89*
4	**0.08**	−0.01	*−0.11*	*−0.25*	*−0.44*	*−0.74*	*−1.22*	*−2.20*	*−5.12*
3	**0.08**	0.02	*−0.07*	*−0.19*	*−0.36*	*−0.61*	*−1.02*	*−1.85*	*−4.34*
2	**0.09**	0.04	−0.04	*−0.13*	*−0.27*	*−0.48*	*−0.82*	*−1.51*	*−3.57*
1	**0.1**	**0.06**	0.00	*−0.08*	*−0.19*	*−0.35*	*−0.62*	*−1.16*	*−2.79*
0	**0.11**	**0.08**	0.04	−0.02	*−0.10*	*−0.22*	*−0.42*	*−0.82*	*−2.02*
−1	**0.12**	**0.10**	**0.07**	0.04	−0.01	*−0.09*	*−0.22*	*−0.48*	*−1.25*
−2	**0.13**	**0.12**	**0.11**	**0.09**	**0.07**	0.04	−0.02	*−0.13*	*−0.47*
−3	**0.14**	**0.14**	**0.15**	**0.15**	**0.16**	**0.17**	**0.18**	**0.21**	**0.30**
−4	**0.15**	**0.17**	**0.18**	**0.21**	**0.24**	**0.30**	**0.38**	**0.56**	**1.08**
−5	**0.16**	**0.19**	**0.22**	**0.27**	**0.33**	**0.43**	**0.58**	**0.90**	**1.85**
−6	**0.17**	**0.21**	**0.26**	**0.32**	**0.42**	**0.55**	**0.78**	**1.24**	**2.62**
CH=CH−CH=CHPh									
6	0.00	*−0.17*	*−0.38*	*−0.67*	*−1.07*	*−1.67*	*−2.67*	*−4.67*	*−10.6*
5	0.01	*−0.14*	*−0.33*	*−0.59*	*−0.95*	*−1.49*	*−2.39*	*−4.19*	*−9.59*
4	0.02	*−0.11*	*−0.28*	*−0.51*	*−0.83*	*−1.31*	*−2.11*	*−3.71*	*−8.51*
3	0.04	*−0.08*	*−0.23*	*−0.43*	*−0.71*	*−1.13*	*−1.83*	*−3.23*	*−7.43*
2	0.05	−0.05	*−0.18*	*−0.35*	*−0.59*	*−0.95*	*−1.55*	*−2.75*	*−6.35*
1	**0.06**	−0.02	*−0.13*	*−0.27*	*−0.47*	*−0.77*	*−1.27*	*−2.27*	*−5.27*
0	**0.08**	0.01	*−0.08*	*−0.19*	*−0.35*	*−0.59*	*−0.99*	*−1.79*	*−4.19*
−1	**0.09**	0.04	−0.02	*−0.11*	*−0.23*	*−0.41*	*−0.71*	*−1.31*	*−3.11*
−2	**0.10**	**0.07**	0.03	*−0.03*	*−0.11*	*−0.23*	*−0.43*	*−0.83*	*−2.03*
−3	**0.12**	**0.10**	**0.08**	0.05	0.01	−0.05	*−0.15*	*−0.35*	*−0.95*
−4	**0.13**	**0.13**	**0.13**	**0.13**	**0.13**	**0.13**	**0.13**	**0.13**	**0.13**
−5	**0.14**	**0.16**	**0.18**	**0.21**	**0.25**	**0.31**	**0.41**	**0.61**	**1.21**
−6	**0.16**	**0.19**	**0.22**	**0.29**	**0.37**	**0.49**	**0.69**	**1.09**	**2.29**
$(CH=CH)_2$−CH=CH_2									
6	−0.02	*−0.19*	*−0.41*	*−0.70*	*−1.11*	*−1.73*	*−2.75*	*−4.80*	*−10.9*
5	0.00	*−0.16*	*−0.36*	*−0.62*	*−0.99*	*−1.54*	*−2.47*	*−4.32*	*−9.87*
4	0.01	*−0.13*	*−0.30*	*−0.54*	*−0.87*	*−1.37*	*−2.19*	*−3.84*	*−8.79*
3	0.02	*−0.10*	*−0.25*	*−0.46*	*−0.75*	*−1.19*	*−1.91*	*−3.36*	*−7.71*
2	0.04	*−0.07*	*−0.20*	*−0.38*	*−0.63*	*−1.01*	*−1.63*	*−2.88*	*−6.63*
1	0.05	−0.04	*−0.15*	*−0.30*	*−0.51*	*−0.83*	*−1.35*	*−2.40*	*−5.55*
0	**0.06**	−0.01	*−0.10*	*−0.22*	*−0.39*	*−0.65*	*−1.07*	*−0.92*	*−4.47*

(*continued overleaf*)

TABLE 2. (*continued*)

	P_D								
η	10	20	30	40	50	60	70	80	90
$(CH{=}CH)_2{-}CH{=}CH_2$									
−1	**0.08**	0.02	−0.05	*−0.14*	*−0.27*	*−0.46*	*−0.79*	*−1.44*	*−3.39*
−2	**0.09**	0.05	0.00	*−0.06*	*−0.15*	*−0.28*	*−0.51*	*−0.96*	*−2.31*
−3	**0.10**	**0.08**	**0.06**	0.02	−0.03	*−0.11*	*−0.23*	*−0.48*	*−1.23*
−4	**0.12**	**0.11**	**0.11**	**0.10**	**0.09**	**0.07**	0.05	0.00	*−0.15*
−5	**0.13**	**0.14**	**0.16**	**0.18**	**0.21**	**0.25**	**0.33**	**0.48**	**0.93**
−6	**0.14**	**0.17**	**0.21**	**0.26**	**0.33**	**0.43**	**0.61**	**0.96**	**2.01**
$H_2C{=}C{-}CH{=}CH{-}CH{=}CH_2$									
6	0.00	*−0.11*	*−0.25*	*−0.44*	*−0.70*	*−1.09*	*−1.75*	*−3.07*	*−7.02*
5	0.01	*−0.09*	*−0.21*	*−0.38*	*−0.62*	*−0.97*	*−1.56*	*−2.73*	*−6.26*
4	0.02	*−0.07*	*−0.18*	*−0.32*	*−0.53*	*−0.84*	*−1.36*	*−2.39*	*−5.49*
3	0.03	−0.04	*−0.14*	*−0.27*	*−0.44*	*−0.71*	*−1.16*	*−2.05*	*−4.72*
2	0.04	−0.02	*−0.10*	*−0.21*	*−0.36*	*−0.58*	*−0.96*	*−1.71*	*−3.96*
1	0.05	0.00	*−0.07*	*−0.15*	*−0.28*	*−0.46*	*−0.76*	*−1.37*	*−3.20*
0	**0.06**	0.02	−0.03	*−0.10*	*−0.19*	*−0.33*	*−0.56*	*−1.03*	*−2.43*
−1	**0.07**	0.04	0.01	−0.04	*−0.10*	*−0.20*	*−0.36*	*−0.69*	*−1.66*
−2	**0.08**	**0.06**	0.04	0.02	−0.02	*−0.07*	*−0.17*	*−0.35*	*−0.90*
−3	**0.09**	**0.08**	**0.08**	**0.07**	**0.07**	0.05	0.03	−0.01	*−0.14*
−4	**0.10**	**0.11**	**0.12**	**0.13**	**0.15**	**0.18**	**0.23**	**0.33**	**0.63**
−5	**0.11**	**0.13**	**0.15**	**0.19**	**0.24**	**0.31**	**0.43**	**0.67**	**1.40**
−6	**0.12**	**0.15**	**0.19**	**0.24**	**0.32**	**0.43**	**0.63**	**1.01**	**2.16**
$(CH{=}CH)_3Ph$									
6	*−0.08*	*−0.27*	*−0.51*	*−0.83*	*−1.28*	*−1.96*	*−3.08*	*−5.33*	*−12.0*
5	*−0.06*	*−0.23*	*−0.44*	*−0.73*	*−1.13*	*−1.73*	*−2.73*	*−4.73*	*−10.7*
4	−0.05	*−0.19*	*−0.38*	*−0.63*	*−0.98*	*−1.50*	*−2.38*	*−4.13*	*−9.38*
3	−0.03	*−0.16*	*−0.32*	*−0.53*	*−0.83*	*−1.28*	*−2.03*	*−3.53*	*−8.03*
2	−0.01	*−0.12*	*−0.25*	*−0.43*	*−0.68*	*−1.06*	*−1.68*	*−2.93*	*−6.68*
1	0.00	*−0.08*	*−0.19*	*−0.33*	*−0.53*	*−0.83*	*−1.33*	*−2.33*	*−5.33*
0	0.02	*−0.04*	*−0.12*	*−0.23*	*−0.38*	*−0.60*	*−0.98*	*−1.73*	*−3.98*
−1	0.04	0.00	*−0.06*	*−0.13*	*−0.23*	*−0.38*	*−0.63*	*−1.13*	*−2.63*
−2	0.05	0.03	0.01	−0.03	*−0.08*	*−0.15*	*−0.28*	*−0.53*	*−1.28*
−3	**0.07**	**0.07**	**0.07**	**0.07**	**0.07**	**0.07**	**0.07**	**0.07**	**0.07**
−4	**0.09**	**0.11**	**0.13**	**0.17**	**0.22**	**0.30**	**0.42**	**0.67**	**1.42**
−5	**0.10**	**0.15**	**0.20**	**0.27**	**0.37**	**0.52**	**0.77**	**1.27**	**2.77**
−6	**0.12**	**0.18**	**0.26**	**0.37**	**0.52**	**0.75**	**1.12**	**1.87**	**4.12**
$(CH{=}CH)_3{-}CH{=}CH_2$									
6	*−0.09*	*−0.28*	*−0.52*	*−0.85*	*−1.30*	*−1.98*	*−3.11*	*−5.38*	*−12.1*
5	*−0.07*	*−0.24*	*−0.46*	*−0.75*	*−1.16*	*−1.76*	*−2.76*	*−4.78*	*−10.8*
4	*−0.06*	*−0.21*	*−0.39*	*−0.65*	*−1.00*	*−1.53*	*−2.41*	*−4.18*	*−9.48*
3	*−0.04*	*−0.17*	*−0.33*	*−0.55*	*−0.85*	*−1.31*	*−2.06*	*−3.58*	*−8.13*
2	−0.02	*−0.13*	*−0.27*	*−0.45*	*−0.70*	*−1.08*	*−1.71*	*−2.98*	*−6.78*
1	−0.01	*−0.09*	*−0.20*	*−0.35*	*−0.55*	*−0.86*	*−1.36*	*−2.38*	*−5.43*
0	0.01	*−0.06*	*−0.14*	*−0.25*	*−0.40*	*−0.63*	*−1.01*	*−1.78*	*−4.08*
−1	0.03	−0.02	*−0.07*	*−0.15*	*−0.25*	*−0.41*	*−0.66*	*−1.18*	*−2.73*
−2	0.04	0.02	−0.01	−0.05	*−0.10*	*−0.18*	*−0.31*	*−0.58*	*−1.38*
−3	**0.06**	**0.06**	**0.06**	0.05	0.05	0.05	0.04	0.02	−0.03
−4	**0.08**	**0.10**	**0.12**	**0.15**	**0.20**	**0.27**	**0.39**	**0.62**	**1.32**
−5	**0.09**	**0.13**	**0.18**	**0.25**	**0.35**	**0.50**	**0.74**	**1.22**	**2.67**
−6	**0.11**	**0.17**	**0.25**	**0.35**	**0.50**	**0.72**	**1.09**	**1.82**	**4.02**

TABLE 2. (*continued*)

	P_D								
η	10	20	30	40	50	60	70	80	90
CH=C(CH=CH$_2$)$_2$									
6	−0.03	*−0.25*	*−0.54*	*−0.92*	*−1.45*	*−2.25*	*−3.58*	*−6.25*	*−14.2*
5	−0.01	*−0.21*	*−0.46*	*−0.80*	*−1.28*	*−2.00*	*−3.19*	*−5.57*	*−12.7*
4	0.01	*−0.16*	*−0.39*	*−0.69*	*−1.11*	*−1.74*	*−2.79*	*−4.89*	*−11.1*
3	0.03	*−0.12*	*−0.32*	*−0.58*	*−0.94*	*−1.48*	*−2.39*	*−4.21*	*−9.66*
2	0.05	*−0.08*	*−0.24*	*−0.46*	*−0.77*	*−1.23*	*−2.00*	*−3.53*	*−8.13*
1	**0.07**	−0.04	*−0.17*	*−0.35*	*−0.60*	*−0.98*	*−1.60*	*−2.85*	*−6.60*
0	**0.09**	0.01	*−0.10*	*−0.24*	*−0.43*	*−0.72*	*−1.20*	*−2.17*	*−5.07*
−1	**0.10**	0.05	−0.03	*−0.12*	*−0.26*	*−0.46*	*−0.81*	*−1.49*	*−3.54*
−2	**0.12**	**0.09**	0.05	−0.01	*−0.09*	*−0.21*	*−0.41*	*−0.81*	*−2.01*
−3	**0.14**	**0.13**	**0.12**	**0.10**	**0.08**	0.05	−0.01	*−0.13*	*−0.48*
−4	**0.16**	**0.18**	**0.19**	**0.22**	**0.25**	**0.30**	**0.38**	**0.55**	**1.05**
−5	**0.18**	**0.22**	**0.27**	**0.33**	**0.42**	**0.56**	**0.78**	**1.23**	**2.58**
−6	**0.20**	**0.26**	**0.34**	**0.44**	**0.59**	**0.81**	**1.18**	**1.91**	**4.11**
CH=C=CH$_2$									
6	0.04	−0.05	*−0.17*	*−0.33*	*−0.56*	*−0.90*	*−1.47*	*−2.60*	*−6.00*
5	**0.06**	−0.02	*−0.12*	*−0.26*	*−0.46*	*−0.74*	*−1.21*	*−2.16*	*−5.01*
4	**0.07**	0.00	*−0.08*	*−0.19*	*−0.34*	*−0.57*	*−0.95*	*−1.72*	*−4.02*
3	**0.08**	0.03	−0.03	*−0.11*	*−0.23*	*−0.40*	*−0.70*	*−1.28*	*−3.03*
2	**0.09**	**0.06**	0.02	−0.04	*−0.12*	*−0.24*	*−0.44*	*−0.84*	*−2.04*
1	**0.11**	**0.09**	**0.06**	0.03	−0.01	*−0.07*	*−0.18*	*−0.40*	*−1.05*
0	**0.12**	**0.12**	**0.11**	**0.11**	**0.10**	**0.09**	**0.07**	0.04	*−0.06*
−1	**0.13**	**0.14**	**0.16**	**0.18**	**0.21**	**0.26**	**0.33**	**0.48**	**0.93**
−2	**0.14**	**0.17**	**0.21**	**0.25**	**0.32**	**0.42**	**0.59**	**0.92**	**1.92**
−3	**0.15**	**0.20**	**0.25**	**0.33**	**0.43**	**0.59**	**0.84**	**1.36**	**2.91**
−4	**0.17**	**0.23**	**0.30**	**0.40**	**0.54**	**0.75**	**1.10**	**1.80**	**3.90**
−5	**0.18**	**0.25**	**0.35**	**0.47**	**0.65**	**0.91**	**1.36**	**2.24**	**4.89**
−6	**0.19**	**0.28**	**0.39**	**0.55**	**0.76**	**1.08**	**1.61**	**2.68**	**5.88**
C≡C−C≡CH									
6	**0.33**	**0.25**	**0.15**	0.02	*−0.17*	*−0.46*	*−0.92*	*−1.85*	*−4.66*
5	**0.34**	**0.27**	**0.19**	**0.08**	*−0.07*	*−0.30*	*−0.68*	*−1.45*	*−3.75*
4	**0.35**	**0.30**	**0.24**	**0.15**	0.03	*−0.15*	*−0.45*	*−1.05*	*−2.85*
3	**0.36**	**0.33**	**0.28**	**0.22**	**0.13**	0.00	*−0.22*	*−0.65*	*−1.95*
2	**0.37**	**0.36**	**0.32**	**0.28**	**0.22**	**0.15**	0.02	*−0.25*	*−1.05*
1	**0.38**	**0.38**	**0.36**	**0.35**	**0.33**	**0.30**	**0.25**	**0.15**	*−0.15*
0	**0.39**	**0.40**	**0.41**	**0.42**	**0.43**	**0.45**	**0.48**	**0.55**	**0.75**
−1	**0.41**	**0.43**	**0.45**	**0.48**	**0.53**	**0.60**	**0.72**	**0.95**	**1.65**
−2	**0.42**	**0.45**	**0.49**	**0.55**	**0.63**	**0.75**	**0.95**	**1.35**	**2.55**
−3	**0.43**	**0.48**	**0.54**	**0.62**	**0.73**	**0.90**	**1.18**	**1.75**	**3.45**
−4	**0.44**	**0.50**	**0.58**	**0.68**	**0.83**	**1.05**	**1.42**	**2.15**	**4.35**
−5	**0.45**	**0.53**	**0.62**	**0.75**	**0.93**	**1.20**	**1.65**	**2.55**	**5.25**
−6	**0.46**	**0.55**	**0.66**	**0.82**	**1.03**	**1.35**	**1.88**	**2.95**	**6.15**
C$_6$H$_4$Ph-4									
6	0.03	*−0.09*	*−0.25*	*−0.46*	*−0.76*	*−1.21*	*−1.95*	*−3.43*	*−7.88*
5	0.04	*−0.06*	*−0.20*	*−0.38*	*−0.64*	*−1.03*	*−1.67*	*−2.95*	*−6.80*
4	**0.06**	−0.03	*−0.15*	*−0.30*	*−0.52*	*−0.85*	*−1.39*	*−2.47*	*−5.72*
3	**0.07**	0.00	*−0.10*	*−0.22*	*−0.40*	*−0.66*	*−1.11*	*−1.99*	*−4.64*
2	**0.08**	0.03	−0.05	*−0.14*	*−0.28*	*−0.49*	*−0.83*	*−1.51*	*−3.56*
1	**0.10**	**0.06**	0.01	*−0.06*	*−0.16*	*−0.31*	*−0.55*	*−1.03*	*−2.48*
0	**0.11**	**0.09**	**0.06**	0.02	−0.04	*−0.13*	*−0.27*	*−0.55*	*−1.40*

(*continued overleaf*)

TABLE 2. (*continued*)

	P_D								
η	10	20	30	40	50	60	70	80	90
C_6H_4Ph-4									
−1	**0.12**	**0.12**	**0.11**	**0.10**	**0.08**	0.05	0.01	*−0.07*	*−0.32*
−2	**0.14**	**0.15**	**0.16**	**0.18**	**0.20**	**0.23**	**0.29**	**0.41**	**0.76**
−3	**0.15**	**0.18**	**0.21**	**0.26**	**0.32**	**0.41**	**0.57**	**0.89**	**1.84**
−4	**0.16**	**0.21**	**0.26**	**0.34**	**0.44**	**0.60**	**0.85**	**1.37**	**2.92**
−5	**0.18**	**0.24**	**0.31**	**0.42**	**0.56**	**0.77**	**1.13**	**1.85**	**4.00**
−6	**0.19**	**0.27**	**0.37**	**0.50**	**0.68**	**0.95**	**1.41**	**2.33**	**5.08**
C≡CPh									
6	**0.21**	**0.06**	*−0.14*	*−0.40*	*−0.76*	*−1.31*	*−2.21*	*−4.03*	*−9.48*
5	**0.22**	**0.09**	*−0.08*	*−0.30*	*−0.62*	*−1.09*	*−1.89*	*−3.47*	*−8.22*
4	**0.24**	**0.13**	−0.02	*−0.21*	*−0.48*	*−0.89*	*−1.56*	*−2.91*	*−6.96*
3	**0.26**	**0.16**	0.04	*−0.12*	*−0.34*	*−0.67*	*−1.23*	*−2.35*	*−5.70*
2	**0.27**	**0.20**	**0.10**	−0.02	*−0.20*	*−0.46*	*−0.91*	*−1.79*	*−4.44*
1	**0.29**	**0.23**	**0.16**	**0.07**	*−0.06*	*−0.25*	*−0.58*	*−1.23*	*−3.18*
0	**0.30**	**0.27**	**0.22**	**0.16**	**0.08**	−0.04	*−0.25*	*−0.67*	*−1.92*
−1	**0.32**	**0.30**	**0.28**	**0.26**	**0.22**	**0.17**	**0.07**	*−0.11*	*−0.66*
−2	**0.33**	**0.34**	**0.34**	**0.35**	**0.36**	**0.38**	**0.40**	**0.45**	**0.60**
−3	**0.35**	**0.37**	**0.40**	**0.44**	**0.50**	**0.59**	**0.73**	**1.01**	**1.86**
−4	**0.36**	**0.41**	**0.46**	**0.54**	**0.64**	**0.80**	**1.05**	**1.57**	**3.12**
−5	**0.38**	**0.44**	**0.52**	**0.63**	**0.78**	**1.01**	**1.38**	**2.13**	**4.38**
−6	**0.40**	**0.48**	**0.58**	**0.72**	**0.92**	**1.22**	**1.71**	**2.69**	**5.64**
CH=CHPh									
6	0.01	*−0.13*	*−0.32*	*−0.57*	*−0.92*	*−1.44*	*−2.32*	*−4.07*	*−9.32*
5	0.03	*−0.10*	*−0.27*	*−0.49*	*−0.80*	*−1.27*	*−2.04*	*−3.59*	*−8.24*
4	0.04	*−0.07*	*−0.22*	*−0.41*	*−0.68*	*−1.09*	*−1.76*	*−3.11*	*−7.16*
3	0.05	−0.04	*−0.17*	*−0.33*	*−0.56*	*−0.91*	*−1.48*	*−2.63*	*−6.08*
2	**0.07**	−0.01	*−0.11*	*−0.25*	*−0.44*	*−0.73*	*−1.20*	*−2.15*	*−5.00*
1	**0.08**	0.02	*−0.06*	*−0.17*	*−0.32*	*−0.55*	*−0.92*	*−1.67*	*−3.92*
0	**0.09**	0.05	−0.01	*−0.09*	*−0.20*	*−0.37*	*−0.64*	*−1.19*	*−2.84*
−1	**0.11**	**0.08**	0.04	−0.01	*−0.08*	*−0.19*	*−0.36*	*−0.71*	*−1.76*
−2	**0.12**	**0.11**	**0.09**	**0.07**	0.04	−0.01	*−0.08*	*−0.23*	*−0.68*
−3	**0.13**	**0.14**	**0.14**	**0.15**	**0.16**	**0.17**	**0.20**	**0.25**	**0.40**
−4	**0.15**	**0.17**	**0.19**	**0.23**	**0.28**	**0.35**	**0.48**	**0.73**	**1.48**
−5	**0.16**	**0.20**	**0.25**	**0.31**	**0.40**	**0.53**	**0.76**	**1.21**	**2.56**
−6	**0.17**	**0.23**	**0.30**	**0.39**	**0.52**	**0.71**	**1.04**	**1.69**	**3.64**

[a]Values in boldface are electron accepting, values in italics are electron donating, and values in ordinary type face show no significant electrical effect.

type of phenomenon studied, the medium and the reagent if any. These are the factors that control the values of P_D and η, which in turn determine the contributions of σ_l, σ_d and σ_e.

a. Conjugated alternating multiply doubly bonded substituents. Values are available for the 1-(1,3-butadienyl), 1-(4-phenyl-1,3-butadienyl) and 1-(1,3,5-hexatrienyl) groups. The substituent constants for the 1,3-butadienyl group were used successfully in the correlation of ionization potentials for 1-substituted 1,3-butadienes. Additional values were estimated for the 2-(1,3-butadienyl), 1-(6-phenyl-1,3,5-hexatrienyl), 1-(1,3,5,7-octatetraenyl) and 2-(1,3,5-hexatrienyl) groups from equations 24a, 26a and 27a. With the exception of the 2-(1,3-butadienyl) group which is of the AM type, all of the conjugated alternating groups appear to be of the LD type. This is in contrast to the behavior of aryl groups which are generally of the LA type.

TABLE 3. Values of P_{EA}, P_0 and P_{ED}

X	P_{EA}	P_0	P_{ED}	Group type
Alternating Dienes and Polyenes				
Conjugated				
CH=CH−CH=CH_2	37	11	52	LD
H_2C=C−CH=CH_2	45	11	44	AM
CH=CH−CH=CHPh	30	12	58	LD
(CH=CH)$_2$CH=CH_2	27	13	61	LD
H_2C=C−CH=CH−CH=CH_2	32	16	52	LD
(CH=CH)$_3$Ph	26	9	59	LD
(CH=CH)$_3$CH=CH_2	27	12	61	LD
Cross-conjugated				
CH=C(CH=CH_2)$_2$	32	11	57	LD
Adjacent				
CH=C=CH_2	59	9	32	LA
Vinyl				
CH=CH_2	53	9	38	LA
CH=CHPh	39	10	50	LD
Ethynyl				
C≡CH	74	4	22	LA
C≡C−C≡CH	80	3	17	PA
C≡CPh	62	3	35	LA
Aryl				
Ph	53	9	39	LA
C_6H_4Ph-4	50	9	41	LA
1-Naph	48	9	49	AM
2-Naph	50	9	40	LA
Other groups				
Me	3	32	65	LD
Et	10	32	57	LD
i-Pr	10	32	57	LD
t-Bu	7	29	64	LD
c-Pr	23	22	55	LD
CF_3	100	0	0	EA
CHO	89	3	8	PA
Ac	89	3	8	PA
$CONH_2$	90	3	8	PA
CO_2Me	90	2	9	PA
CO_2Et	92	3	5	PA
CN	96	0	4	PA
NH_2	25	9	66	LD
NHAc	51	5	44	LA
NMe_2	37	7	56	LD
NO_2	95	1	4	PA
N_3	65	3	32	LA
PMe_2	39	7	54	LD
$POMe_2$	95	2	3	PA
$PO(OMe)_2$	100	0	0	EA
OH	33	9	58	LD
OMe	34	7	59	LD
OEt	32	9	59	LD
OAc	58	9	33	LA
OPh	47	7	46	AM

(*continued overleaf*)

TABLE 3. (*continued*)

X	P_{EA}	P_0	P_{ED}	Group type
SH	48	7	45	AM
SMe	52	6	42	LA
SAc	79	3	18	PA
SEt	48	8	44	AM
SPh	56	4	39	LA
SOMe	92	1	7	PA
SOPh	87	3	10	PA
SO_2Me	97	0	3	PA
SO_2Ph	89	1	10	PA
SeMe	50	7	44	LA
F	53	3	44	LA
Cl	61	7	32	LA
Br	62	6	32	LA
I	70	3	27	LA
H	0	100	0	AM

b. Cross-conjugated alternating multiply doubly bonded substituents. No data are available for these substituents. Values were estimated for the 1-(2-vinyl-1,3-butadienyl) group from equations 24a, 26a and 27a assuming additivity. It seems to be of the LD type. This resembles the behavior of the ethynyl groups.

c. Adjacent multiply doubly bonded substituents. The only group of this type for which substituent constants are available is the allenyl group. The parameters for this group have been used successfully in the correlation of vertical ionization potentials of substituted allenes (see Section VI.C.3 below). This group is of the LA type.

C. Estimation of Electrical Effect Parameters for Dienyl and Polyenyl Substituents

It is often necessary to estimate values of electrical effect parameters for groups for which no measured values are available[27]. The equations available for the estimation of σ_1 values for *trans*-vinylene (CH=CHZ) and vinylidene ($CZ{=}CH_2$) groups are:

$$\sigma_{1X} = 0.291\sigma_{lZ} + 0.174\sigma_{dZ} - 0.279\sigma_{eZ} + 0.0903 \tag{23}$$

and

$$\sigma_{1_{M^1Z^1M^2Z^2}} = 0.292\sigma_{lZ^2} + 0.175\sigma_{dZ^2} + 0.0814\chi_{M^1} + 0.205\chi_{M^2} + 0.394\sigma_{lZ^1} + 0.206\sigma_{dZ^1} + 0.201n_x - 0.803 \tag{24}$$

The equations for the estimation of σ_d for *trans*-vinylene and vinylidene groups are:

$$\sigma_{dX} = 0.239\sigma_{lZ} + 0.500\sigma_{dZ} + 2.19\sigma_{eZ} - 0.0640 \tag{25}$$

and

$$\sigma_{d,M^1Z^1M^2Z^2} = 0.473\sigma_{lZ^2} + 0.272\sigma_{dZ^2} + 2.19\sigma_{eZ^2} + 0.229\chi_{M^1} + 0.432\chi_{M^2} + 0.148\sigma_{dZ^1} + 0.877\sigma_{eZ^1} - 1.77 \tag{26}$$

The only equation available for the estimation of σ_e constants is:

$$\sigma_{eM^1Z^1M^2Z^2} = 0.169\sigma_{lZ^2} - 0.0540\sigma_{dZ^2} + 0.422\sigma_{eZ^2} + 0.0694\chi_{M^1} + 0.0878\sigma_{lZ^1} - 0.269 \quad (27)$$

Equations 24, 26 and 27 apply to $M^1Z^1{=}M^2Z^2$ and $M^1{\equiv}M^2Z^2$ groups. They may be used to calculate substituent constants for both *trans*-vinylene and vinylidene groups. For these groups the value of χ_{M^1} and χ_{M^2}, the Allred–Rochow[28] electronegativity of carbon is 2.50; and the value of n_π, the number of bonds in the $M^1{-}M^2$ bond, is 1. Thus, equations 24, 26 and 27 simplify to:

$$\sigma_{l_{M^1Z^1M^2Z^2}} = 0.292\sigma_{lZ^2} + 0.175\sigma_{dZ^2} + 0.394\sigma_{lZ^1} + 0.206\sigma_{dZ^1} + 0.114 \quad (24a)$$

$$\sigma_{d_{M^1Z^1M^2Z^2}} = 0.473\sigma_{lZ^2} + 0.272\sigma_{dZ^2} + 2.19\sigma_{eZ^2} + 0.148\sigma_{dZ^1} + 0.877\sigma_{eZ^1} - 0.118 \quad (26a)$$

$$\sigma_{e_{M^1Z^1M^2Z^2}} = 0.169\sigma_{lZ^2} + 0.0540\sigma_{dZ^2} + 0.422\sigma_{eZ^2} + 0.0878\sigma_{lZ^1} - 0.0955 \quad (27a)$$

Values of σ_l, σ_d and σ_e for alternating dienyl substituents of the type $(CH{=}CH)_nX$ can be calculated by the following procedure:

1. Values of σ_l, σ_d and σ_e for the appropriate substituted vinylene or vinylidene group are calculated.
2. Taking the *trans*-vinylene or vinylidene group as Z, the values of σ_l, σ_d and σ_e for the appropriate dienyl group can be calculated from the estimation equations 24a, 26a and 27a given above.

Estimated values of σ_D parameters may be calculated from the equations[25]:

$$\sigma_{RX} = 0.934\sigma_{dX} + 0.308\sigma_{eX} - 0.0129 \quad (28)$$

$$\sigma_{RX}{}^{+} = 1.05\sigma_{dX} + 2.14\sigma_{eX} - 0.0731 \quad (29)$$

$$\sigma_{RX}{}^{-} = 1.13\sigma_{dX} - 1.58\sigma_{eX} + 0.00272 \quad (30)$$

$$\sigma_{RX}{}^{\bullet} = 1.15\sigma_{dX} + 3.81\sigma_{eX} - 0.0262 \quad (31)$$

$$\sigma_{RX}{}^{\bullet} = 1.01\sigma_{dX} - 3.01\sigma_{eX} - 0.00491 \quad (32)$$

$$\sigma_{RX}{}^{\circ} = 0.770\sigma_{dX} - 0.288\sigma_{eX} - 0.0394 \quad (33)$$

Values of these parameters are reported in Table 4. Estimated values of Hammett σ constants can be calculated from the relationships[25]:

$$\sigma_{mX} = 1.02\sigma_{lX} + 0.385\sigma_{dX} + 0.661\sigma_{eX} + 0.0152 \quad (34)$$

$$\sigma_{pX} = 1.02\sigma_{lX} + 0.989\sigma_{dX} + 0.837\sigma_{eX} + 0.0132 \quad (35)$$

$$\sigma_{pX}{}^{\circ} = 1.06\sigma_{lX} + 0.796\sigma_{dX} + 0.278\sigma_{eX} - 0.00289 \quad (36)$$

$$\sigma_{pX}{}^{+} = 1.10\sigma_{lX} + 0.610\sigma_{dX} + 2.76\sigma_{eX} + 0.0394 \quad (37)$$

$$\sigma_{pX}{}^{-} = 1.35\sigma_{lX} + 1.36\sigma_{dX} - 1.28\sigma_{eX} + 0.0176 \quad (38)$$

Table 5 reports values of the Hammett substituent constants.

TABLE 4. Values of σ_D^a

X	$\sigma_R^{\ominus}$	σ_R^{-}	σ_R^{0}	σ_R	σ_R^{+}	$\sigma_R^{\oplus}$
Alternating Dienes and Polyenes						
Conjugated						
CH=CH−CH=CH_2	*−0.02*	*−0.23*	*−0.29*	*−0.38*	*−0.57*	*−0.91*
H_2C=C−CH=CH_2	*0.01*	*−0.13*	*−0.20*	*−0.26*	*−0.51*	*−0.63*
CH=CH−CH=CHPh	*−0.13*	*−0.35*	*−0.37*	*−0.49*	*−0.53*	*−1.04*
$(CH=CH)_2$CH=CH_2	*−0.16*	*−0.38*	*−0.40*	*−0.51*	*−0.72*	*−1.07*
H_2C=C−CH=CH−CH=CH_2	*−0.03*	*−0.18*	*−0.23*	*−0.30*	*−0.55*	*−0.67*
$(CH=CH)_3$Ph	*−0.01*	*−0.27*	*−0.34*	*−0.48*	*−0.87*	*−1.12*
$(CH=CH)_3$CH=CH_2	*−0.02*	*−0.28*	*−0.35*	*−0.49*	*−0.88*	*−1.15*
Cross-conjugated						
CH=C$(CH=CH_2)_2$	*−0.08*	*−0.39*	*−0.44*	*−0.61*	*−1.05*	*−1.34*
Adjacent						
CH=C=CH_2	*0.31*	*0.15*	*−0.02*	*−0.05*	*−0.18*	*−0.47*
Vinyl						
CH=CH_2	0.45	−0.08	−0.15	−0.15	−0.15	−0.56
CH=CHPh	*0.02*	−0.23	−0.30	−0.30	−0.30	−1.01
Ethynyl						
C≡CH	0.28	0.13	−0.04	−0.04	−0.12	−0.45
C≡C−C≡CH	*0.34*	0.19	*0.02*	*0.01*	−0.17	*−0.36*
C≡CPh	*0.16*	−0.14	−0.21	−0.21	−0.21	−1.03
Aryl						
Ph	0.28	−0.04	−0.11	−0.11	−0.17	−0.69
C_6H_4Ph-4	*0.18*	*0.00*	*−0.14*	*−0.20*	*−0.36*	*−0.68*
1-Naph	*0.12*	*−0.07*	*−0.18*	*−0.26*	*−0.57*	*−0.75*
2-Naph	*0.19*	*0.01*	*−0.13*	*−0.20*	*−0.50*	*−0.67*
Other groups						
Me	−0.03	−0.09	−0.16	−0.16	−0.16	−0.25
Et	−0.01	−0.07	−0.14	−0.14	−0.14	−0.28
i-Pr	*−0.04*	−0.09	−0.16	−0.16	−0.16	−0.34
t-Bu	*−0.05*	−0.11	−0.18	−0.18	−0.18	−0.33
c-Pr	0.01	*−0.08*	*−0.15*	−0.19	−0.27	−0.43
CF_3	*0.20*	0.18	0.11	0.11	0.15	0.00
CHO	*0.57*	0.53	0.15	0.15	0.15	−0.04
Ac	0.56	0.41	0.20	0.20	0.06	−0.05
$CONH_2$	*0.28*	0.23	0.08	0.08	0.08	−0.10
CO_2Me	*0.37*	0.30	0.11	0.11	0.11	−0.12
CO_2Et	*0.37*	0.31	0.11	0.11	0.11	*−0.06*
CN	0.26	0.26	0.08	0.08	0.08	−0.10
NH_2	*−0.30*	−0.55	−0.42	−0.80	−1.10	−1.05
NHAc	*−0.09*	−0.28	−0.25	−0.35	−0.47	−0.75
NMe_2	*0.05*	−0.30	−0.44	−0.88	−1.22	−1.38
NO_2	0.41	0.37	0.10	0.10	0.10	−0.08
N_3	*0.08*	*−0.11*	*−0.21*	−0.31	*−0.47*	−0.67
PMe_2	*0.30*	*−0.14*	*−0.35*	*−0.55*	*−1.03*	*−1.63*
$POMe_2$	*0.24*	*0.22*	*0.08*	*0.12*	*0.14*	*0.00*
$PO(OMe)_2$	*0.34*	*0.33*	*0.15*	*0.21*	*0.25*	*0.12*
OH	*−0.45*	−0.45	−0.46	−0.62	−0.64	−0.71
OMe	−0.36	−0.51	−0.44	−0.58	−0.66	−0.83
OEt	*−0.35*	−0.51	−0.44	−0.57	−0.65	−0.86
OAc	*−0.23*	−0.16	*−0.22*	−0.23	−0.26	*−0.32*
OPh	*−0.27*	*−0.44*	−0.42	−0.48	*−0.64*	−0.96
SH	*−0.11*	*−0.29*	*−0.32*	*−0.41*	*−0.56*	−0.81

TABLE 4. (*continued*)

X	$\sigma_R^{\ominus}$	σ_R^{-}	σ_R^{0}	σ_R	σ_R^{+}	$\sigma_R^{\oplus}$
SMe	0.01	−0.24	−0.31	−0.38	−0.55	−0.97
SAc	*0.09*	*0.00*	−0.08	*−0.09*	*−0.13*	*−0.34*
SEt	*−0.04*	−0.10	−0.30	−0.30	*−0.59*	−0.99
SPh	*0.16*	−0.11	−0.24	−0.34	*−0.65*	−1.00
SOMe	0.13	0.05	0.00	0.00	−0.10	−0.70
SOPh	*0.03*	*0.06*	−0.07	−0.07	*−0.21*	−0.81
SO_2Me	0.18	0.35	0.11	0.11	0.11	−0.12
SO_2Ph	*0.32*	*0.22*	0.12	0.12	*−0.16*	−0.42
SeMe	*0.01*	*−0.23*	*−0.31*	*−0.42*	*−0.65*	*−1.02*
F	*−0.61*	−0.58	−0.44	−0.48	−0.37	*−0.25*
Cl	*−0.25*	−0.30	−0.25	−0.25	−0.21	−0.41
Br	−0.21	−0.28	−0.25	−0.25	−0.19	−0.44
I	*−0.06*	−0.18	−0.16	−0.16	−0.16	−0.57
H	0	0	0	0	0	0

[a]Values are from References 24, 25 and 27 unless otherwise noted. Those in italics are estimates.

TABLE 5. Values of Hammett substituent constants[a]

X	σ_m	σ_p^{-}	σ_p^{0}	σ_p	σ_p^{+}
Alternating Dienes and Polyenes					
Conjugated					
$CH{=}CH{-}CH{=}CH_2$	−0.08	−0.17	−0.20	−0.33	−0.76
$H_2C{=}C{-}CH{=}CH_2$	*0.01*	*−0.01*	*−0.07*	*−0.15*	*−0.19*
$CH{=}CH{-}CH{=}CHPh$	−0.12	−0.31	−0.28	−0.43	−0.42
$(CH{=}CH)_2CH{=}CH_2$	−0.14	−0.36	−0.32	−0.47	−0.98
$H_2C{=}C{-}CH{=}CH{-}CH{=}CH_2$	*−0.06*	*−0.13*	*−0.15*	*−0.24*	*−0.27*
$(CH{=}CH)_3Ph$	*−0.19*	*−0.31*	*−0.33*	*−0.49*	*−0.57*
$(CH{=}CH)_3CH{=}CH_2$	*−0.20*	*−0.34*	*−0.35*	*−0.51*	*−0.59*
Cross-conjugated					
$CH{=}C(CH{=}CH_2)_2$	*−0.17*	*−0.35*	*−0.35*	*−0.55*	*−0.62*
Adjacent					
$CH{=}C{=}CH_2$	0.06	0.29	0.08	0.02	−0.16
Vinyl					
$CH{=}CH_2$	0.02	0.21	0.02	−0.05	−0.30
$CH{=}CHPh$	−0.06	0.13	−0.16	−0.28	−0.68
Ethynyl					
$C{\equiv}CH$	0.24	0.50	0.26	0.21	0.05
$C{\equiv}C{-}C{\equiv}CH$	0.36	0.72	0.41	0.37	0.26
$C{\equiv}CPh$	0.16	0.39	0.11	−0.01	−0.39
Aryl					
Ph	0.01	0.08	0.00	−0.08	−0.51
C_6H_4Ph-4	0.00	0.11	−0.03	−0.12	−0.42
1-Naph	*−0.02*	*0.05*	*−0.07*	*−0.17*	*−0.28*
2-Naph	*0.01*	*0.13*	*−0.03*	*−0.11*	*−0.25*
Other groups					
Me	−0.06	−0.15	−0.15	−0.17	−0.31
Et	−0.06	−0.09	−0.12	−0.15	−0.28
i-Pr	*−0.04*	*−0.12*	*−0.12*	−0.15	−0.28
t-Bu	0.00	*−0.15*	*−0.14*	−0.19	−0.26
c-Pr	−0.08	−0.09	−0.15	−0.22	−0.46

(*continued overleaf*)

TABLE 5. (*continued*)

X	σ_m	σ_p^-	σ_p^0	σ_p	σ_p^+
CF_3	0.46	0.74	0.52	0.53	0.61
CHO	0.36	0.91	0.50	0.45	0.53
Ac	0.38	0.82	0.46	0.50	0.51
$CONH_2$	0.31	0.62	0.37	0.37	0.39
CO_2Me	0.36	0.74	0.46	0.44	0.49
CO_2Et	0.35	0.74	0.46	0.44	0.49
CN	0.61	1.02	0.69	0.65	0.66
NH_2	−0.21	−0.51	*−0.40*	−0.63	−1.30
NHAc	0.11	0.03	0.00	−0.12	−0.46
NMe_2	−0.22	−0.35	−0.44	−0.67	−1.50
NO_2	0.74	1.29	0.82	0.77	0.79
N_3	0.27	0.38	0.20	0.08	−0.25
PMe_2	−0.25	−0.18	−0.37	−0.61	−1.40
$POMe_2$	0.35	0.65	0.42	0.43	0.50
$PO(OMe)_2$	0.46	0.87	0.56	0.59	0.73
OH	0.13	*−0.24*	−0.10	−0.38	−0.61
OMe	0.11	−0.25	−0.12	−0.28	−0.78
OEt	*0.07*	*−0.27*	−0.16	*−0.29*	*−0.73*
OAc	0.31	0.20	0.21	0.16	0.06
OPh	*0.23*	*−0.04*	*−0.01*	*−0.08*	*−0.57*
SH	*0.07*	*−0.04*	*−0.06*	*−0.19*	*−0.58*
SMe	0.09	0.04	−0.02	−0.17	−0.60
SAc	0.34	0.50	0.33	0.28	0.18
SEt	*0.16*	*−0.01*	*−0.07*	*−0.04*	*−0.63*
SPh	*0.23*	0.18	*0.01*	*−0.15*	*−0.64*
SOMe	0.47	0.74	0.47	0.54	0.21
SOPh	*0.50*	*0.75*	*0.51*	*0.44*	*0.44*
SO_2Me	0.63	1.13	0.71	0.70	0.75
SO_2Ph	*0.62*	0.95	*0.68*	*0.68*	*0.48*
SeMe	0.05	0.03	−0.06	−0.21	−0.68
F	0.34	0.03	0.17	0.06	−0.07
Cl	0.37	0.28	0.27	0.22	0.11
Br	0.34	0.30	0.26	0.22	0.15
I	0.35	0.35	0.27	0.24	0.13
H	0	0	0	0	0

[a]Values are from the references cited in Table 4. Those in italics are estimates.

IV. STERIC EFFECTS

A. Introduction

The concept of steric effects was introduced by Kehrmann[30] over a century ago. Meyer[31] and Sudborough and Lloyd[32] shortly thereafter presented kinetic results supporting the steric effect explanation of rate retardation in the esterification of 2-substituted and 2,6-disubstituted benzoic and 3-*cis*-substituted acrylic acids. Major early reviews of steric effects are given by Stewart[33], Wittig[34] and somewhat later by Wheland[35] and in a volume edited by Newman[36].

B. The Nature of Steric Effects

1. Primary steric effects

Primary steric effects are due to repulsions between electrons in valence orbitals on adjacent atoms which are not bonded to each other. They are believed to result from the

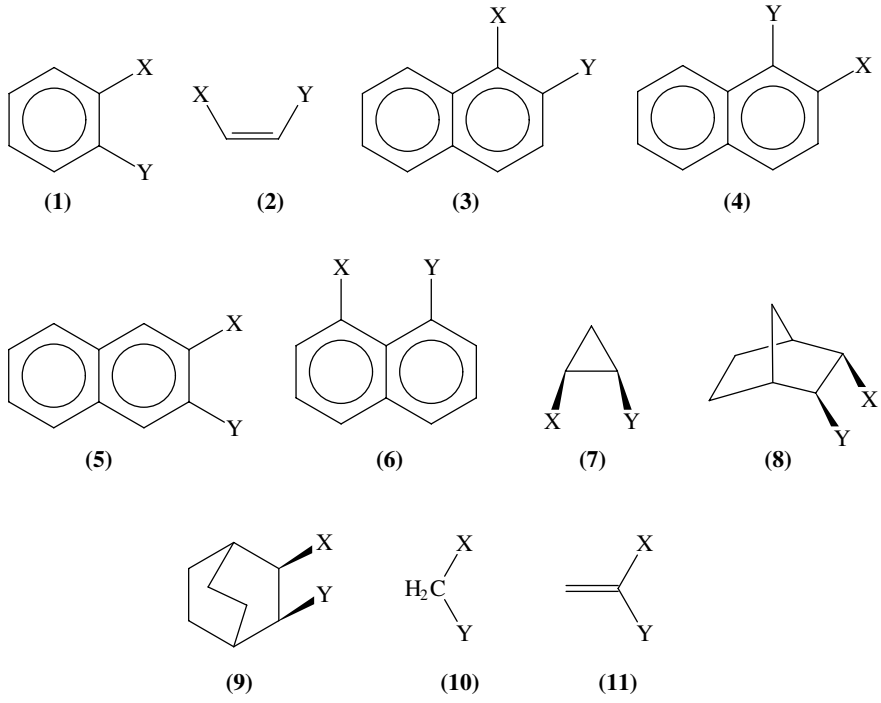
interpenetration of occupied orbitals on one atom by electrons on the other resulting in a violation of the Pauli exclusion principle. *All steric interactions raise the energy of the system in which they occur*. Their effect on chemical reactivity is to either decrease or increase a rate or equilibrium constant depending on whether steric repulsions are greater in the reactant or in the product (equilibria) or transition state (rate).

2. Secondary steric effects

Secondary steric effects on chemical reactivity can result from the shielding of an active site from the attack of a reagent, from solvation, or both. They may also be due to a steric effect on the reacting conformation of a chemical species that determines its concentration.

3. Direct steric effects

These effects can occur when the active site at which a measurable phenomenon occurs is in close proximity to the substituent. Among the many systems exhibiting direct steric effects are *ortho*-substituted benzenes, **1**, *cis*-substituted ethylenes, **2**, and the *ortho*- (1,2-, 2,1- and 2,3-) and peri- (1,8-) substituted naphthalenes, **3**, **4**, **5** and **6**, respectively. Other examples are *cis*-1,2-disubstituted cyclopropanes, *cis*-2,3-disubstituted norbornanes and *cis*-2,3-disubstituted [2.2.2]-bicyclooctanes, **7**, **8** and **9**, respectively. Some systems generally do not show steric effects. Vicinally substituted systems such as disubstituted methanes, **10**, and 1,1-disubstituted ethenes, **11**, are examples, 2,3-Disubstituted heteroarenes with five-membered rings such as thiophenes and selenophenes



(1) **(2)** **(3)** **(4)**

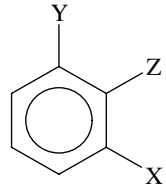
(5) **(6)** **(7)** **(8)**

(9) **(10)** **(11)**

are also generally free of steric effects. This is probably due to the larger XCC angle in these systems as compared with benzenoid systems.

4. Indirect steric effects

These effects are observed when the steric effect of the variable substituent is relayed by a constant substituent between it and the active site as in **12** where Y is the active site, Z is the constant substituent and X is the variable substituent. This is a buttressing effect.



(12)

5. The directed nature of steric effects

There is a regrettable tendency to regard steric effects as being related to 'bulk'. Unfortunately, the word bulk is invariably used without a precise definition of its meaning. The latest form of this verbal handwaving is the use of the phrase steric bulk. Presumably, this is intended to imply size in some vague ill-defined way. Steric effects are vector quantities. This is easily shown by considering, for example, the ratio r of the steric parameter for any five-carbon alkyl group to that for 1-pentyl (Pe). Values of r are: 1-Pe, 1; 2-Pe, 1.54; 3-Pe, 2.22; CH_2Bu-s; 1.47; CH_2Bu-i, 1.00; CH_2Bu-t, 1.97; CMe_2Pr, 2.40; CH-iPrMe, 1.90. All of these groups have the same volume and therefore the same bulk, but they differ in steric effect. In order to account for this it is necessary to consider what happens when a nonsymmetric substituent is in contact with an active site. Taking as an example the simple case of a spherical active site Y in contact with a nonsymmetric substituent, $CZ^LZ^MZ^S$, where the superscripts, L, M and S represent the largest, the medium-sized and the smallest Z groups, respectively, there are three possible conformations of this system. They are shown in top views in Figure 1. As all steric repulsions raise the energy of the system, the preferred conformation will be the one that results in the lowest energy increase. This is the conformation which presents the smallest face to the active site, conformation **A**. This is the basis of the minimum steric interaction (MSI) principle which states: *a nonsymmetric substituent prefers that conformation which minimizes steric interactions*. The directed nature of steric effects results in a conclusion of vital importance: that in general *the volume of a substituent is not an acceptable measure of its steric effect*[37–39]. Although there are still some workers who are unable to comprehend this point, it is nevertheless true that group volumes are not useful as steric parameters. They are actually measures of group polarizability. In short, for a range of different substituent shapes in a data set *steric effects are not directly related to bulk, polarizability is*.

C. The Monoparametric Model of Steric Effects

Stewart[33], who proposed a parallel between the rate of esterification of 2-substituted benzoic acids and the molecular weights of the substituents (the nitro group strongly deviating from this relationship) was the first to attempt to relate the steric effect of a

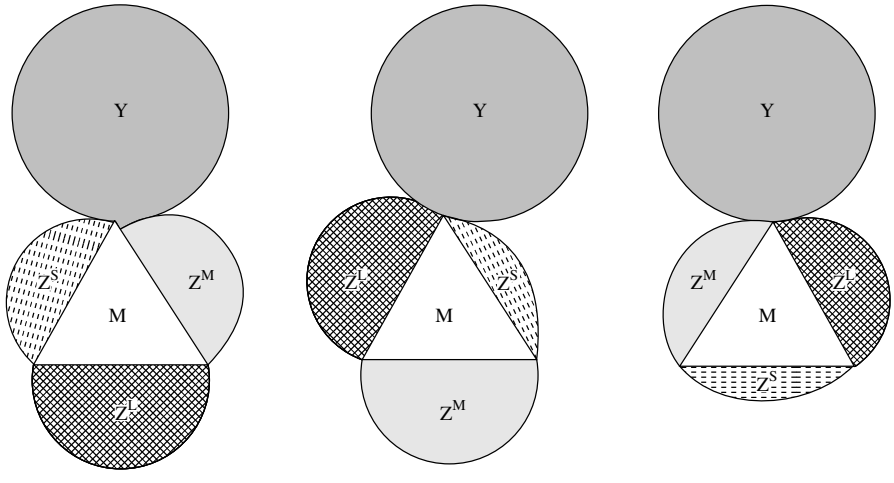


FIGURE 1. Possible conformations of a spherical active site Y adjacent to a tetrahedral substituent $MZ^LZ^MZ^S$ where L, M and S designate the largest, medium-sized and smallest groups, respectively. Conformation **A** has the lowest energy, conformation **C** the highest

group to some property that might at least in part be a measure of size. Kindler[40] made the first attempt at defining a set of steric parameters. These parameters were later shown to be a function of electrical effects. The first successful parameterization of the steric effect is due to Taft[41], who defined the steric parameter E_s for aliphatic systems by the expression:

$$E_{s,X} \equiv \delta \log \frac{k_X}{k_{Me}} \tag{39}$$

where k_X and k_{Me} are the rate constants for the acid-catalyzed hydrolysis of the corresponding alkyl esters XCO_2Alk and $MeCO_2Alk$, respectively. The value of δ is taken as 1.000 for this purpose; $E_{So,X}$ parameters intended to represent the steric effects of substituents in the *ortho* position of a benzene derivative were defined for a few groups from the rates of acid-catalyzed hydrolysis of 2-substituted alkyl benzoates. These parameters are a mix of electrical and steric effects with the former predominating, and are therefore of no use as steric parameters.

The original Taft $E_{S,X}$ values suffered from several deficiencies:

1. Their validity as measures of steric effects was unproven.
2. They were determined from average values of rate constants obtained under varying experimental conditions, often in different laboratories.
3. They were available only for those groups in which the atom bonded to G or Y (the first atom of the substituent) is an sp^3 hybridized carbon atom, and for hydrogen. Values were therefore unavailable for many if not most of the substituents generally encountered.
4. The use of the methyl group as the reference substituent meant that they were not compatible with electrical effect substituent constants for which the reference substituent is hydrogen.

The first problem was resolved when it was shown that the E_S values for symmetric groups are a linear function of van der Waals radii[42]. The latter have long been held to be an effective measure of atomic size. The second and third problems were solved by

Charton, who proposed the use of the van der Waals radius as a steric parameter[43] and developed a method for the calculation of group van der Waals radii for tetracoordinate symmetric top substituents MZ_3 such as the methyl and trifluoromethyl groups[44]. In later work the hydrogen atom was chosen as the reference substituent and the steric parameter υ was defined as:

$$\upsilon_X \equiv r_{VX} - r_{VH} = r_{VX} - 1.20 \tag{40}$$

where r_{VX} and r_{VH} are the van der Waals radii of the X and H groups in Angstrom units[45]. Expressing r_V in these units is preferable to the use of picometers because the coefficient of the steric parameter is then comparable in magnitude to the coefficients of the electrical effect parameters. Whenever possible, υ parameters are obtained directly from van der Waals radii or calculated from them. Recently, an equation has been derived which makes possible the calculation of υ values for nonsymmetric tetrahedral groups of the types $MZ_2^SZ^L$ and $MZ^SZ^MZ^L$ in which the Z groups are symmetric. These are considered to be primary values. For the greater number of substituents however, υ parameters must be calculated from the regression equations obtained for correlations of rate constants with primary values. The values obtained in this manner are considered to be secondary υ values. All other measures of atomic size are a linear function of van der Waals radii. There is therefore no reason for preferring one measure of atomic size over another. As values of υ were developed for a wide range of substituent types with central atoms including oxygen, nitrogen, sulfur and phosphorus as well as carbon, these parameters provide the widest structural range of substituents for which a measure of the steric effect is available.

1. Steric classification of substituents

Substituents may be divided into three categories based on the degree of conformational dependence of their steric effects:

1. No conformational dependence (NCD). Groups of this type include monatomic substituents such as hydrogen and the halogens: cylindrical substituents such as the ethynyl and cyano groups, and tetracoordinate symmetric top substituents such as the methyl, trifluoromethyl and silyl groups.

2. Minimal conformational dependence (MCD). Among these groups are:

a. Nonsymmetric substituents with the structure MH_n $(lp)_{3-n}$, such as the hydroxyl and amino groups (lp is a lone pair)

b. Nonsymmetric substituents with the structure $MZ_2^SZ^L$, where S stands for small and L for large.

3. Strong conformational dependence (SCD). These groups have the structures:

a. $MZ_2^LZ^S$ and $MZ^LZ^MZ^S$, where the superscript M indicates medium.

b. Planar π-bonded groups MZ^LZ^S, where M and either or both Z's are sp^2 hybridized, such as phenyl, acetyl, nitro ($X_{p\pi}$ groups). (Figure 2).

c. Quasi-planar π-bonded groups such as dimethylamino and cyclopropyl.

The steric parameter for NCD groups can be obtained directly from van der Waals radii or calculated from them. The values for MCD groups are often obtainable from van der Waals radii, although in some cases they must be derived as secondary values from regression equations obtained by correlating rate constants with known values of the steric parameter. Steric parameters for SCD groups of the nonsymmetric type are usually obtainable only from regression equations. In the case of planar π-bonded groups the maximum and minimum values of the steric parameter are available from the van der Waals radii. These groups are sufficiently common and important to require a more detailed discussion.

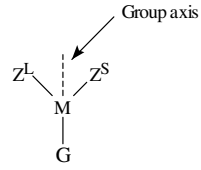


FIGURE 2. Planar π-bonded ($X_{p\pi}$) group. Superscripts L and S designate the larger and smaller, respectively of the Z groups attached to the central M atom. The bond order of the MZ^L and/or the MZ^S bonds is not less than 1.5. The MG bond is collinear with the group axis

2. Planar π-bonded groups

These $X_{p\pi}$ groups represent an especially difficult problem because their delocalized electrical effect depends on the steric effect when they are bonded to planar π-bonded skeletal groups, $G_{p\pi}$. An approach to the problem has been developed[45,46]. The σ_d and σ_e electrical effect parameters are a function of the dihedral angle formed by $X_{p\pi}$ and $G_{p\pi}$. The relationship generally used has the form:

$$P = P_0 \cos^2 \theta \tag{41}$$

where P is the property of interest, P_0 is its value when the dihedral angle is zero and θ is the dihedral angle. Thus:

$$\sigma_{dX,\theta} = \sigma_{dX,0} \cos^2 \theta \tag{42}$$

and:

$$\sigma_{eX,\theta} = \sigma_{eX,0} \cos^2 \theta \tag{43}$$

where $\sigma_{dX,0}$ and $\sigma_{eX,0}$ are the values of σ_d and σ_e when the substituent and skeletal group are coplanar ($\theta = 0$). The steric parameter does not depend on equation 41. The effective value of υ, which is derived from the geometry of the system, is given by the expression:

$$\upsilon = d' \cos\theta + r_{VZ^S} - 1.20 \tag{44}$$

where Z^S is the smaller of the two Z groups attached to the central atom, M of the $X_{p\pi}$ group and d' is the distance between the center of Z^S and the perpendicular to the line joining that center with the group axis. There is no simple *a priori* way to determine θ. It could conceivably be estimated by molecular mechanics calculations, but there is some reason to believe that θ is a function of the medium. Alternatively, the $X_{p\pi}$ group can be included in the data set by means of an iteration procedure. The method requires an initial correlation of the data set with all $X_{p\pi}$ and other SCD groups excluded. This constitutes the basis set. The correlation equation used for this purpose is the LDRS equation which takes the form:

$$Q_X = L\sigma_{IX} + D\sigma_{dX} + R\sigma_{eX} + S\upsilon + h \tag{45}$$

The correlation is then repeated for each $X_{p\pi}$ group using υ values increasing incrementally by some convenient amount from the minimum, which represents the half-thickness of the group, to the maximum, which occurs when $X_{p\pi}$ is nearly perpendicular to $G_{p\pi}$. The proper value of θ is that which:

1. Results in the best fit of the data to the correlation equation. The best fit is indicated by the minimal value of the S_{est} and S^0 statistics, and the maximal value of the F and $100R^2$ statistics. The statistics used in this work are described in the appendix.
2. Has the L, D, R, S and h values that are in best agreement with those of the basis set.

D. Multiparametric Models of Steric Effects

In some cases a simple monoparametric model of the steric effect is insufficient. Examples are, when the active site is itself large and nonsymmetric, or alternatively when the phenomenon studied is some form of bioactivity in which binding to a receptor is the key step. The failure of the monoparametric model is due to the fact that a single steric parameter cannot account for the variation of the steric effect at various points in the substituent. The use of a multiparametric model of steric effects that can represent the steric effect at different segments of the substituent is required. Five multiparametric models are available; that of Verloop and coworkers[48], the simple branching model, the expanded branching model, the segmental model and the composite model. The Verloop model suffers from the fact that its parameters measure maximum and minimum distances perpendicular to the group axis. These maxima and minima may occur at any point in the group skeleton (the longest chain in the group). The steric effect, however, may be very large at one segment of the chain and negligible at others. If a data set is large, as it must be if a multiparametric model is to be used, the likelihood that the maximum and minimum distances of all groups are located at the same segment and that it is this segment at which the steric effect is important is very small. The Verloop model will therefore not be discussed further.

1. The branching equations

The simple branching model[45,47] for the steric effect is given by the expression:

$$S\psi = \sum_{i=1}^{m} a_i n_i + a_\mathrm{b} n_\mathrm{b} \tag{46}$$

where $S\psi$ represents the steric effect parameterization, the a_i and a_b are coefficients, n_i is the number of branches attached to the i-th atom, and n_b is the number of bonds between the first and last atoms of the group skeleton. It follows that n_b is a measure of group length. Unfortunately, it is frequently highly collinear in group polarizability, which greatly limits its utility. For saturated cyclic substituents it is necessary to determine values of n_i from an appropriate regression equation. For planar π-bonded groups n_i is taken to be 1 for each atom in the group skeleton. For other groups n_i is obtained simply by counting branches. The model makes the assumption that all of the branches attached to a skeleton atom are equivalent. This is at best only a rough approximation. Distinguishing between branches results in an improved model called the expanded branching equation:

$$S\psi = \sum_{i=1}^{m} \sum_{j=1}^{3} a_{ij} n_{ij} + a_\mathrm{b} n_\mathrm{b} \tag{47}$$

which allows for the difference in steric effect that results from the order of branching[45,47]. This difference follows from the MSI principle. The first branch has the smallest steric effect because a conformation in which it is rotated out of the way of the active site is preferred. In this conformation the active site is in contact with two hydrogen atoms. The preferred conformation in the case of a second branch has the larger of the two branches directed out of the way. The smaller branch and a hydrogen atom are in contact with the active site. When there are three branches, the largest will be directed out of the way and the other two will be in contact with the active site.

The problem with the expanded branching method is that it requires a large number of parameters. Data sets large enough to permit its use are seldom seen.

2. The segmental model

As both branching methods have problems associated with them, the segmental method[47] is often the simplest and most effective of the multiparametric models. In this model each atom of the group skeleton together with the atoms attached to it constitutes a segment of the substituent. Applying the MSI principle, the segment is considered to have that conformation which presents its smallest face to the active site. The segment is assigned the υ value of the group which it most resembles. Values of the segmental steric parameters υ_i, where i designates the segment number, are given in Table 6. Numbering starts from the first atom of the group skeleton which is the atom that is attached to the rest of the system. The segmental model is given by the expression:

$$S\psi = \sum_{i=1}^{m} S_i \upsilon_i \tag{48}$$

TABLE 6. Values of segmental and simple steric parameters[a]

X	υ_1	υ_2	υ_3	υ
Alternating Dienes and Polyenes				
Conjugated				
CH=CH−CH=CH_2	*0.57*	*0.57*	*0.57*	*0.57*
H_2C=C−CH=CH_2	*0.57*	*0.57*	*0.57*	*0.57*
CH=CH−CH=CHPh	*0.57*	*0.57*	*0.57*	*0.57*
$(CH=CH)_2$CH=CH_2	*0.57*	*0.57*	*0.57*	*0.57*
H_2C=C−CH=CH−CH=CH_2	*0.57*	*0.57*	*0.57*	*0.57*
$(CH=CH)_3$Ph	*0.57*	*0.57*	*0.57*	*0.57*
$(CH=CH)_3$CH=CH_2	*0.57*	*0.57*	*0.57*	*0.57*
Cross-conjugated				
CH=C$(CH=CH_2)_2$	*0.57*	*0.57*	*0.57*	*0.57*
Adjacent				
CH=C=CH_2	*0.57*	0.58	*0.57*	*0.57*
Vinyl				
CH=CH_2	*0.57*	*0.57*	0	
CH=CHPh	*0.57*	*0.57*	*0.57*	
Ethynyl				
C≡CH	0.58	0.58	0	0.58
C≡C−C≡CH	0.58	0.58	0.58	0.58
C≡CPh	0.58	0.58	*0.57*	0.58
Aryl				
Ph	*0.57*	*0.57*	*0.57*	*0.57*
C_6H_4Ph-4	*0.57*	*0.57*	*0.57*	*0.57*
1-Naph	*0.57*	*0.57*	*0.57*	*0.57*
2-Naph	*0.57*	*0.57*	*0.57*	*0.57*
Other groups				
Me	0.52	0		0.52
Et	0.52	0.52	0	0.56
i-Pr	0.76	0.52	0	0.76
t-Bu	1.24	0.52	0	1.24
c-Pr				0.64
CF_3	0.90	0.27	0	0.90
CHO	*0.50*	0.32		*0.50*

(*continued overleaf*)

TABLE 6. (*continued*)

X	υ_1	υ_2	υ_2	υ_2
Ac	*0.50*	0.32	0	*0.50*
$CONH_2$	*0.50*	0.32	0	*0.50*
CO_2Me	*0.50*	0.32	0.52	*0.50*
CO_2Et	*0.50*	0.32	0.52	*0.50*
CN	0.40	0.40	0	0.40
NH_2	0.35	0		0.35
NHAc	0.35	*0.50*	0.32	0.50
NMe_2	0.35	0.52	0	0.52
NO_2	0.35	0.32		0.35
N_3	0.35	0.35	0.35	0.35
PMe_2	1.09	0.52	0	0.84
$POMe_2$	1.39	0.52	0	1.22
$PO(OMe)_2$	1.29	0.32	0.52	1.04
OH	0.32	0		0.32
OMe	0.32	0.52	0	0.36
OEt	0.32	0.52	0.52	0.48
OAc	0.32	*0.52*	0.32	0.50
OPh	0.52	*0.57*	*0.57*	0.57
SH	0.60	0		0.60
SMe	0.60	0.52	0	0.64
SAc	0.60	*0.50*	*0.32*	1.09
SEt	0.60	0.52	0.52	0.94
SPh	0.60	*0.57*	*0.57*	1.00
SOMe	0.74	0.52	0	0.76
SOPh	0.74	*0.57*	*0.57*	1.10
SO_2Me	1.03	0.52	0	1.13
SO_2Ph	1.03	*0.57*	*0.57*	
SeMe	0.70	0.52	0	0.74
F	0.27			0.27
Cl	0.55			0.55
Br	0.65			0.65
I	0.78			0.78
H	0			0

[a] Values are from References 24, 25, 27, 47 and 75. Those in italics are half thicknesses of planar π-bonded groups.

When only steric effects are present:

$$Q_X = S\psi_X \tag{49}$$

In the general case electrical effects are also present and the general form of the LDRS equation:

$$Q_X = L\sigma_{DX} + D\sigma_{dX} + R\sigma_{eX} + S\psi_X + h \tag{50}$$

is required.

3. The composite model

The composite model is a combination of the monoparametric υ model with the simple branching model. This method has proven useful in modelling amino acid, peptide and protein properties[49]. It is an improvement over the simple branching model and requires only one additional parameter.

V. INTERMOLECULAR FORCES

A. Introduction

Inter- and intramolecular forces (imf) are of vital importance in the quantitative description of structural effects on bioactivities and chemical properties. They can make a significant contribution to chemical reactivities and some physical properties as well. Types of intermolecular forces and their present parameterization are listed in Table 7[50].

B. Parameterization of Intermolecular Forces

1. Hydrogen bonding

Hydrogen bonding requires two parameters for its description, one to account for the hydrogen atom donating capacity of a substituent and another to account for its hydrogen atom accepting capacity. A simple approach is to use of n_H, the number of OH and/or NH bonds in the substituent, and n_n, the number of lone pairs on oxygen and/or nitrogen atoms, as parameters[49,52]. The use of these parameters is based on the argument that if one of the phases involved in the phenomenon studied includes a protonic solvent, particularly water, then all of the hydrogen bonds that the substituent is capable of forming will indeed form. For such a system, hydrogen bond parameters defined from equilibria in highly dilute solution in an 'inert' solvent are unlikely to represent a suitable model. This parameterization accounts only for the number of hydrogen-donor and hydrogen-acceptor sites in a group. It does not take into account differences in hydrogen bond energy. A more sophisticated parameterization than that described above would be to use the hydrogen bond energy for each type of hydrogen bond formed[50]. Thus for each substituent the parameter E_{hbX}, would be given by the equation:

$$E_{hbX} = \sum_{i=1}^{m} n_{hbi} E_{hbi} \tag{51}$$

where E_{hbX} is the hydrogen bonding parameter, E_{hbi} is the energy of the i-th type of hydrogen bond formed by the substituent X and n_{hbi} is the number of such hydrogen bonds. The validity of this parameterization is as yet untested. In any event, the site number parameterization suffers from the fact that though it accounts for the number of

TABLE 7. Intermolecular forces and the quantities upon which they depend[50]

Intermolecular force	Quantity
molecule–molecule	
Hydrogen bonding (hb)	E_{hb}, n_H, n_n
Dipole–dipole (dd)	dipole moment
Dipole–induced dipole (di)	dipole moment, polarizability
Induced dipole–induced dipole (ii)	polarizability
Charge transfer (ct)	ionization potential, electron affinity
ion–molecule	
ion–dipole (Id)	ionic charge, dipole moment
ion–induced dipole (Ii)	ionic charge, polarizability

Abbreviations are in parentheses. The dd interactions are also known as Keesom interactions; di interactions are also known as Debye interactions; ii interactions are also known as London or dispersion interactions. Collectively, dd, di and ii interactions are known as van der Waals interactions. Charge transfer interactions are also known as donor–acceptor interactions.

hydrogen bonds formed, it does not differentiate between their energies and can therefore be only an approximation. A recent definition of a scale of hydrogen-bond acceptor values from 1-octanol–water partition coefficients of substituted alkanes shows that the site number method strongly overestimates the hydrogen acceptor capability of the nitro group and seriously underestimates that of the methylsulfoxy group[51]. Much remains to be done in properly parameterizing hydrogen bonding.

2. van der Waals interactions

These interactions (dd, di, ii) are a function of dipole moment and polarizability. It has been shown that the dipole moment cannot be replaced entirely by the use of electrical effect substituent constants as parameters[52]. This is because the dipole moment has no sign. Either an overall electron donor group or an overall electron acceptor group may have the same value of μ. It has also been shown that the bond moment rather than the molecular dipole moment is the parameter of choice. The dipole moments of MeX and PhX were taken as measures of the bond moments of substituents bonded to sp^3- and sp^2-hybridized carbon atoms, respectively, of a skeletal group. Application to substituents bonded to sp-hybridized carbon atoms should require a set of dipole moments for substituted ethynes.

The polarizability parameter used in this work, α, is given by the expression:

$$\alpha \equiv \frac{MR_X - MR_H}{100} = \frac{MR_X}{100} - 0.0103 \tag{52}$$

where MR_X and MR_H are the group molar refractivities of X and H, respectively[49,52]. The factor 1/100 is introduced to scale the α parameter so that its coefficients in the regression equation are roughly comparable to those obtained for the other parameters used. There are many other polarizability parameters including parachor, group molar volumes of various kinds, van der Waals volumes and accessible surface areas, any of which will do as well because they are all highly collinear in each other[53]. Proposing other polarizability parameters has been a cottage industry in the past.

Values of α can be estimated by additivity from the values for fragments or from group molar refractivities calculated from the equation:

$$MR_X = 0.320n_c + 0.682n_b - 0.0825n_n + 0.991 \tag{53}$$

where n_c, n_b and n_n are the number of core, bonding and nonbonding electrons, respectively, in the group X[53].

3. Charge transfer interactions

These interactions can be roughly parameterized by the indicator variables n_A and n_D, where n_A takes the value 1 when the substituent is a charge transfer acceptor and 0 when it is not; n_D takes the value 1 when the substituent is a charge transfer donor and 0 when it is not. An alternative parameterization makes use of the first ionization potential of MeX (ip_{MeX}) as the electron donor parameter and the electron affinity of MeX as the electron acceptor parameter. Usually, the indicator variables n_A and n_D are sufficient. This parameterization accounts for charge transfer interactions directly involving the substituent. If the substituent is attached to a π-bonded skeletal group, then the skeletal group is capable of charge transfer interaction the extent of which is modified by the substituent. This is accounted for by the electrical effect parameters of the substituent.

4. The intermolecular force (IMF) equation

A general relationship for the quantitative description of intermolecular forces, called the intermolecular force (IMF) equation, is:

$$Q_X = L\sigma_{lX} + D\sigma_{dX} + R\sigma_{eX} + M\mu_X + A\alpha_X + H_1 n_{HX} + H_2 n_{nX} + Ii_X + B_{DX} n_{DX} + B_{AX} n_{AX} + S\psi_X + B^0 \quad (54)$$

Some values of the IMF parameters for diene and polyene substituents are presented in Table 8.

TABLE 8. Values of intermolecular force parameters[a]

X	μ_{Ph}	μ_{Me}	α	n_H	n_n	i
Alternating Dienes and Polyenes						
Conjugated						
CH=CH−CH=CH_2	*0*	0585	0.190	0	0	0
H_2C=C−CH=CH_2	*0*	0.26	0.190	0	0	0
CH=CH−CH=CHPh	*0*	*0.6*	0.423	0	0	0
$(CH=CH)_2CH=CH_2$	*0*	*0.6*	0.270	0	0	0
H_2C=C−CH=CH−CH=CH_2	*0*	*0.3*	0.270	0	0	0
$(CH=CH)_3$Ph	*0*	*0.6*	0.513	0	0	0
$(CH=CH)_3CH=CH_2$	*0*	*0.6*	0.360	0	0	0
Cross-conjugated						
CH=C$(CH=CH_2)_2$	*0*	*0.6*	0.270	0	0	0
Adjacent						
CH=C=CH_2			0.138	0	0	0
Vinyl						
CH=CH_2	0.13	0.364	0.100	0	0	0
CH=CHPh	0	0.72	0.331	0	0	0
Ethynyl						
C≡CH	0.71	0.7809	0.085	0	0	0
C≡C−C≡CH			0.170	0	0	0
C≡CPh	0		0.322	0	0	0
Aryl						
Ph	0	0.37	0.243	0	1	0
C_6H_4Ph-4	*0*	*0.37*	0.476	0	1	0
1-Naph	*0*	0.223	0.404	0	1	0
2-Naph	*0*	0.44	0.404	0	1	0
Other groups						
Me	0.37	0	0.046	0	0	0
Et	0.37	0	0.093	0	0	0
i-Pr	0.37	0	0.140	0	0	0
t-Bu	0.52	0	0.186	0	0	0
c-Pr	0.48	0.139	0.125	0	0	0
CF_3	2.86	2.321	0.040	0	0	0
CHO	2.92	2.69	0.059	0	2	0
Ac	2.88	2.93	0.102	0	2	0
$CONH_2$	3.42	3.72	0.088	2	3	0
CO_2Me	1.92	1.706	0.118	0	4	0
CO_2Et	1.849	1.84	0.164	0	4	0
CN	4.14	3.9185	0.053	0	0	0

(*continued overleaf*)

TABLE 8. (*continued*)

X	μ_{Ph}	μ_{Me}	α	n_H	n_n	i
NH_2	1.49	1.296	0.044	2	1	1
NHAc	3.75	3.71	0.212	1	3	0
NMe_2	1.60	0.612	0.145	0	1	1
NO_2	4.26	3.56	0.063	0	4	0
N_3	1.56	2.17	0.092	0	1	0
PMe_2	1.31	1.192	0.202	0	0	0
$POMe_2$	4.39	4.29	0.189	0	2	0
$PO(OMe)_2$			0.208	0	6	0
OH	1.40	1.77	0.018	1	2	0/1
OMe	1.36	1.31	0.068	0	2	0
OEt	1.38	1.22	0.114	0	2	0
OAc	1.69	1.706	0.114	0	4	0
OPh	1.13	1.17	0.267	0	2	0
SH	1.21	1.52	0.082	0	0	0/1
SMe	1.29	*1.06*	0.128	0	0	0
SAc			0.174	0	2	0
SEt			0.174	0	0	0
SPh	1.37	1.50	0.333	0	1	0
SOMe	3.98	3.96	0.127	0	2	0
SOPh	4.02		0.320	0	2	0
SO_2Me	4.73		0.125	0	4	0
SO_2Ph	5.00	4.73	0.322	0	4	0
SeMe	1.31		0.160	0	0	0
F	1.66	1.8549	−0.001	0	0	0
Cl	1.70	1.895	0.050	0	0	0
Br	1.70	1.84	0.079	0	0	0
I	1.71	1.618	0.129	0	0	0
H	0	0	0	0	0	0

[a] Values are from References 24, 25, 27, 51 and 53. Those in italics are estimates. μ_{ph} and μ_{Me} parameterize the bond moments of the X-C(sp^2) and X-C(sp^3) bonds, respectively i values reported as 0/1 take the value 1 when bonded to sp^2-hybridized carbon and 0 when bonded to sp^3-hybridized carbon. Dipole moments for alternating dienyl and polyenyl groups are assumed to be approximately equal to those for the 1- and 2-(1,3-butadienyl) groups.

VI. APPLICATIONS

A. Introduction

Examples of the application of correlation analysis to diene and polyene data sets are considered below. Both data sets in which the diene or polyene is directly substituted and those in which a phenylene lies between the substituent and diene or polyene group have been considered. In that best of all possible worlds known only to Voltaire's Dr. Pangloss, all data sets have a sufficient number of substituents and cover a wide enough range of substituent electronic demand, steric effect and intermolecular forces to provide a clear, reliable description of structural effects on the property of interest. In the real world this is not often the case. We will therefore try to demonstrate how the maximum amount of information can be extracted from small data sets.

The choice of correlation equations. In choosing a correlation equation there are several factors that must be considered. They include the number of data points in the set to be studied, the experimental conditions, the type of data to be correlated and the possibility of steric effects.

a. *The number of data points*. The number of data points, n, and the number of independent variables, N_v, determine the number of degrees of freedom, N_{DF}. Thus:

$$N_{DF} = n - N_V - 1 \tag{55}$$

In order to obtain reliable models (minimize the probability of chance correlations) it is necessary to consider the ratio $R_{DF/V}$:

$$R_{DF/V} = \frac{N_{DF}}{N_V} \tag{56}$$

The minimum value of $R_{DF/V}$ required for a reliable model depends on the quality of the determination of the data to be correlated. The smaller the experimental error in the data, the smaller the value of $R_{DF/V}$ required for dependable results. Experience indicates that in the case of chemical reactivity data $R_{DF/V}$ should be not less than 3. For bioactivity studies $R_{DF/V}$ depends heavily on the type of data; for rate and equilibrium constants obtained from enzyme kinetics a value of not less than 3 is reasonable while for toxicity studies on mammals at least 7 is required.

b. *Steric effects*. If substituent and active site are proximal, then steric effects may occur. In that event it is necessary to include a steric effect parameterization in the correlation equation. The choice of parameterization depends on the number of data points in the set. If N_{DF} is sufficiently large, then the segmental method is a good choice of parameterization. If this is not the case, then it is best to use a monoparametric method.

c. *Intermolecular forces*. If intermolecular forces are likely to be significant, as is the case with bioactivity data and many types of chemical properties, then it is necessary to use the intermolecular force equation or some relationship derived from it. If N_{DF} is too small, it may be necessary to use composite parameters such as log P in order to get a reliable model.

d. *Small chemical reactivity data sets*. Chemical reactivity data sets which involve only electrical effects are best modelled by the LDR equation. Although data sets are often encountered which are too small to give reliable results with the LDR equation, it is still possible to extract from them useful information regarding structural effects. There are two ways to handle this problem. The best approach is to combine two or more small data sets into a single large data set. This can be done if all of the data sets to be combined have been studied under experimental conditions such that all but one are kept constant and the variation in that one can be parameterized. Consider, for example, the case in which the data are rate constants that have been determined at various temperatures. Addition to the correlation equation of the term $T\tau$, where

$$\tau \equiv \frac{100}{t} \tag{57}$$

and t is the absolute temperature, makes possible the combination of rate constants at different temperatures into a single data set. Thus, the LDR equation becomes the LDRT equation:

$$Q_X = L\sigma_{lX} + D\sigma_{dX} + R\sigma_{eX} + T\tau_X + h \tag{58}$$

If the data sets were studied in aqueous organic solvents, they can be combined into a single large set by the addition of the term $F\phi$ where ϕ is the mole fraction of organic solvent in the medium. Thus, the LDR equation becomes the LDRF equation:

$$Q_X = L\sigma_{lX} + D\sigma_{dX} + R\sigma_{eX} + F\phi_X + h \tag{59}$$

In general, if a number of data sets are available that have the same skeletal group and active site but vary in one of the experimental conditions, they can be combined into a

single larger data set by parameterizing the variable condition. Taking the LDR equation as the example once more gives the relationship:

$$Q_X = L\sigma_{lX} + D\sigma_{dX} + R\sigma_{eX} + \Sigma P_i\zeta_{iX} + h \tag{60}$$

where $\Sigma P_i\zeta_{iX}$ is the parameterization of the variable condition. This approach can be extended to data sets involving chemical and physical properties and bioactivities.

e. *The use of composite variables*. When faced with small data sets, the alternative to combining them is to decrease the number of independent variables. This can be done by replacing two or more pure parameters with composite parameters of an appropriate composition. Consider, for example, a chemical reactivity data set of five members ($n = 5$). The problem is to determine the magnitude of the electrical effect (L, C or ρ), the composition of the electrical effect (P_D) and the electronic demand of the reactivity (η) without assuming prior knowledge. This can be done by the following procedure:

1.(a) If the substituent is attached to an sp^2- or sp-hybridized carbon atom of the skeletal group that is directly conjugated with the reaction site, then the data set is correlated with the CR equation using the σ_{c50} constants.

(b) The data set is correlated with the LD equation in the form:

$$Q_X = L\sigma_{lX} + D\sigma_{dX} + h \tag{61}$$

If further correlations are necessary, the appropriate parameters can be chosen on the basis of the approximate η and P_D values obtained in the first two correlations.

2. If the substituent is attached to an sp^2-hybridized carbon atom that is not directly conjugated with the reaction site, then it is correlated with the Hammett equation using the σ_m constants.

3. If the substituent is bonded to an sp^3-hybridized carbon atom, it is correlated with the L equation:

$$Q_X = L\sigma_{lX} + h \tag{62}$$

The final regression equation obtained will give a reasonable model of the electrical effect on the chemical reactivity in the data set of interest.

B. Conjugated Alternating Dienes and Polyenes

1. Chemical reactivity (QSRR)

Two types of chemical reactivity of data sets can be distinguished: those in which the diene or polyene system acts simply as a skeletal group, and those in which it acts in whole or in part as a reaction site.

a. *Diene and polyene skeletal groups*. Molko and Grand[54] have reported pK_a values for *trans*,*trans*- and *cis*,*trans*-4′-substituted-5-phenyl-2,4-pentadienoic acids in 50% v/v aqueous ethanol at 25 °C. The pK_a values are: X, pK_a EE, pK_a ZE: H, 5.81, 6.17; Cl, 5.73, 6.06; OMe, 5.96, 6.27; Me, 5.90, 6.21; NMe_2, 6.10, 6.43. The data were correlated with the CR equation using the σ_{c50} substituent constants and with the LD equation using the σ_d constants. The best regression equations are for the *trans*,*trans* acids:

$$pK_{aX} = -0.518\ (\pm 0.0201)\sigma_{lX} - 0.563\ (\pm 0.0149)\sigma_{dX} + 5.81\ (\pm 0.00561) \tag{63}$$

$100R^2$, 99.87; A$100R^2$, 99.82; F, 755.68; S_{est}, 0.00730; S^0, 0.0575; n, 5; P_D, 52.0 (±1.83); η, 0.

For the *Z*,*E* acids:

$$pK_{aX} = -0.527\ (\pm 0.0419)\sigma_{c50X} + 6.15\ (\pm 0.0113) \tag{64}$$

$100R^2$, 98.14; F, 158.5; S_{est}, 0.0215; S^0, 0.176; n, 5; P_D, 50; η, 0.

Yanovskaya and coworkers[55] have reported rate constants for the alkaline hydrolysis of ethyl *trans,trans*-4′-substituted 5-phenyl-2,4-pentadienoates in 60% aqueous dioxan giving the values: X, log k; H, −2.60; Cl, −2.23; Br, −2.31; NO_2, −1.83; OMe, −2.61; NMe_2, −3.00. Correlation with the CR equation gave as the best regression equation:

$$\log k_X = 0.724\ (\pm 0.0453)\sigma_{c50X} + 1.12\ (\pm 0.253)\sigma_{eX} - 2.37\ (\pm 0.0246) \qquad (65)$$

$100R^2$, 99.34; A$100R^2$, 99.17; F, 224.7; S_{est}, 0.0412; S^0, 0.115; n, 6; P_D, 50; η, 1.55 (±0.0150).

The value of η is in accord with the attack of a nucleophile on the carbonyl carbon atom to form a negatively charged tetrahedral intermediate in the rate-determining step.

Doyle and coworkers[56] have reported polarographic half-wave potentials in aqueous ethanol for 1- and 2-substituted perfluoro-1,3-cyclohexadienes. The $E_{0.5}$ values are: X, $E_{0.5}$ (1-X), $E_{0.5}$ (2-X): H, −1.24, −1.22; CF_3, −0.87, —; OMe, —, −1.39; OEt, —, −1.40; Me, −1.42, −1.37; F, −1.19, −1.19. Correlation with the CR equation gave as the best regression equations for the 1-substituted compounds:

$$E_{0.5,X} = 0.772\ (\pm 0.0785)\sigma_{c50,X} - 1.26\ (\pm 0.0217) \qquad (66)$$

$100R^2$, 97.98; F, 96.87; S_{est}, 0.0399; S^0, 0.201; n, 4; P_D, 50; η, 0
and for the 2-substituted compounds:

$$E_{0.5,X} = 0.667\ (\pm 0.0832)\sigma_{c50,X} - 1.23\ (\pm 0.0150) \qquad (67)$$

$100R^2$, 95.54; F, 64.21; S_{est}, 0.0246; S^0, 0.273; n, 5; P_D, 50; η, 0.

There is no significant difference between the values of C for 1- and for 2-substitution; the values of P_D and η are the same.

b. *Diene and polyene reactions at the double bonds*. Tidwell and coworkers[57] have reported second-order rate constants for the acid-catalyzed hydration of 2-substituted 1,3-butadienes at 25 °C; their values are: X, k_2: *c*-Pr, 122,000; Me, 3.19; Cl, 0.201; H, 0.396; OEt, 60,000,000.

Correlation with the LD and CR equations gave as the best regression equation:

$$k_{2X} = -8.85\ (\pm 1.27)\sigma_{c60,X} - 50.3\ (\pm 9.33)\sigma_{eX} - 0.673\ (\pm 0.218) \qquad (68)$$

$100R^2$, 99.66; A$100R^2$, 99.55; F, 292.5; S_{est}, 0.299; S^0, 0.0923; n, 5; P_D, 60; η, 3.79 (±0.447).

The large values of P_D and η and the negative sign of C are in accord with a large electron deficiency in the transition state; the large value of C suggests a directly substituted active site.

The Diels-Alder reaction ($4\pi + 2\pi$ cycloaddition) is by far the best studied reaction of dienes from both theoretical and experimental viewpoints. Frontier molecular orbital theory predicts three types of Diels-Alder reaction. Structural effects on rate constants show the existence of two types of reaction:

1. Donor (electron-rich) diene and acceptor (electron-poor) ene (dienophile), designated D_dE_a.

2. Acceptor diene and donor ene, designated D_aE_d.

The great majority of the reactions studied are of the D_dE_a type. Thus, DeWitt and coworkers[58] have reported relative rate constants (k_X/k_H) for the reaction of 4′-substituted 1-phenyl-1,3-butadienes with maleic anhydride in dioxan at 25 °C, 35 °C, and 45 °C. Their data are: X, $k_r(25)$, $k_r(35)$, $k_r(45)$: H, 1, 1, 1; Me, 1.11, 1.29, 1.37; Cl, 0.580, 0.632; 0.636; OMe, 2.65, 2.33, 2.40; NO_2, 0.275, 0.300, 0.280.

Writing the LDRT equation for log (k_X/k_H) gives:

$$\log k_{rX} = \log k_X/k_H = \log k_X - \log k_H \tag{69}$$

$$\log k_X = L\sigma_{lX} + D\sigma_{dX} + R\sigma_{eX} + T\tau + h \tag{70}$$

$$\log k_H = L\sigma_{lH} + D\sigma_{dH} + R\sigma_{eH} + T\tau + h \tag{71}$$

$$\log k_X - \log k_H = L\sigma_{lX} + D\sigma_{dX} + R\sigma_{eX} + T\tau + h - L\sigma_{lH} - D\sigma_{dH} - R\sigma_{eH} - T\tau - h \tag{72}$$

As $\sigma_{lH} = \sigma_{dH} = \sigma_{eH} = 0$, equation 72 simplifies to:

$$\log k_{rX} = L\sigma_{lX} + D\sigma_{dX} + R\sigma_{eX} \tag{73}$$

which is a form of the LDR equation. Relative rate constants are independent of temperature. All of the data were therefore combined into a single data set and correlated with the LDR equation giving as the best regression equation:

$$k_{rX} = -0.856\ (\pm 0.0711)\sigma_{lX} - 0.866\ (\pm 0.0608)\sigma_{dX} - 3.07\ (\pm 0.626)\sigma_{eX} - 0.0579\ (\pm 0.0266) \tag{74}$$

$100R^2$, 97.55; A$100R^2$, 97.14; F, 145.9; S_{est}, 0.0573; S^0, 0.183; n, 15; P_D, 50.4 (±4.47); η, 3.55 (±0.679).

That this is an example of the D_dE_a type of reaction is shown by the negative signs of L and D.

Sauer, Sustmann and coworkers[59] have reported second-order rate constants for the reaction of *trans*-1-substituted 1,3-butadienes with tetracyanoethylene (TCNE) in dichloromethane at 20 °C; their values are: X, $\log k_2 + 6$: OMe, 7.935, vinyl, 5.456; Ph, 5.814; Me, 5.243; H, 3.228. The data were correlated with the CR equation; the best regression equation is:

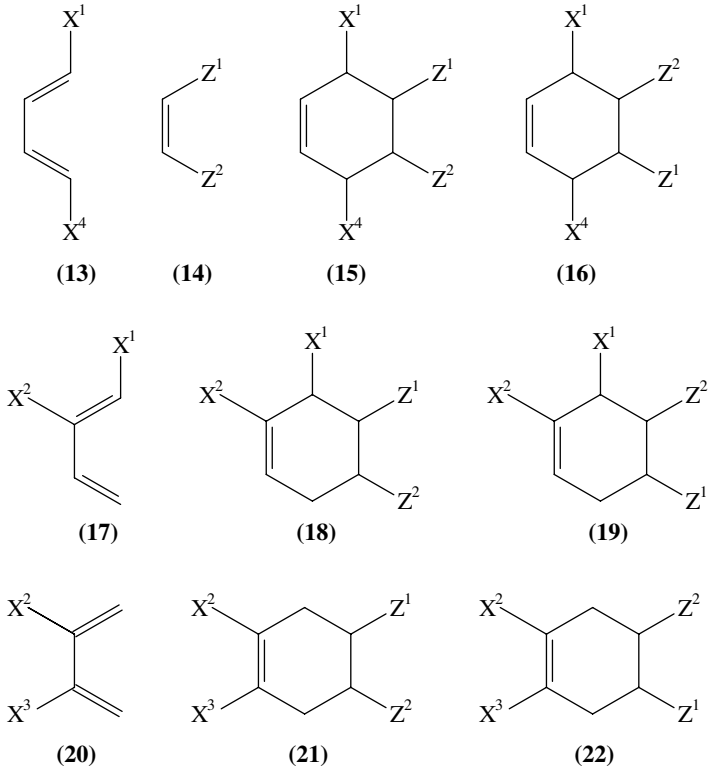
$$\log 10^6 k_2X = -6.70\ (\pm 0.0258)\sigma_{c60,X} - 18.1\ (\pm 0.107)\sigma_{eX} + 3.227\ (\pm 0.0101) \tag{75}$$

$100R^2$, 99.998; A$100R^2$, 99.997; F, 43239; S_{est}, 0.0114; S^0, 0.00760; n, 5; P_D, 60; η, 1.80 (±0.0811).

The excellent fit of the data in this case is undoubtedly fortuitous. The reaction is of the D_dE_a type. The large value of C is due to the substituent being directly attached to the reaction site.

If both diene and ene are nonsymmetric, it is possible to obtain two products from this type of cycloaddition. Consider the reaction of the diene **13** with the ene **14**. The possible product types are **15** and **16**. Reaction of the diene **17** with the ene **14** can give as product types **18** and **19** while that of the diene **20** with **14** as product types can give **21** and **22**. Both products are not always obtained. Thus, Kresze and coworkers[60] have determined rate constants for the reaction of 4′-substituted 1-phenyl-1,3-butadienes with 4-chloronitrosobenzene in benzene at temperatures from 15 °C to 35 °C. Their values are: X, k(15), k(20), k(25), k(30), k(35): NO_2, 0.94, —, 1.94, —, 3.98; Cl, 1.12, 1.60, 2.22, 3.17, 4.29; H, 1.47, 2.11, 3.08, 4.32, 5.73; Me, 1.52, 2.32, 3.20, 4.19, 5.68; OMe, 2.21, 3.19, 4.46, 6.27, 8.48. In this case the diene is **17** with X^1 equal to substituted phenyl and X^4 equal to H, while in the ene which is the N=O group Z^1 is 4-chlorophenyl and there is no Z^2. The only product formed was **16**. The data were correlated with the LDRT equation; the best regression equation was:

$$\log k_X = -0.365\ (\pm 0.0414)\sigma_{lX} - 0.311\ (\pm 0.0381)\sigma_{dX} - 2.02\ (\pm 0.371)\sigma_{eX} - 26.8\ (\pm 1.11) + 9.408\ (\pm 0.372) \tag{76}$$



(13) **(14)** **(15)** **(16)**

(17) **(18)** **(19)**

(20) **(21)** **(22)**

$100R^2$, 97.66; A$100R^2$, 97.29; F, 187.5; S_{est}, 0.0423; S^0, 0.173; n, 23; P_D, 46.0 (±6.81); η, 6.49 (±0.891).

Again, the reaction is of the D_dE_a type. The electronic demand is very large; its sign indicates the need to stabilize an electron-deficient carbon atom.

In a later paper Kresze and coworkers[61] reported partial rate factors for the reaction of methyl 4′-substituted 5-phenyl-2,4-dienoates with nitrosobenzene (the ene is the N=O group) in benzene at temperatures ranging from 20 °C to 40 °C to form product types **15** and **16** with X^1 equal to substituted phenyl, X^4 equal to carbomethoxy, Z^1 equal to phenyl and no Z^2. Their partial rate factors are: X, $k_{\mathbf{15}}(20)$, $k_{\mathbf{15}}(25)$, $k_{\mathbf{15}}(30)$, $k_{\mathbf{15}}(35)$, $k_{\mathbf{15}}(40)$, $k_{\mathbf{16}}(20)$, $k_{\mathbf{16}}(25)$, $k_{\mathbf{16}}(30)$, $k_{\mathbf{16}}(35)$, $k_{\mathbf{16}}(40)$: NMe_2, 0.84, 1.53, 2.03, 3.81, 4.85, 1.66, 3.18, 4.35, 8.51, 11.22; OMe, 0.48, 0.82, 1.44, 1.87, 3.05, 1.68, 2.90, 5.06, 6.60, 10.8; Me, 0.37, 0.63, 1.13, 1.57, 2.38, 1.59, 2.72, 4.84, 6.71, 10.2; H, 0.34, 0.58, 1.05, 1.47, 2.22, 1.42, 2.44, 4.44, 6.22, 9.41; Cl, 0.37, 0.55, 0.81, 1.48, 1.92, 1.18, 1.78, 2.62, 4.78, 6.20; CN, 0.62, 0.89, 1.23, 2.16, 3.21, 0.95, 1.48, 2.17, 4.07, 6.40.

The data were correlated with the LDRT equation. The best regression equation obtained for the $\log k_{\mathbf{15}}$ values is:

$$\log k_{\mathbf{15},X} = -0.363\ (\pm 0.0395)\sigma_{lX} - 0.222\ (\pm 0.0310)\sigma_{dX} - 37.2\ (\pm 1.13)\tau + 12.9\ (\pm 0.373) \quad (77)$$

$100R^2$, 97.94; A$100R^2$, 97.79; F, 412.7; S_{est}, 0.0473; S^0, 0.154; n, 30; P_D, 37.9 (± 6.2); η, 0

while that for the $\log k_{\mathbf{16}}$ values, obtained by excluding the points for the cyano group, is:

$$\log k_{\mathbf{16},X} = -0.196\ (\pm 0.0727)\sigma_{lX} - 0.250\ (\pm 0.0922)\sigma_{dX} - 1.06\ (\pm 0.228)\sigma_{eX} - 36.2\ (\pm 1.06)\tau + 11.9\ (\pm 0.360) \quad (78)$$

$100R^2$, 98.60; A$100R^2$, 98.40; F, 352.6; S_{est}, 0.0416; S^0, 0.132; n, 25; P_D, 56.1 (±25.4); η, 4.24 (± ?); r_{de}, 0.812.

Both reactions are of the D_dE_a type. Equations 76 and 78 are in accord with a transition state in which the C−O bond is almost completely formed while the C−N bond formation is much less advanced. This is indicated by the large positive values of η which are evidence of a large electron deficiency at the carbon atom of the diene to which the substituted phenyl group is attached. The lack of a significant dependence on σ_e in equation 77 is in accord with this transition state, as in this case the substituted phenyl group is bonded to the carbon atom which forms a bond with the oxygen atom of the nitroso group. The P_D and η values are in fairly good agreement with each other.

Craig and coworkers[62] have reported rate constants for the reaction of 2-substituted 1,3-butadienes with maleic anhydride in benzene at 25 °C; their values are: X, k: Cl, 0.019; H, 0.19; Me, 0.57; Et, 1.15; *i*-Pr, 2.2; *t*-Bu, 5.6; OMe, 1.9. As the Diels-Alder reaction proceeds through the s-*cis* conformation of the diene, and substituents in the 2- and 3-positions can affect the fraction of the diene in this conformation, steric effects must be considered. The data set was correlated therefore with the CRS equation:

$$Q_X = C\sigma_{cX} + R\sigma_{eX} + S\upsilon_X + h \quad (79)$$

The best regression obtained is:

$$\log k_X = -4.83\ (\pm 0.762)\sigma_{c50,X} + 0.696\ (\pm 0.288)\upsilon_X - 1.01\ (\pm 0.190) \quad (80)$$

$100R^2$, 93.21; A$100R^2$, 91.86; F, 22.47; S_{est}, 0.263; S^0, 0.345; n, 7; P_D, 50; η, 0.

The sign of C shows that the reaction is of the D_dE_a type. As expected, steric effects are significant.

2. Chemical properties (QSCR)

As an example of chemical properties we consider the boiling points of 1-substituted 1,3-butadienes, 1-substituted 4-methyl-1,3-butadienes and 2-substituted 1,3-butadienes[63]. The data points available are for the 1-substituted, the 1-substituted 4-methyl- and the 2-substituted compounds: X, bp(1-X), bp(1-X-4-Me), bp(2-X): H, 268.75, 315.15, 268.75; Me, 315.15, 355.15, 307.15; Et, 346.15, 381.15, —; OMe, 364.65, —, 348.15; OEt, 383.15, —, 368.15; Cl, 341.15, —, 332.55; F, —, —, 285.15; I, —, —, 385.15; CHO, —, 446.65, —; CO_2Me, —, 453.15, —; CO_2Et, —, 468.15, —; CN, 409.65, —, —; CH=CHMe, —, 420.65, —; Vinyl, 371.65, —, —; C_2H, 356.55, —, —. The model for chemical properties is the IMF equation. As the only interactions expected to be significant in these data sets are dipole–dipole, dipole-induced–dipole and induced-dipole–induced-dipole forces, we have dropped from the IMF equation all terms other than μ_{PhX}, which represents the X−C(sp^2) bond moment, and the polarizability parameter α. The resulting correlation equation is:

$$bp_X = M\mu_X + A\alpha_X + h \quad (81)$$

Correlation of the boiling points of 2-substituted 1,3-butadienes with equation 81 gave, as the best regression equation:

$$bp_X = 14.0\ (\pm 5.92)\mu_X + 703\ (\pm 81.4)\alpha_X + 269.27\ (\pm 7.20) \quad (82)$$

$100R^2$, 96.90; A$100R^2$, 96.27; F, 62.42; S_{est}, 8.97; S^0, 0.233; n, 7.

The boiling points of the 1-substituted and 1-substituted 4-methyl-1,3-butadienes were combined into a single data set by introducing the variable n_{Me}, which takes the value 1 when there is a 4-methyl group and 0 when there is not. Thus the correlation equation is:

$$bp_X = M\mu_X + A\alpha_X + B_{Me}n_{Me} + h \tag{83}$$

The best regression obtained is:

$$bp_X = 24.9\ (\pm 6.04)\mu_X + 715\ (\pm 67.3)\alpha_X + 40.7\ (\pm 5.50)n_{Me} + 274.38\ (\pm 5.88) \tag{84}$$

$100R^2$, 96.97; A$100R^2$, 96.50; F, 128.1; S_{est}, 10.6; S^0, 0.201; n, 16.

The IMF equation in the form of equations 81 and 83 represents boiling points effectively.

3. Physical properties (QSPR)

Ionization potentials (IP) of 1- and 2-substituted 1,3-butadienes and of 1,4-disubstituted 1,3-butadienes[64] were correlated with the LDRA, CR and CRA equations, respectively. The choice of correlation equation was made on the basis of the number of data points in the set. The values of the ionization potential were: 1-X, IP: H, 9.03; Me, 8.61; Et, 8.51; *i*-Pr, 8.47; *t*-Bu, 8.43; vinyl, 8.29; Ph, 8.16; OMe, 8.62; CH=CH−CH=CH_2, 7.79; CH=CHMe, 7.96; C_2H, 9.20. 2-X, IP; OMe, 8.62; Ph, 8.15; Cl, 8.828; Me, 8.845; H, 9.03. 1-X, 4-X, IP; OMe, OMe, 7.67; Ph, Ph, 8.09; vinyl, vinyl, 7.79; Me, Me, 8.18; Me, Et, 8.18; Me, vinyl, 7.96.

The best regression equations are for the 1-substituted 1,3-butadienes:

$$IP_{1X} = 2.94\ (\pm 0.259)\sigma_{1X} + 2.21\ (\pm 0.162)\sigma_{dX} + 7.58\ (\pm 0.598)\sigma_{ex} + 9.08\ (\pm 0.0474) \tag{85}$$

$100R^2$, 97.89; A$100R^2$, 97.36; F, 108.1; S_{est}, 0.0730; S^0, 0.182; n, 11; P_D, 42.9 (±4.06); η, 3.43 (±0.0976).

For the 2-substituted 1,3-butadienes:

$$IP_{2X} = -0.383\ (\pm 0.0910)\sigma_{c50,X} + 7.20\ (\pm 0.314)\sigma_{eX} + 9.00\ (\pm 0.0189) \tag{86}$$

$100R^2$, 91.49; A$100R^2$, 89.78; F, 21.49; S_{est}, 0.139; S^0, 0.386; n, 5; P_D, 50; η, −18.8 (± ?).

For the 1,4-disubstituted 1,3-butadienes:

$$IP_{1X,4X} = 1.51\ (\pm 0.242)\sigma_{c50X} + 6.13\ (\pm 0.867)\sigma_{eX} + 1.21\ (\pm 0.512)\alpha_X + 8.94\ (\pm 0.0995) \tag{87}$$

$100R^2$, 96.73; A$100R^2$, 95.09; F, 29.55; S_{est}, 0.113; S^0, 0.276; n, 7; P_D, 50; η, 4.06 (± ?).

Landesberg and Katz[65] have reported three sets of carbonyl stretching frequencies of 4′-substituted 1-phenyl-1,3-butadiene iron tricarbonyl complexes. Their values are: X, $\nu_{CO}(1)$, $\nu_{CO}(2)$, $\nu_{CO}(3)$: NH_2, 2047, 1980, 1973; OMe, 2048, 1983, 1975; H, 2049, 1986, 1979; NHAc, 2050, 1986, 1979, Br, 2052, 1989, 1981; Ac, 2053, 1990, 1982; CN, 2055, 1993, 1984. The data were correlated with the CR and LD equations. The best regression equations obtained are for $\nu_{CO}(1)$:

$$\nu_{CO,X}(1) = 9.27\ (\pm 1.27)\sigma_{lX} + 5.60\ (\pm 0.685)\sigma_{dX} + 2049\ (\pm 0.484) \tag{88}$$

$100R^2$, 97.41; A$100R^2$, 96.90; F, 75.34; S_{est}, 0.570; S^0, 0.213; n, 7; P_D, 37.7 (±5.88); η, 0.

For ν_{CO} (2):

$$\nu_{CO}(2) = 11.6\ (\pm 3.05)\sigma_{lX} + 9.51\ (\pm 1.64)\sigma_{dX} + 1985\ (\pm 1.16) \quad (89)$$

$100R^2$, 93.71; A$100R^2$, 92.45; F, 29.79; S_{est}, 1.37; S^0, 0.332; n, 7; P_D, 45.0 ($\pm$10.7); η, 0.

For ν_{CO} (3):

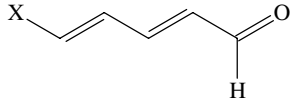
$$\nu_{CO}(3) = 8.43\ (\pm 3.12)\sigma_{lX} + 8.86\ (\pm 1.67)\sigma_{dX} + 1978\ (\pm 1.19) \quad (90)$$

$100R^2$, 91.49; A$100R^2$, 89.78; F, 21.49; S_{est}, 1.39; S^0, 0.386; n, 7; P_D, 51.2 ($\pm$14.3); η, 0.

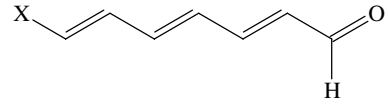
Yanovskaya and coworkers[55] have reported ν_{CO} for 5-substituted 2,4-pentadienals, **23**, and 7-substituted 2,4,6-heptatrienals, **24**, in chloroform. Their values are: X, ν_{CO} **(23)**, ν_{CO} **(24)**: Me, 1680, 1678; CO_2Et, 1689, 1682; CN, 1692, 1687; NMe_2, 1584, 1640; Ph, 1675, 1675; CH=CHMe, 1678, —; CH=CHCN, 1687, 1678; CH=CHPh, 1675, —. The data were correlated with the CRA equation. The best regression equations were for **23**:

$$\nu_{CO,X} = 14.1\ (\pm 6.74)\sigma_{c75,X} + 415\ (\pm 98.1)\sigma_{eX} + 129\ (\pm 46.8)\alpha_X + 1696\ (\pm 10.8) \quad (91)$$

$100R^2$, 94.72; A$100R^2$, 92.61; F, 23.93; S_{est}, 10.7; S^0, 0.325; n, 8; P_D, 75, η, 9.81.



(23)



(24)

For **24**:

$$\nu_{CO,X} = 8.86\ (\pm 2.91)\sigma_{c75,X} + 114\ (\pm 39.2)\sigma_{eX} + 1680\ (\pm 4.24) \quad (92)$$

$100R^2$, 96.35; A$100R^2$, 95.44; F, 39.65; S_{est}, 4.15; S^0, 0.270; n, 6; P_D, 75; η, 4.28 ($\pm$0.450).

Kajimoto and Fueno[66] have reported ^{13}C chemical shifts for 2-substituted 1,3-butadienes at each carbon atom of the dienyl moiety. Their values are: X, δ^1, δ^2, δ^3, δ^4: OEt, −24.5, 15.3, −7.5, 19.3; Me, −4.4, −0.5, −9.0, 14.5; Ph, −1.3, −5.0^u, −9.3^u, 10.6; H, 11.7, −8.8, −8.8, 11.7; CO_2Me, 6.1, −16.3, −6.9, 3.1; CN, 29.5, −21.3, −4.6, 1.1. Values labelled u are uncertain. The data sets were correlated with the CR and LD equations. The best regression equations are for the δ^1 values:

$$\Delta\delta^1_X = 61.5\ (\pm 16.8)\sigma_{dX} + 8.28\ (\pm 4.20) \quad (93)$$

$100R^2$, 77.10; F, 13.47; S_{est}, 9.62; S^0, 0.586; n, 6; P_D, 100; η, 0.

For δ^2 values:

$$\Delta\delta^2_X = -11.3\ (\pm 4.25)\sigma_{lX} - 46.7\ (\pm 3.68)\sigma_{dX} - 7.82\ (\pm 1.33) \quad (94)$$

$100R^2$, 98.48; A$100R^2$, 98.10; F, 97.13; S_{est}, 2.05; S^0, 0.174; n, 6; P_D, 80.5 ($\pm$10.0); η, 0.

For δ^3:

$$\Delta\delta^3_X = 7.60\ (\pm 1.22)\sigma_{lX} - 9.31\ (\pm 0.359) \quad (95)$$

$100R^2$, 90.68; F, 38.94; S_{est}, 0.606; S^0, 0.374; n, 6; P_D, 0; η, 0.

For δ^4:

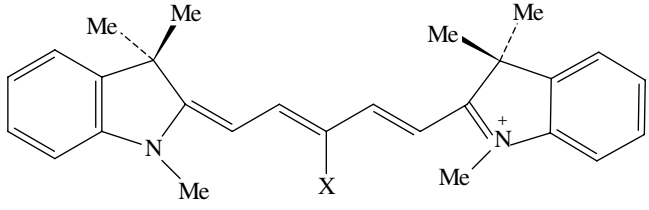
$$\Delta\delta_X^4 = -13.4\ (\pm 1.95)\sigma_{lX} - 21.5\ (\pm 1.69)\sigma_{dX} + 11.0\ (\pm 0.611) \tag{96}$$

$100R^2$, 98.87; A$100R^2$, 98.59; F, 131.0; S_{est}, 0.945; S^0, 0.150; n, 6; P_D, 61.7 (±6.67); η, 0.

^{13}C chemical shifts in $CDCl_3$ of the 12-substituted indocyanines **25** were reported by Grahn and Reichardt[67]. Their values for C^2 are: X, $\Delta\delta^2$: H, 0; OMe, −0.23; *c*-Pr, 0.26; *c*-Bu, −0.16; *c*-Hx, −0.02; Me, 0.08; Ph, 0.27; F, 0.08; Cl, 1.51; Br, 1.71; I, 1.78; N_2Ph, 4.18; CHO, 4.75; CN, 3.25; NO_2, 6.14. Correlation of the set with the LDRA equation gave equation 97 as the best regression equation:

$$\Delta\delta_X^2 = 4.52\ (\pm 0.941)\sigma_{lX} + 5.85\ (\pm 0.923)\sigma_{dX} + 1.16\ (\pm 0.372) \tag{97}$$

$100R^2$, 85.77; A$100R^2$, 84.68; F, 36.17; S_{est}, 0.842; S^0, 0.422; n, 15; P_D, 56.4 (±11.4); η, 0.



(25)

C. Adjacent Dienes and Polyenes

1. Chemical reactivity (QSRR)

Battioni and coworkers[68] have reported rate constants for the reaction of 4′-substituted 6,6-diphenyl-3,4,5-hexatrien-2-one with diazomethane in dimethylformamide at 29.7 °C. The values are: X, 10^5 k (s^{-1}): OMe, 3.76; Me, 5.05; H, 7.36; Br, 11.6; NO_2, 66.6. The triene is a 50:50 mixture of *cis* and *trans* isomers. The data set was correlated with the CR equation. The best regression equation is:

$$k_X = 1.13\ (\pm 0.0172)\sigma_{c50,X} + 0.860\ (\pm 0.00708) \tag{98}$$

$100r^2$, 99.93; F, 4285; S_{est}, 0.0150; S^0, 0.0341; n, 5; P_D, 50; η, 0.

2. Chemical properties (QSCR)

Boiling points of 1-substituted 1,2-propadienes[63,69] were correlated with the MA equation. The values used are: X, bp: H, 238.65; Me, 283.95; Et, 318.05; Pr, 349.15; CH_2Br, 383.15; CH_2Cl, 361.15; CH_2I, 403.15; CH_2OMe, 361.15; $SiMe_3$, 364.15. The best regression equation is:

$$bp_X = 14.0\ (\pm 5.92)\mu_X + 703\ (\pm 81.4)\alpha_X + 269.27\ (\pm 7.20) \tag{99}$$

$100R^2$, 96.90; A$100R^2$, 96.27; F, 62.42; S_{est}, 8.97; S^0, 0.233; n, 9.

3. Physical properties (QSPR)

The application of correlation analysis to physical properties of alkenes and cumulenes was reviewed by Runge[70]. Vertical ionization potentials of 1-substituted 1,2-propadienes were correlated with the LDRA equation. The values are: X, IP(ν): H, 10.07; Me, 9.33, Et, 9.22; CO_2Me, 10.02; CN, 10.35; OMe, 8.75; Cl, 9.57; Br, 9.46; Ph, 8.29; $CH{=}C{=}CH_2$, 8.53; CH_2C_2H, 9.65; $CMe{=}CH_2$, 8.54; E−CH=CHMe, 8.32. The best regression equation is:

$$\mathrm{IP}(\nu)_X = 1.13\ (\pm 0.306)\sigma_{lX} + 2.06\ (\pm 0.330)\sigma_{dX} + 8.18\ (\pm 1.86)\sigma_{eX} - 2.89\ (\pm 1.39)\alpha_X + 10.02\ (\pm 0.147) \quad (100)$$

$100R^2$, 93.40; A$100R^2$, 91.42; F, 31.85; S_{est}, 0.208; S^0, 0.320; n, 14; P_D, 64.6 (±13.8); η, 3.97 (±0.638); $r_{e\alpha}$, 0.705.

Runge and Firl[71] have reported ^{13}C chemical shifts for 1-substituted allenes. Their values are: X, δ^1, δ^2, δ^3: H, 73.5, 212.6, 73.5; Me, 84.2, 209.4, 73.4; Et, 91.6, 208.8, 74.7; *i*-Pr, 99.8, 207.8, 76.2; *t*-Bu, 102.1, 207.0, 77.0; Ph, 94.0, 209.6, 78.8; OMe, 123.0, 201.1, 91.4; OEt, 121.7, 202.3, 89.6; SMe, 88.5, 206.9, 80.9; Cl, 88.7, 202.4, 84.8; Br, 71.9, 206.9, 83.1; F, 128.5, 199.1, 92.6; CO_2H, 88.1, 217.7, 80.0; CN, 67.4, 218.6, 80.7. Correlation with the LDRA equation gave as the best regression equation for C^1 on exclusion of the values for Br and CO_2H:

$$\delta^1_X = -82.4\ (\pm 9.78)\sigma_{dX} + 219\ (\pm 63.2)\sigma_{eX} + 135\ (\pm 41.2)\alpha_X + 75.1\ (\pm 4.13) \quad (101)$$

$100R^2$, 90.55; A$100R^2$, 88.44; F, 25.54; S_{est}, 6.94; S^0, 0.377; n, 12; P_D, 100; η, −2.66; $r_{e\alpha}$, 0.712.

For C^2:

$$\delta^2_X = 2.89\ (\pm 1.28)\sigma_{lX} + 23.7\ (\pm 1.13)\sigma_{dX} - 46.0\ (\pm 7.88)\sigma_{eX} - 20.8\ (\pm 5.53)\alpha_X + 212\ (\pm 0.596) \quad (102)$$

$100R^2$, 98.20; A$100R^2$, 97.66; F, 122.9; S_{est}, 0.888; S^0, 0.167; n, 14; P_D, 89.1 (±7.10); η, −1.94 (±0.319); $r_{e\alpha}$, 0.697.

Although a statistically significant correlation was obtained for δ^3, it must be fortuitous as L and D had opposite signs.

D. Cross-conjugated Alternating Dienes and Polyenes

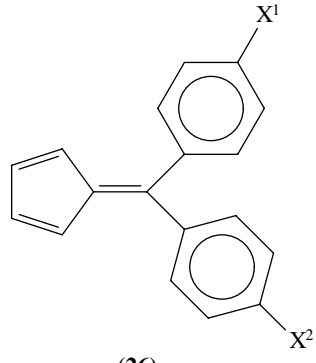
1. Chemical reactivity (QSRR)

Norton and Knoblich[72] have reported $E_{0.5}$ versus the standard calomel electrode in 75% aqueous dioxan at 25 °C for 6,6-di(4′-substituted-phenyl)-pentafulvenes **26**. Their values are: X^1, X^2, $-E_{0.5}$: Cl, Cl, 1.47; Cl, H, 1.51; Br, H, 1.51; F, F, 1.53; F, H, 1.54; H, H, 1.55; Me, H, 1.58; Me, Me, 1.60; OMe, H, 1.60; OMe, OMe, 1.63. The data set was correlated with the LDR equation in the form:

$$Q_X = L\Sigma\sigma_{lX} + D\Sigma\sigma_{dX} + R\Sigma\sigma_{eX} + h \quad (103)$$

on the assumption that the substituent effects are approximately additive. The best regression equation obtained is:

$$E_{0.5,X} = 0.199\ (\pm 0.00691)\Sigma\sigma_{lX} + 0.193\ (\pm 0.00712)\Sigma\sigma_{dX} - 0.0945\ (\pm 0.0316)\Sigma\sigma_{eX} - 1.55\ (\pm 0.00229) \quad (104)$$



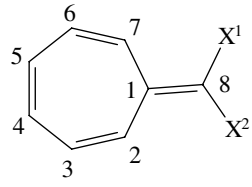
(26)

$100R^2$, 99.57; A$100R^2$, 99.45; F, 466.6; S_{est}, 0.00399; S^0, 0.0843; n, 10; P_D, 49.2 (±2.20); η, −0.490 (±0.163); r_{ld}, 0.731.

2. Physical properties (QSPR)

Bönzli and Neuenschwander[73] have reported ^{13}C and ^{1}H chemical shifts for 8,8-disubstituted heptafulvenes, **27**. In some cases the substituents are segments of a ring. Values of the ^{13}C shifts are: X^1, X^2, δ^2, δ^3, δ^4, δ^5, δ^7, δ^8: CN, H, 133.02, 132.99, 133.54, 132.37, 156.72, 87.22; Ph, H, 128.78, 131.80, 131.49, 127.05, 139.1, 125.83; OMe, H, 126.38, 129.82, 131.71, 124.55, 122.51, 144.75; $COCF_3$, CN, 142.84, 141.58, 140.46, 142.65, 165.20, 88.19; CN, CN, 138.65, 137.42, 137.42, 138.65, 163.70, 70.10; $CO(CH_2)_4CO$, 142.93, 140.60, 140.60, 142.93, 158.94, 114.52; Cl, Cl, 130.15, 132.35, 132.35, 130.15, 135.94, 113.15; H, H, 126.90, 130.80, 130.80, 126.90, 146.60, 111.90; Ph, Ph, 127.48, 132.00, 132.00, 127.48, 136.61, 135.62, $(CH_2)_4$, 125.36, 131.00, 131.00, 125.36, 129.37, 139.73; NMe_2, $OSiMe_3$, 122.82, 130.61, 131.61, 123.63, 107.48; 148.76; NMe_2, NMe_2, 120.80, 130.80, 130.80, 120.80, 105.70, 157.50. The data sets were correlated with the LDRA equation in the form:

$$Q_X = L\Sigma\sigma_{lX} + D\Sigma\sigma_{dX} + R\Sigma\sigma_{eX} + \Sigma\alpha_X + h \tag{105}$$



(27)

The best regression equations are for C^2:

$$\delta^2_X = 8.07\ (\pm1.35)\Sigma\sigma_{lX} + 10.8\ (\pm1.17)\Sigma\sigma_{dX} - 10.8\ (\pm2.32)\Sigma\sigma_{eX} + 128\ (\pm0.983) \tag{106}$$

$100R^2$, 96.26; A$100R^2$, 95.43; F, 68.62; S_{est}, 1.68; S^0, 0.237; n, 12; P_D, 57.2 (±8.22); η, −1.00 (±0.419); r_{de}, 0.597.

For C^3:

$$\delta_X^3 = 4.66\ (\pm 1.11)\Sigma\sigma_{lX} + 6.07\ (\pm 0.961)\Sigma\sigma_{dX} - 14.1\ (\pm 3.85)\Sigma\sigma_{eX} + 131\ (\pm 0.811) \quad (107)$$

$100R^2$, 91.53; A$100R^2$, 89.65; F, 28.81; S_{est}, 1.38; S^0, 0.356; n, 12; P_D, 57.0 (±11.8); η, −2.32 (±0.517); r_{de}, 0.597.

For C^4:

$$\delta_X^4 = 4.46\ (\pm 1.13)\Sigma\sigma_{lX} + 5.25\ (\pm 0.974)\Sigma\sigma_{dX} - 11.9\ (\pm 3.90)\Sigma\sigma_{eX} + 131\ (\pm 0.821) \quad (108)$$

$100R^2$, 89.48; A$100R^2$, 87.14; F, 22.68; S_{est}, 1.40; S^0, 0.397; n, 12; P_D, 54.1 (±13.0); η, −2.27 (±0.611); r_{de}, 0.597.

For C^5:

$$\delta_X^5 = 8.55\ (\pm 1.39)\Sigma\sigma_{lX} + 10.7\ (\pm 1.20)\Sigma\sigma_{dX} - 12.7\ (\pm 4.80)\Sigma\sigma_{eX} + 127\ (\pm 1.01) \quad (109)$$

$100R^2$, 96.08; A$100R^2$, 95.21; F, 65.45; S_{est}, 1.40; S^0, 0.242; n, 12; P_D, 55.6 (±8.16); η, −1.18 (±0.427); r_{de}, 0.597.

For C^7:

$$\delta_X^7 = 11.2\ (\pm 3.25)\Sigma\sigma_{lX} + 31.4\ (\pm 2.26)\Sigma\sigma_{dX} + 141\ (\pm 2.16) \quad (110)$$

$100R^2$, 96.71; A$100R^2$, 96.38; F, 132.4; S_{est}, 4.07; S^0, 0.209; n, 12; P_D, 73.8 (±8.68); η, 0; r_{de}, 0.597.

For C^8:

$$\delta_X^8 = -30.9\ (\pm 8.96)\Sigma\sigma_{lX} - 26.1\ (\pm 6.47)\Sigma\sigma_{dX} + 47.5\ (\pm 24.1)\Sigma\sigma_{eX} + 119\ (\pm 7.58) \quad (111)$$

$100R^2$, 87.79; A$100R^2$, 85.08; F, 19.17; S_{est}, 11.2; S^0, 0.428; n, 12; P_D, 45.8 (±14.4); η, 0; r_{de}, 0.597.

C^1 and C^6 chemical shifts were not well modelled by equation 105. The 1 and 6, 2 and 5, and 3 and 4 positions of heptafulvene are equivalent to each other when groups in position 8 are the same. Results for these positions are comparable, as expected in view of the fact that for seven of the twelve compounds in the data set $X^1 = X^2$. The cyclic 8,8 substituents $CO(CH_2)_4CO$ and $(CH_2)_4$ were assumed equivalent to two Ac and two Et groups, respectively, in the parameterization of the substituents.

The values of the ^1H chemical shifts are: X^1, X^2, δ^1, δ^2, δ^3: CN, H, 6.73, 6.36, 6.29; Ph, H, 6.40, 5.77, 5.85; OMe, H, 5.74, 5.13, 5.23; $COCF_3$, CN, 9.43, 7.41, 7.88; CN, CN, 7.37, 7.28, 7.16; $CO(CH_2)_4CO$, 9.62, 7.67, 7.55; Cl, Cl, 6.30, 6.20, 6.15; H, H, 5.97, 5.48, 5.65; Ph, Ph, 6.14, 5.62, 5.88; $(CH_2)_4$, 5.82, 5.51, 5.70; NMe_2, $OSiMe_3$, 5.44, 5.11, 5.31; NMe_2, NMe_2, 4.84, 4.37, 4.71. Correlation with equation 105 gave for H^1:

$$\delta_X^{1H} = 1.15\ (\pm 0.521)\Sigma\sigma_{lX} + 2.38\ (\pm 0.450)\Sigma\sigma_{dX} - 3.56\ (\pm 1.80)\Sigma\sigma_{eX} + 6.16\ (\pm 0.379) \quad (112)$$

$100R^2$, 86.19; A$100R^2$, 83.12; F, 16.64; S_{est}, 0.647; S^0, 0.455; n, 12; P_D, 67.4 (±18.3); η, −1.50 (±0.703); r_{de}, 0.597.

For H^2:

$$\delta_X^{2H} = 1.35\ (\pm 0.188)\Sigma\sigma_{lX} + 1.41\ (\pm 0.136)\Sigma\sigma_{dX} + 1.03\ (\pm 0.505)\Sigma\alpha_X + 5.52\ (\pm 0.159) \quad (113)$$

$100R^2$, 96.64; A$100R^2$, 95.90; F, 76.81; S_{est}, 0.235; S^0, 0.224; n, 12; P_D, 51.0 (±6.32); η, 0; r_{de}, 0.597.

For H^3:

$$\delta_X^{3H} = 1.14\ (\pm 0.171)\Sigma\sigma_{lX} + 1.27\ (\pm 0.124)\Sigma\sigma_{dX} + 1.24\ (\pm 0.460)\Sigma\alpha_X + 5.62\ (\pm 0.145) \quad (114)$$

$100R^2$, 96.36; A$100R^2$, 95.55; F, 70.65; S_{est}, 0.214; S^0, 0.234; n, 12; P_D, 52.8 (±6.89); η, 0; r_{de}, 0.597.

VII. CONCLUSION

Methods have been presented, with examples, for obtaining quantitative structure–property relationships for alternating conjugated and cross-conjugated dienes and polyenes, and for adjacent dienes and polyenes. The examples include chemical reactivities, chemical properties and physical properties. A method of estimating electrical effect substituent constants for dienyl and polyenyl substituents has been described. The nature of these substituents has been discussed, but unfortunately the discussion is very largely based on estimated values. A full understanding of structural effects on dienyl and polyenyl systems awaits much further experimental study. It would be particularly useful to have more chemical reactivity studies on their substituent effects, and it would be especially helpful if chemical reactivity studies on the transmission of electrical effects in adjacent multiply doubly bonded systems were available. Only further experimental work will show how valid our estimates and predictions are.

VIII. APPENDIX (GLOSSARY)

This appendix is an updated and slightly modified version of one we have published elsewhere[50].

General

X A variable substituent.
Y An active site. The atom or group of atoms at which a measurable phenomenon occurs.
G A skeletal group to which X and Y may be attached.

Parameter An independent variable.
Pure parameter A parameter which represents a single effect.
Composite parameter A parameter which represents two or more effects.
Modified composite parameter A composite parameter whose composition has been altered by some mathematical operation.
Monoparametric equation A relationship in which the effect of structure on a property is represented by a single generally composite parameter. Examples are the Hammett and Taft equations.
Diparametric equation A relationship in which the effect of structure on a property is represented by two parameters, one of which is generally composite. Examples discussed in this work include the LD, CR and MYT equations. Other examples are the Taft, Ehrenson and Brownlee DSP (dual substituent parameter), Yukawa–Tsuno YT and the Swain, Unger, Rosenquist and Swain SURS equations. The DSP equation is a special case of the LDR equation with the intercept set equal to zero. It is inconvenient to use and has no advantages. The SURS equation uses composite parameters which are of poorer quality than

those used with the LDR and DSP equations. The MYT equation has all the advantages of the YT equation and gives results which are easier to interpret.

Multiparametric equation An equation which uses three or more parameters any of which may be either pure or composite.

Electrical effect parameterization

σ_1 The localized (field) electrical effect parameter. It is identical to σ_I. Though other localized electrical effect parameters such as σ_I^q and σ_F have been proposed, there is no advantage to their use. The σ^* parameter has sometimes been used as a localized electrical effect parameter; such use is generally incorrect. The available evidence is strongly in favour of an electric field model for transmission of the effect.

σ_d The intrinsic delocalized (resonance) electrical effect parameter. It represents the delocalized electrical effect in a system with zero electronic demand.

σ_e The electronic demand sensitivity parameter. It adjusts the delocalized effect of a group to meet the electronic demand of the system.

σ_D A composite delocalized electrical effect parameter which is a function of σ_d and σ_e. Examples of σ_D constants are the σ_R^+ and σ_R^- constants. The $\sigma_{R,k}$ constants, where k designates the value of the electronic demand η, are also examples of σ_D constants.

σ_R A composite delocalized electrical effect parameter of the σ_D type with η equal to 0.380. It is derived from 4-substituted benzoic acid pK_a values.

σ_R° A composite delocalized electrical effect parameter of the σ_D type with η equal to -0.376. It is derived from 4-substituted phenylacetic acid pK_a values.

σ_R^+ A composite delocalized electrical effect parameter of the σ_D type with η equal to 2.04. It is derived from rate constants for the solvolysis of 4-substituted cumyl chlorides.

$\sigma_R^\oplus$ A composite delocalized electrical effect parameter of the σ_D type with η equal to 3.31. It is derived from ionization potentials of the lowest-energy π orbital in substituted benzenes.

$\sigma_R^\ominus$ A composite delocalized electrical effect parameter of the σ_D type with η equal to -2.98. It is derived from pK_a values of substituted nitriles.

σ_R^- A composite delocalized electrical effect parameter of the σ_D type with η equal to -1.40. It is derived from pK_a values of substituted anilinium ions.

$\sigma_{k'/k}$ A composite parameter which is a function of σ_1, σ_d and σ_e. Its composition is determined by the values of k and k'. The Hammett σ_m and σ_p constants are of this type.

$\sigma_{Ck'}$ A composite constant that is a function of σ_1 and σ_d; its composition is determined by the value of k'.

$\sigma^\blacklozenge$ An electrical effect modified composite parameter.

σ Any electrical effect parameter.

η The electronic demand of a system or of a composite electrical effect parameter that is a function of both σ_d and σ_e. It is represented in subscripts as k. It is a descriptor of the nature of the electrical effect. It is given by R/D, where R and D are the coefficients of σ_e and σ_d, respectively.

P_D The percent delocalized effect. It too is a descriptor of the nature of the electrical effect. It is represented in subscripts as k'.

LDR equation A triparametric model of the electrical effect.

P_{EA} The percent of the $\sigma_{k'/k}$ values in a substituent matrix which exhibit an electron acceptor electrical effect.

P_{ED} The percent of the $\sigma_{k'/k}$ values in a substituent matrix which exhibit an electron donor electrical effect.

P_0 The percent of the $\sigma_{k'/k}$ values in a substituent matrix which do not exhibit a significant electrical effect.

Steric effect parameterization

r_v The van der Waals radius. A useful measure of group size. The internuclear distance of two nonbonded atoms in contact is equal to the sum of their van der Waals radii.

υ A composite steric parameter based on van der Waals radii. For groups whose steric effect is at most minimally dependent on conformation, it represents the steric effect due to the first atom of the longest chain in the group and the branches attached to that atom. The only alternative monoparametric method for describing steric effects is that of Taft which uses the E_s parameter. This was originally developed only for alkyl and substituted alkyl groups and for hydrogen. Kutter and Hansch[74] have estimated E_s values for other groups from the υ values using a method which, in many cases, disregards the MSI principle. It is best to avoid their use.

Simple branching equation (SB) A topological method for describing steric effects which takes into account the order of branching by using as parameters n_i, the number of atoms other than H that are bonded to the i-th atoms of the substituent.

n_i The number of branches on the i-th atoms of a substituent. These are the steric parameters used in the SB equation.

Expanded branching equation (XB) A topological method for describing steric effects which takes into account the order of branching by using as parameters n_{ij}, the number of j-th branching atoms bonded to the i-th atoms of the substituent.

n_{ij} The number of j-th branches on the i-th atoms of a substituent. These are the steric parameters used in the XB model of steric effects.

n_b The number of bonds in the longest chain of a substituent. It is a steric parameter which serves as a measure of the length of a group along the group axis.

Segmental equation A steric effect model that separately parameterizes each segment of a substituent. It requires fewer parameters than the XB equation and is generally more effective than the SB equation.

υ_i A steric parameter based on van der Waals radii that is a measure of the steric effect of the i-th segment of a substituent. The i-th segment consists of the i-th atom of the longest chain in the substituent and the groups attached to it. The MSI principle is assumed to apply and the segment is assigned the conformation that gives it the smallest possible steric effect.

MSI principle The principle of minimal steric interaction which states that the preferred conformation of a group is that which results in the smallest possible steric effect.

Intermolecular force parameterization

α A polarizability parameter defined as the difference between the group molar refractivities for the group X and for H divided by 100. Many other polarizability

parameters, such as the van der Waals volume, the group molar volume and the parachor, can be used in its place. All of these polarizability parameters are very highly linear in each other.

n_H A hydrogen-bonding parameter which represents the lone-pair acceptor (proton donor) capability of a group. It is defined as the number of OH and/or NH bonds in the group.

n_n A hydrogen-bonding parameter which represents the lone-pair donor (proton acceptor) capability of the group. It is defined as the number of lone pairs on O and/or N atoms in the group.

i A parameter which represents ion–dipole and ion–induced dipole interactions. It is defined as one for ionic groups and 0 for nonionic groups.

n_D A charge transfer donor parameter which takes the values 1 when the substituent can act as a charge transfer donor and 0 when it cannot.

n_A A charge transfer acceptor parameter which takes the values 1 when the substituent can act as a charge transfer acceptor and 0 when it cannot.

IMF equation A multiparametric equation which models phenomena that are a function of the difference in intermolecular forces between an initial and a final state.

Statistics

Correlation equation An equation with which a data set is correlated by simple (one parameter) or multiple (two or more parameters) linear regression analysis.

Regression equation The equation obtained by the correlation of a data set with a correlation equation.

n The number of data points in a data set.

Degrees of freedom (DF) Defined as the number of data points (n) minus the number of parameters (N_p), plus 1 [$DF = n - (N_p + 1)$].

F statistic A statistic which is used as a measure of the goodness of fit of a data set to a correlation equation. The larger the value of F, the better the fit. Confidence levels can be assigned by comparing the F value calculated with the values in an F table for the N_p and DF values of the data set.

$100R^2$ A statistic which represents the percent of the variance of the data accounted for by the regression equation. It is a measure of the goodness of fit.

S_{est} The standard error of the estimate. It is a measure of the error to be expected in predicting a value of the dependent variable from the appropriate parameter values.

S^0 Defined as the ratio of S_{est} to the root-mean-square of the data. It is a measure of the goodness of fit. The smaller the value of S^0, the better the fit.

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CHAPTER **16**

Acidity of alkenes and polyenes

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I. INTRODUCTION

Little quantitative data, either experimental or theoretical, are available on the acidities of dienes and polyenes. Accordingly, this chapter will review recent work on the acidities of alkenes and the data available on dienes and polyenes will be placed in this context.

Alkenes frequently have two kinds of C−H bonds, vinyl and allyl, that are generally more acidic than the C−H bonds of saturated alkanes. Quantitative measures of acidity are related to the chemistry of the corresponding carbanions and carbanion salts or organometallic compounds. Several methods have been used for the study of anions in the gas phase[1]. For many acids it is possible to measure equilibrium constants for equilibria of the type in equation 1. From such equilibrium constants with compounds RH of independently known gas-phase acidity, it has been possible to determine the acidities of a wide range of compounds[2].

$$RH + R'^{-} \rightleftharpoons R^{-} + R'H \tag{1}$$

An alternative approach to acidities is via a thermodynamic cycle using the bond dissociation energy (DH°), electron affinity (EA) and ionization potential (IP) as follows:

$$\begin{array}{ll} AH \longrightarrow A^{\bullet} + H^{\bullet} & DH^{\circ} \\ A^{\bullet} + e^{-} \longrightarrow A^{-} & -EA \\ H^{\bullet} \longrightarrow H^{+} + e^{-} & IP \\ \hline AH \longrightarrow A^{-} + H^{+} & \Delta H^{\circ} = \text{Acidity} \end{array}$$

$$\therefore \Delta H^{\circ}_{\text{acid}} = DH^{\circ}(\text{A}{-}\text{H}) + \text{IP}(\text{H}^{\bullet}) - \text{EA}(\text{A}^{\bullet})$$

Thus, acidity can be determined from independent measures of the bond dissociation energy and electron affinity, or the acidity provides a measure of the electron affinity of the corresponding radical if the bond dissociation energy is known.

Alkenes are not acidic enough for their acidities to be measured in terms of the usual solution definition of dissociation into anion and proton (equation 2).

$$\text{RH} \rightleftharpoons \text{R}^{-} + \text{H}^{+} \tag{2}$$

$$K_{\text{eq}} = [\text{R}^{-}][\text{H}^{+}]/[\text{RH}]$$

Such equilibrium constants, K_{eq}, are known only for highly conjugated carbanions, such as in cyclopentadienyl anion in water or triphenylallyl anion in DMSO[3]. Some values are known for equilibrium constants and enthalpies of equation 1 in the gas phase. Additional energies are available for many compounds by computation — with modern methods, computed energies for equation 2 are reliable to a few kcal mol^{-1}.

Other experimental values are available for *ion pair acidities* defined by the transmetallation reaction of equation 3, where the acid R′H of known pK_{a} serves as a reference, and are thermodynamic in nature.

$$\text{RH} + \text{R}'^{-}\text{M}^{+} \rightleftharpoons \text{R}^{-}\text{M}^{+} + \text{R}'\text{H} \tag{3}$$

$$-\log K = \text{p}K_{\text{RH}} - \text{p}K_{\text{R}'\text{H}}$$

These equilibria give directly only acidity differences between RH and R′H and can vary with solvent and counterion. The corresponding $-\log K$ values have been converted to pK scales by choosing one compound as the standard and referring others to it. The standard chosen for tetrahydrofuran (THF) solutions is fluorene and it is assigned a pK of 22.9, its value in the DMSO scale (statistically corrected per hydrogen; for fluorene the measured pK is 22.6)[3,4].

Finally, in many cases the acidity equilibria cannot be measured but the *rate* of proton transfer or transmetallation can be measured to give an *ionic* or *ion pair kinetic acidity*. Studies using the rates of proton transfer have included the use of isotopes such as tritium and deuterium[5,6]. The rate is then used to calculate the Brønsted slope, α, by plotting the logarithm of the proton transfer rate against the pK_{a}, as determined by the equilibrium acidity, for a series of compounds. From this plot, the approximate pK_{a} of an unknown compound can be determined by comparison of the same type of compounds.

Alkenes and polyalkenes have two fundamentally different types of relatively acidic protons, the vinyl and allylic hydrogens. Vinyl hydrogens are bound by approximately sp^2 hybrid orbitals on carbon and the corresponding carbanions are relatively localized; their relative acidity is due in part to the higher degree of s-character in the carbon orbital of the vinyl C−H bond. The allylic C−H bond is conjugated to the double bond and the corresponding carbanions are delocalized; the higher acidity of these protons stems primarily from such charge delocalization in the corresponding carbanion. These two types of protons will be treated separately in the following sections.

II. VINYL HYDROGENS

A. Gas-phase Acidities

Acetylene is sufficiently acidic to allow application of the gas-phase proton transfer equilibrium method described in equation 1[7]. For ethylene, the equilibrium constant was determined from the kinetics of reaction in both directions with NH_2^-[8]. Since the acidity of ammonia is known accurately, that of ethylene can be determined. This method actually gives ΔG_{acid} at the temperature of the measurement. Use of known entropies allows the calculation of ΔH_{acid} from $\Delta G = \Delta H - T\Delta S$. The value of ΔH_{acid} found for ethylene is 409.4 ± 0.6 kcal mol^{-1}. But hydrocarbons in general, and ethylene in particular, are so weakly acidic that such equilibria are generally not observable. From net proton transfers that are observed it is possible sometimes to put limits on the acidity range. Thus, ethylene is not deprotonated by hydroxide ion whereas allene and propene are[9]; consequently, ethylene is less acidic than water and allene and propene (undoubtedly the allylic proton) are more acidic. Unfortunately, the acidity of no other alkene is known as precisely as that of ethylene.

A further measure of acidity is provided by rates of deuterium exchange between a labeled base such as DO^- and a proton acid. The mechanism involves exchange within weak ion–molecule encounter complexes as shown in equation 4.

$$RH + DO^- \rightleftharpoons RH \cdot DO^- \rightleftharpoons R^- \cdot DOH \rightleftharpoons RD \cdot HO^- \rightleftharpoons RD + HO^- \quad (4)$$

Using a selected ion flow tube (SIFT) technique, DePuy and coworkers studied such rates of deuterium–hydrogen exchange for a series of neutral carbon acids[10]. Table 1 contains some selected rates of exchange with DO^- from DePuy's work; these rates are approximate measures of relative acidity in the gas phase.

Accurate values of these acidities are not known experimentally because these compounds are in the weakly acidic range, but some qualitative conclusions can be made. For example, on bombardment of butadiene or methyl vinyl ether with NH_2^-, the corresponding deprotonated anions (R^-) were present but not in the case of *tert*-butylethylene. Butadiene and methyl vinyl ether are therefore more acidic than *tert*-butylethylene. The

TABLE 1. Selected rate constants for the deuterium isotope exchange reactions, $DO^- + MH \longrightarrow HO^- + RD$ at 299 ($\pm$1) K

RH	k_{obsd}[a]	$\Delta[\Delta H_{acid}]$[b] kcal mol^{-1}
$H_2C{=}CHCH{=}CH_2$	9.6	<12.8
$H_2C{=}CHOCH_3$	10	<12.8
Norbornadiene	10	11.2[c]
$C_6H_5C(CH_3)_3$	19	<12.8
$H_2C{=}CHC(CH_3)_3$	1.1	<12.8
CH_4	$\leqslant$0.002	25.8[d]
CH_3OCH_3	$\leqslant$0.003	>12.8
$H_2C{=}CH_2$	$\leqslant$0.002	>12.8
$H_2C{=}O$	exchange observed	<12.8

[a] In units of 10^{-10}cm^3 particle^{-1} s^{-1}.
[b] Relative value to that in water.
[c] Reference 11.
[d] Reference 12.

protons at the 2- (or β) C positions of butadiene and the proton on the carbon adjacent to the oxygen of methyl vinyl ether were found to be kinetically more acidic than the protons at other positions by labeling experiments. The greater acidity observed for *tert*-butylethylene relative to ethylene was attributed to the charge stabilizing polarization effect of the *tert*-butyl group. Further investigation of the mechanism for isotope exchange showed that the acidity of ethylene is close to that of ammonia ($\Delta H_{\text{acid}} = 403.6$ kcal mol^{-1}) because the vinyl anion is detected in other SIFT experiments but is produced at a slow rate.

Alternatively, some conclusions can be derived from the relative reactivities of carbanions. For example, DePuy and colleagues[13] made use of a clever method involving reactions of silanes with hydroxide ion to deduce acidities of such weak acids as alkanes and ethylene. The silane reacts with hydroxide ion to form a pentacoordinate anion that ejects a carbanion held as a complex with the hydroxysilane; rapid proton transfer gives the stable silanoxide ion and the carbon acid (equation 5).

$$HO^- + (CH_3)_3SiR \longrightarrow [(CH_3)_3SiOH \cdots R]^- \longrightarrow (CH_3)_3SiO^- + RH \qquad (5)$$

The relative amounts of $(CH_3)_3SiO^-$ or $R(CH_3)_2SiO^-$ produced were assumed to be inversely proportional to the basicities of R^- and $CH_3{}^-$ and were used to determine acidities of RH by comparison with the known pK_a values of methane and benzene. Some derived values are summarized in Table 2. The reliability of this method can be judged by noting that the value for ethylene differs by only 2 kcal mol^{-1} from the more accurate value described above. The methyl hydrogen in 1-butene is 8 kcal mol^{-1} more acidic than ethane, undoubtedly because of the electron-attracting inductive effect of the vinyl group. The 2-H in propene is also found to be more acidic than the hydrogen of ethylene, showing again that polarizable alkyl groups appear to stabilize carbanions in the gas phase. The DePuy group points out that one possible problem with this method is that the carbanions are not formed free but rather within a complex with the silanol, and are essentially solvated by the silanol[13].

Another measurement of the pK_a for ethylene comes from the formation of carbanions in the gas phase by decarboxylation of carboxylate anions[14]. Carbanions that are too basic will not form in this way; the corresponding carboxylates do not decarboxylate. From the energy thresholds of such decarboxylations Graul and Squires estimated ΔH_{acid} of ethylene <401 kcal mol^{-1}, but this value differs substantially from the accepted value of 409.4 kcal mol^{-1}.

Few other alkenes have been studied. Norbornadiene is deprotonated by $NH_2{}^-$ but not by H^-[11]. Additional bracketing experiments by Lee and Squires provided estimates

TABLE 2. Acidities of RH from reaction of $(CH_3)_3SiR$ with OH^-[13a]

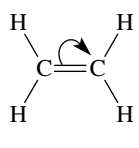
MH	$\Delta H^\circ_{\text{acid}}$ (kcal mol^{-1})
CH_4	416.6
C_6H_6	400.7
C_2H_6	420.1
n-C_4H_{10}(CH_3-H)	412.0
C_2H_4	407.5
$CH_2{=}CHCH_3$(CH_3-H)	405.8

[a]The known acidities of benzene and methane are used as standards for the others.

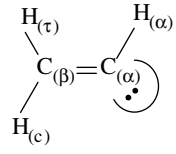
of ΔH_{acid} of norbornene equal to 401 kcal mol^{-1} and of norbornadiene equal to 398 kcal mol^{-1}[15].

B. Theory

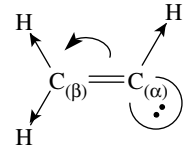
Scheiner and Wang have calculated the geometries of ethylene **1** and vinyl anion **2** at the Self-Consistent Field (SCF) Hartree–Fock level with a 6-31+G** basis set[16]. Both structures are planar (Table 3). Their results differ little from much earlier calculations of Williams and Streitwieser[17]. The β-methylene group of ethylene is almost unchanged on deprotonation. The $C_{(\beta)}-H$ bond lengths elongate by only 0.01–0.02 Å and only one angle changes by as much as 4° ($\beta = \angle C_{(\alpha)}C_{(\beta)}H_{(c)}$). The elongation of the double bond of the vinyl anion is also quite small, 0.034 Å. The largest changes are with the $C_{(\alpha)}-H_{(\alpha)}$ bond length and the $\angle C_{(\alpha)}C_{(\beta)}H_{(\alpha)}$ angle, 0.031 Å and 13°, respectively. According to Mulliken populations, the negative charge is divided almost equally between the α and β positions; however, there is a difference between the σ and π electronic populations. $C_{(\alpha)}$ has a higher σ charge than in ethylene but has a low π electron population; the reverse is true for $C_{(\beta)}$. The electron density function shows that removal of the vinyl proton and formation of the lone pair on carbon polarizes the electrons in the double bond, an effect that can be symbolized as **3**. Much of the increased electron density, however, is associated with the hydrogens[18], a polarization effect that is also symbolized in **3**. Williams and Streitwieser accordingly suggested that the relative acidities of sp^n localized systems (i.e. ethane, ethylene and acetylene) might be due not only to the amount of s-character of the lone pair, but also to the polarizability of the π electrons[17].



(1)



(2)



(3)

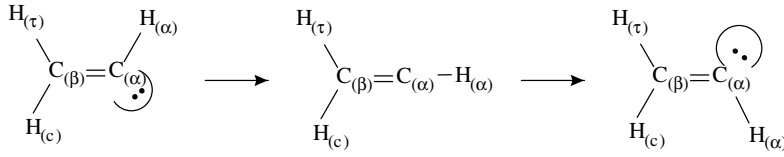
The energy barrier calculated for inversion of the vinyl anion (**2** ⟶ **2′**) by changing ($C_{(\beta)}C_{(\alpha)}H_{(\alpha)}$) through 180° in its linear transition state (**2a**), 34 kcal mol^{-1}, is in good agreement with the previously calculated value (SCF-LCAO-MO) of 39 kcal mol^{-1} by Lehn and coworkers[19]. The corresponding SCF and MP2 energies for the optimized geometries at 6-31+G** as well as the corresponding deprotonation energies are given in Table 4.

The calculated deprotonation energies of ethane, ethylene and acetylene by SCF Hartree–Fock (HF) and MP2 methods follow the expected order: 456, 455 (basis

TABLE 3. Bond distances (in Å) and angles (in degrees) in ethylene, **1**, and vinyl anion, **2**[a]

Compounds	C–H bond distances	C=C bond distances	∠CCH angles
1	1.076	1.321	121.7
2	$C_{(\beta)}-H_{(\tau)}$ 1.087	$C_{(\alpha)}-C_{(\beta)}$ 1.354	$\angle C_{(\alpha)}C_{(\beta)}H_{(\tau)}$ 121.6
	$C_{(\beta)}-H_{(c)}$ 1.096		$\angle C_{(\alpha)}C_{(\beta)}H_{(c)}$ 125.5
	$C_{(\alpha)}-H_{(\alpha)}$ 1.107		$\angle C_{(\alpha)}C_{(\beta)}H_{(\alpha)}$ 108.6

[a]Reference 16.



(2) **(2a)** **(2′)**

TABLE 4. SCF and MP2 energies for ethylene and vinyl anion and the deprotonation energy (ΔE_{acid}) for ethylene[a,b]

	Absolute SCF energy[c,d]	Absolute MP2 energy[c,d]	G2 total energy[d,e,f]	SCF ΔE_{acid}[g]	MP2 ΔE_{acid}[g]	G2 ΔE_{acid}[b]	expt[h]
$H_2C{=}CH_2$	−78.04307	−78.32274	(−78.41593) −78.41193	422.0	410.8[i]	(407.0) 409.0	409.4
$H_2C{=}CH^-$	−77.36881	−77.65292	(−77.76722) −77.76326				

[a] Reference 16.
[b] Reference 20.
[c] 6-31+G** basis set.
[d] Energy in Hartrees.
[e] Corrected for basis set superposition error (BSSE).
[f] Energy in parentheses is calculated at 0 K, the other at 298 K.
[g] Energy in kcal mol^{-1}.
[h] Reference 8.
[i] Calculated value at MP2/6-31+G* = 407.7 kcal mol^{-1}; the corresponding MP4 value is 408.7 kcal mol^{-1}[21].

set 6-31+G*)[22]; 422, 410.8 (6-31+G**)[16]; and 380.3, 384.8 (6-31+G**) kcal mol^{-1}[23], respectively. The added correlation energy of the MP2 method has a variable effect on these energies. Saunders[24] tested a number of theoretical levels and found best overall agreement with the 6-31+G* + MP2 level. This method gave $\Delta H^\circ_{acid} = 408.6$ kcal mol^{-1} for ethylene, in good agreement with the experimental values. Smith and Radom[20] used G2 theory to calculate the absolute acidity resulting in $\Delta H^\circ_{acid} = 409.0$ kcal mol^{-1} and $\Delta H^\circ_{acid} = 378.0$ kcal mol^{-1} for ethylene and acetylene, respectively. These theoretical results are in excellent agreement with experiment[8].

C. Vinylic Anions in Solution

A few measurements are available that relate to the ion pair acidity of ethylene and some other alkenes. Ethylene is difficult to metallate directly, but vinyl bromides and iodides undergo facile transmetallation with alkyllithium reagents. Applequist and O'Brien determined the equilibrium constants of transmetallation exchange reactions as a measure of relative acidity (equations 6 and 7)[25].

$$RLi + R'I \overset{K_{obsd}}{\rightleftharpoons} RI + R'Li \tag{6}$$

$$K_{obsd} = [RI][R'Li]/[RLi][R'I] \tag{7}$$

For R′ = phenyl and R = vinyl, the corresponding $\log K_{obsd}$ is -2.41 ± 0.92; that is, by this measure ethylene is more acidic than benzene with ether as the solvent. It should be

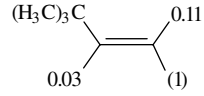


FIGURE 1. Relative rates of tritium exchange with cesium cyclohexylamide in cyclohexylamine[31]

noted that measurements of ion pair acidities may be complicated by aggregation of the phenyllithium and vinyllithium ion pairs which was not taken into account, although the equilibrium constants measured were not sensitive to solvent.

Cram[26] had developed an acidity scale based on the ion pair acidity and used this and other measures (such as the acidity function technique) in compiling his so-called MSAD acidity scale, named after W. K. McEwen, A. Streitwieser, D. E. Applequist and R. E. Dessy. The scale used 9-phenylfluorene ($pK_a = 18.5$) as its standard and is considered at least approximately to refer to the dilute aqueous solution as the standard state. On this scale ethylene is assigned a pK value 0.5 units lower than benzene; however, in another early compilation[27] ethylene is 1 pK unit higher than benzene. In an updated MSAD scale, ethylene was found to be 1 pK unit less acidic than benzene[6,28,29].

Kinetic acidities provide another measure. The rate of isotope exchange of ethylene-d_4 with cesium cyclohexylamide (CsCHA) in cyclohexylamine (CHA)[6] is about 0.1 the rate of exchange of benzene. The corresponding exchange of *trans*-3,3-dimethyl-1-butene-1-d is about 0.02 that of benzene-d, and shows that the *β-tert*-butyl group exerts an electron-donating inductive effect[5,30]. Other positions in *tert*-butylethylene show the effects of steric hindrance to exchange (Figure 1)[31]. Note that this effect differs from that in the gas phase (*vide supra*).

Norbornadiene is readily metallated by butyllithium, in agreement with its higher gas-phase acidity than ethylene (*vide supra*)[32].

III. ALLYL HYDROGENS

Vinyl C−H bonds are more acidic than the C−H bonds in saturated hydrocarbons because of their higher s-character and the polarizability of the double bond, but the corresponding carbanions are essentially localized. Allylic C−H bonds have the s-character of saturated hydrocarbons, but the resulting carbanions now have the possibility of additional stabilization by delocalization. Allylic positions are thus generally the most acidic in alkenes.

A. Gas-phase Acidities

One of the earliest measurements of the gas-phase equilibrium acidity of propene involved measuring the rates of reaction of propene with hydroxide ion in both directions[33]. The resulting equilibrium constant gave $\Delta H_{acid} = 391 \pm 1$ kcal mol^{-1}. In the case of ethylene, the acidity and independently measured electron affinity of vinyl radical were used to determine the bond dissociation energy, a quantity difficult to obtain accurately by other means[8].

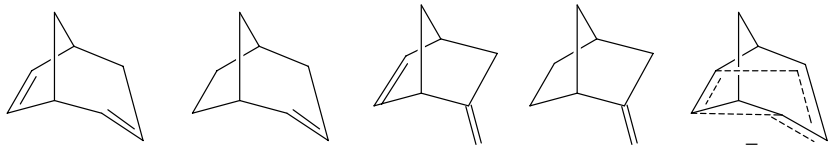
Another early acidity investigation of propene by the thermodynamic method involved the determination of the electron affinity of allyl radical by photodetachment from allyl anion[34]. Extrapolation of the data to a photodetachment threshold gave an electron affinity (EA) of allyl radical of 0.55 eV which, combined with a bond dissociation energy of allyl-H of 89 kcal mol^{-1}, gave $\Delta H_{acid} = 390$ kcal mol^{-1}.

The same method was used to determine the electron affinities of pentadienyl radical (0.91 eV) and heptatrienyl radical (1.27 eV)[35]. The corresponding bond dissociation

energies are not known accurately. Using a reasonable value of 76 kcal mol^{-1} for $CH_2{=}CHCH{=}CHCH_2{-}H$ gives a corresponding $\Delta H_{acid} = 368$ kcal mol^{-1}.

In studies of substituent effects, Bartmess and Burnham measured the acidities of several 2-substituted propenes in the gas phase[36]. Electron-attracting groups have the expected acidity-enhancing effect. 2-Methylpropene was found to be 0.6 kcal mol^{-1} more acidic than propene. Isoprene (2-methylbutadiene) was found to be 6 kcal mol^{-1} more acidic than propene but the experimental error was almost as large. The acidity of isoprene of 385 kcal mol^{-1} is substantially higher than that of its conjugated isomer, 1,3-pentadiene, quoted above as 368 kcal mol^{-1}. Dahlke and Kass studied 3-fluoro-, 3-methoxy- and 3-(dimethylamino)-propene and found almost no change in the acidity of propene within their experimental uncertainty of ± 4 kcal mol^{-1}[37].

Lee and Squires determined the gas-phase acidities of a number of cyclic alkenes and dienes including the bicyclic compounds **4**, **5**, **6** and **7**[15]. Their values are summarized in Table 5 and have estimated uncertainties of 1–2 kcal mol^{-1}. The relatively high acidity of **4** was attributed to bishomoconjugation of the double bond with the allyl anion, as shown in **8**[15].



(4) **(5)** **(6)** **(7)** **(8)**

B. Theory

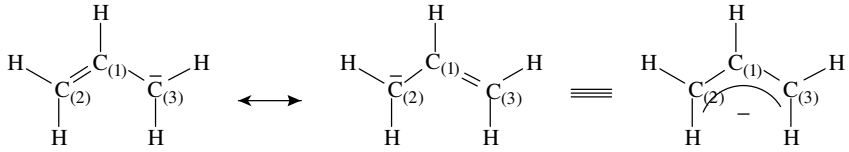
Extensive theoretical studies have been carried out to probe the nature of the allyl anion. These studies supplement and extend the experimental results. Allyl anion is of special interest because it is the simplest π-delocalized carbanion with 4 electrons and 3 p_π-centers. Much recent theoretical discussion has concerned the role of resonance in the stabilization of such conjugated systems, a stabilization defined as the enthalpy difference between the localized double-bonded system and its conjugated state. The stabilization of allyl anion has generally been attributed to the delocalization of charge associated

TABLE 5. Gas-phase acidities of some cyclic and bicyclic unsaturated hydrocarbons[a]

Compound	ΔH_{acid} (kcal mol^{-1})
4	380
5	389
6	389
7	389
Cyclohexene	$\geqslant$387
1,3-Cyclohexadiene	372
Cyclooctene	$\leqslant$386
1,3-Cyclooctadiene	375
1,5-Cyclooctadiene	375

[a]Reference 15.

with the resonance structures **9a** and **9b.** A recent argument based on the magnitudes of stretching vibrations has nevertheless supported some new concepts, namely that it is the σ-system which imposes the equal CC bond lengths[38]. The asymmetric stretching modes of benzene and allyl cation and anion to give alternating double and single bonds are enhanced by the π-electronic systems.



(9a) **(9b)**

In an attempt to assess the importance of the delocalization energies in the allyl system, Gobbi and Frenking have computed various distorted structures of allyl anion and rotational transition states, such as **11a–11d**, and have compared the relative energies with the corresponding allyl cations, **10a–10c**[39]. The structures are shown in Figure 2 and the energies are summarized in Table 6.

The allyl anion ground-state conformation is C_{2v} at 6-31G HF and C_2 at MP2. The energy difference, however, is only 0.2 kcal mol^{-1} and when the zero-point energy (ZPE)

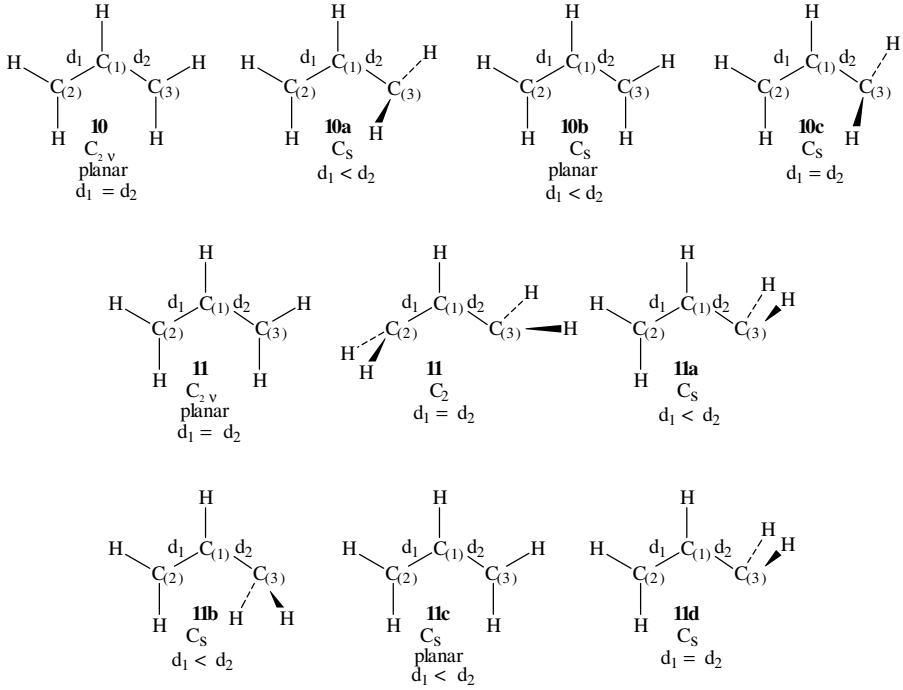


FIGURE 2. Structures of calculated allyl cations, **10**, and allyl anions, **11**

TABLE 6. Calculated results for allyl cations, **10**, and allyl anions, **11**[a]

	10	**10a**	**10b**	**10c**	**11**	**11a**	**11b**	**11c**	**11d**
Symmetry	C_{2v}	C_s	C_s	C_s	C_2 (C_{2v})	C_s	C_s	C_s	C_s
E_{rel}	(0.0)	(34.0)	(4.0)	(38.3)	0.0	22.8	25.3	(7.7)	(27.9)
	0.0	*37.8*	*4.4*	*38.7*	(0.0)	(20.4)	(22.7)	*7.4*	*28.0*
					0.0	*23.1*	*25.4*		
$C_{(1)}-C_{(2)}$	1.382	(1.318)	(1.318)	(1.373)	1.393	1.348	1.351	(1.331)	(1.382)
(d_1)	(1.373)				(1.382)	(1.331)	(1.334)		
$C_{(1)}-C_{(3)}$	1.382	(1.445)	(1.445)	(1.373)	1.393	1.493	1.503	(1.508)	(1.382)
(d_2)	(1.373)				(1.382)	(1.508)	(1.518)		

[a] E_{rel} is the energy relative to the lowest-energy conformation (in kcal mol^{-1}); d_1 and d_2 are calculated bond lengths (in Å). Energies and geometries are given at MP2/6-31G(d); in parentheses for HF/6-31G(d); in italics for MP2/6-31G(d)//HF/6-31G(d).

correction is taken into account, the C_{2v} structure is the minimum. Rotation of the methylene group can proceed through either the **11a** or **11b** transition states. The inward rotation **(11b)** is energetically more favored by 2.3 kcal mol^{-1} with an increase in the negative charge on $C_{(3)}$ of 0.162 *e* (topological analysis) and 0.274 *e* (NBO) accompanying the localization of bonds. For $C_{(1)}-C_{(2)}$ and $C_{(1)}-C_{(3)}$ using the numbering scheme of Frenking, the bond order P_{CC} is 1.832 (more double bond-like) and 1.102 (more single bond-like), respectively. Although the barrier to rotation about the $C_{(1)}-C_{(3)}$ bond in allyl anion is quite large, the distortion energy of the planar structures is relatively small (7.4 kcal mol^{-1}) but higher than in allyl cation by 3.1 kcal mol^{-1}.

With respect to the σ and π interactions towards the geometry in the allyl system, Frenking separated the distortions into the rotation of the methylene group and bond distances. The former 'turns off' π-conjugation while bond-length distortion only changes the π-interactions. From both the topological[40] and Natural Bond Orbital (NBO)[41] analysis, the negative charge resides mostly on the terminal carbons: $q(\rho(\mathbf{r}))$ and q(NBO) for $C_{(2)}$ and $C_{(3)}$ in reference to Frenking's numbering scheme (as pictured in Figure 2) are -0.328 and -0.817, respectively; and including the hydrogens, the charge for $C_{(2)}$ and $C_{(3)}$ is -0.446 and -0.512. Note that the two methods give reasonable agreement for the CH_2 groups but differ in the distribution of charge between C and H.

A second argument concerning resonance stabilization centered on a stabilizing effect in the allyl anion. Wiberg and coworkers challenged the generally accepted point that allyl anion is stabilized by electron delocalization[42]. Their approach is based on large basis-set calculations of allyl cation and anion and their localized counterparts (see Table 7). The reaction of hydride transfer from propene to propyl cation to form the unconjugated allyl cation was computed to be endothermic. The corresponding proton transfer from propene to give unconjugated allyl anion, however, was found to be exothermic. Both effects were attributed to the electron-attracting inductive effect of the C−C double bond. The calculated rotational barrier of allyl anion of 19 kcal mol^{-1} is 17 kcal mol^{-1} lower than for allyl cation. The cation has a calculated barrier of 36 kcal mol^{-1}, but the experimentally approximated barrier is 25 kcal mol^{-1} with a resonance energy stabilization range of 8–18 kcal mol^{-1}[43].

Wiberg split the stabilization of the energy barrier into two parts: (a) electrostatic energy in the planar form and (b) delocalization. Electrostatic stabilization lowers the energy of the planar form because the charge is spread over three atoms rather than being localized on one carbon in the rotated form. An estimation of the electrostatic stabilization was made by calculating a model, methane, for the localized anion and yielded a 23 kcal mol^{-1}

TABLE 7. Calculated ionization energies[a] and energy changes for several reactions[b]

Reaction	ΔE (kcal mol^{-1})						
		6-311++G**//6-31G*					
	6-31G*//6-31G*	RHF	MP2	MP3	MP4	ΔH_{calc}	ΔH_{obs}
propane ⟶ propyl$^+$ + H$^-$	307.5	267.3	288.3	285.8	284.8	276	274 ± 3[c]
propene ⟶ allyl$^+$ + H$^-$	286.0	248.7	268.1	266.9	265.1	258	256 ± 3
propane ⟶ propyl$^-$ + H$^+$	452.6	436.1	425.9	430.1	426.9	417	419 ± 3
propene ⟶ allyl$^-$ + H$^+$	425.4	408.0	399.8	405.2	402.8	392	390 ± 3
propyl$^+$ + propene ⟶ unconj allyl$^+$ + propane	+12.5	+14.5	+16.3	+15.5	+15.9		
propyl$^-$ + propene ⟶ uncon allyl$^-$ + propane	−6.7	−6.8	−5.4	−5.5	−5.1		
unconj allyl$^+$ ⟶ conj allyl$^+$	−34.0	−33.1	−36.5	−34.4	−35.6		
unconj allyl$^-$ ⟶ conj allyl$^-$	−20.4	−21.3	−20.8	−19.4	−19.0		

[a]In kcal mol^{-1}.
[b]Abbreviations: unconj stands for unconjugated and conj stands for conjugated.
[c]The experimental value given for 1-propyl cation is actually that for the ethyl cation. The values should not be much different, for the open propyl cation will receive a small stabilization because of its greater size, but the experimentally studied ethyl cation has a small stabilization from bridging.

difference between the planar and rotated forms, which is close to the observed energy difference between the above two forms. Therefore, he attributed the rotational barrier in the allyl anion to the change in electrostatic energy rather than to resonance stabilization, and concluded: 'whereas the cation has significant resonance stabilization, the anion has little stabilization'[42].

Frenking argued with Wiberg's conclusion that electrostatic effects dominate the barrier in allyl anion rather than resonance stabilization. Among allyl systems, the highest barrier to rotation is that of the allyl cation with the largest change in the charge differences on the CH_2 group in the rotated form (see Table 8). The lowest rotational barrier is that of the allyl radical with basically no change in charge distribution. The barrier for allyl anion lies between that of the cation and radical, but with a significant amount of charge redistribution.

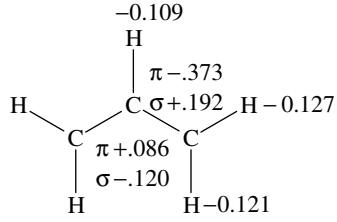
How does this address the difference in the barrier to rotation between allyl cation and anion? The CH_2 methylene group is planar in the transition state in the case of the cation **(10c)** but pyramidal in the anion **(11a)**. Frenking calculated the energy for the transition state of the anion with a planar CH_2 group at the MP2/6-31G(d)//HF/6-31G(d) level to be 9.8 kcal mol^{-1} higher than the pyramidal CH_2 group in **11a**, but 32.9 kcal mol^{-1} higher than the ground-state structure, **11**. Therefore, the total energy for the rotation of the allyl anion with a planar CH_2 group is quite comparable to that of allyl cation. Pyramidalization clearly stabilizes the anion transition state and lowers the rotational barrier.

TABLE 8. Calculated energies (ΔE) for barrier to rotation in the allyl systems and charge differences (Δq) for the CH_2 groups[a]

	Allyl cation, **10**	Allyl radical	Allyl anion, **11**
ΔE (kcal mol^{-1})	37.8	12.6	23.1
Δq(NBO)	0.33	0.02	0.27
$\Delta q(\rho(\mathbf{r}))$	0.17	0.02	0.16

[a]Reference 39.

The actual charge distribution in the allyl anion is of further interest in this connection. The simple resonance structures (**9a** and **9b**) suggest that the negative charge is solely on the two terminal carbons. The actual charge distribution as given by Bader's topological analysis[42] shown in **12** gives a much different picture: the π and σ charges are shown for carbon. Note that 60% of the negative charge is carried by the hydrogens[18]. The terminal carbons have negative charge in the π-system, but the σ-system is positive; the reverse is true for the central carbon. This observation, that charge in one system polarizes the other, is becoming more common. Note also that even a classical electrostatic picture of π-polarization, as in **13**, would leave the central position with a positive charge.



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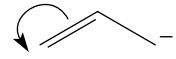


(13)

The theoretical studies of allyl anion lead naturally to those of metal salts and, in particular, allyllithium. Hommes and colleagues considered the effect of the metal on the structure of the allyl ion pair[44]. They calculated the energies of a series of alkali metals for the C_s symmetric bridged ('ion-pair') and C_s symmetric planar (covalent) species at the 6-31G** for C, H, Li and Na and at 6-31G* for Rb and Cs. The optimized structure of the allyl alkali metal is the bridged η^3 ion pair species (Table 9). As one proceeds down the Group I alkali metal column, the natural charge on the metal as well as $C_{(2)}$ becomes more positive and the charge on $C_{(1)}$ and $C_{(3)}$ becomes more negative, with the exception of the carbons in allylcesium. The structural features change as well; the M−C bond length and the CCC bond angle increases as the metal becomes larger. The structure of the metal salt is important because it will influence its behavior in reactions.

The rotational barriers increase from sodium to cesium to yield an estimate of the 'free' allyl anion barrier to rotation. The calculated barrier is higher than that determined experimentally. Hommes and colleagues proposed that the decrease could be due to solvation or dimerization. Considering both dimerization and solvation, the calculated barrier decreases by 5.5 and 0.5 kcal mol^{-1}, respectively.

The theoretical study of the structure of propene was then used as a model to calculate the effect of the structure on the proton affinity, and later to predict the acidity of similar systems such as cycloalkenes[46]. Deformation of the CCC angle as a function of the stability of the anion was probed, and the results were in agreement with the acidities of the hydrogens of propene. The allylic protons were found to be more acidic than the vinylic ones, which is in contrast to the results of Gründler[47].

C. Allylic Anions in Solution

Allyl anion is too strongly basic to be studied as the free anion in solution. Bordwell developed an acidity scale based on equation 1 in dimethyl sulfoxide (DMSO) at 25 °C[3] and applied the method to a number of more acidic substituted allylic systems. A summary of some results is shown in Table 10. DMSO is sufficiently polar that there is little ion

TABLE 9. Calculated energies and rotational barriers of η^3 and η^1 allyllithium and allylalkali metal compounds

Compound		Absolute energies[a]	ZPE[b,h]	rotational barriers	
				(calcd ΔE)[c]	(expl $\Delta G^{\ddagger}$)[c]
C_3H_5Li	η^3	124.32623[d]	45.8(0)		
	η^1	124.29554[d]	45.0(1)	18.5[d]	10.7[i]
$C_3H_5Li{-}OH_2$	η^3	200.56745[d]	61.9(0)		
	η^1	200.53708[d]	61.0(2)	18.2[d]	
$(C_3H_5Li)_2$	η^3	246.52231	93.9(0)[g]		
	η^1	246.50063	93.1(1)[g]	13.0[f]	
C_3H_5Na	η^3	278.70629[d]	44.6(0)		
	η^1	278.68461[d]	44.4(1)	13.4[d]	11.5[j]
C_3H_5K	η^3	715.42691[d,f]	44.3(0)		
	η^1	715.39919[d,f]	43.8(1)	17.4[d]	14.3, 16.7[i]
C_3H_5Rb	η^3	3052.62835[d,f]	44.2(0)		
	η^1	3052.59752[d,f]	43.8(1)	19.0[d]	18.1[j]
C_3H_5Cs	η^3	7665.39864[d,f]	44.0(0)		
	η^1	7665.36314[d,f]	43.5(1)	21.8[d]	18.0[i]
$C_3H_5^-$	η^1	116.88560[e]	39.9(0)[f]		
	syn	116.85163[e]	40.2(1)[f]	21.7[h]	
	anti	116.84806[e]	40.3(1)[f]	24.0[h]	

[a] Absolute energies in au.
[b] Zero-point energies.
[c] In kcal mol^{-1}.
[d] MP2(fc)/(6-31+G*).
[e] MP2(fu)/(6-31G*) (fu = full) with 6-31+G** basis sets on C used for $C_3H_5^-$.
[f] 3-21G.
[g] 6-31G* and Huzinaga basis sets used for K, Rb and Cs, 6-31+G* and 6-31+G** on C used for $C_3H_5^-$.
[h] 6-31+G**. Number of imaginary frequencies is given in parentheses: (1) a transition state; (2) a second-order saddle point.
[i] Reference 45.
[j] Reference 71.

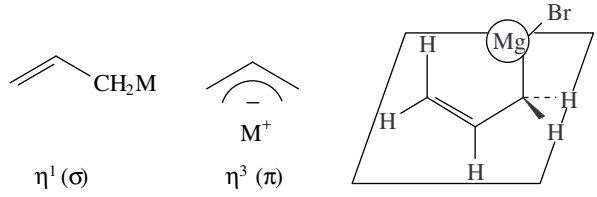
TABLE 10. Equilibrium acidities of selected allylic compounds in dimethyl sulfoxide at 25 °C[a]

Acid	pK_a[b]
$CH_2{=}CHCH_2NO_2$	7.7
$PhCH{=}CHCH_2SO_2Ph$	20.2
$CH_2{=}CHCH_2SO_2Ph$	22.5
$Ph_2C{=}CHCH_2Ph$	25.6[c]
$Ph_2C{=}CHCHPh_2$	25.8
$CH_2{=}CHCH_3$	(44)[d,e]

[a] Reference 3.
[b] pK_a values of acids forming chelating anions have been corrected for ion-pairing with K^+. Most pK_a values were measured by using two or more indicators or standard acids and are believed to be accurate to 0.1 unit.
[c] This number is comparable (26.76) to the cesium ion-pair acidity for the same compound measured in THF at 25 °C[49].
[d] Reference 50.
[e] Reference 48.

pairing and the results pertain to the ionic pK values with the dilute DMSO solution as the standard state. The results were extrapolated to give the approximate corresponding pK_a of propene[48]. The derived value of 44 is comparable to that of toluene.

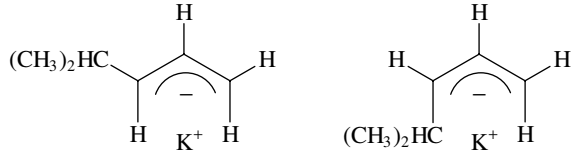
With less polar solvents and more basic allyl anions the compounds are present as ion pairs. The carbon–metal bond with the alkali and alkaline earth metals are known to have high ionic character. The allyl compounds behave accordingly as salts. The structures of allyl compounds of the alkali and alkaline earth metals are of two fundamental types, a η^1 (or σ) type, **14**, in which the metal cation is associated closely with a single terminal allylic carbon, and the η^3 (or π) type, **15**, in which the cation bridges the two terminal allylic positions.



(14) **(15)** **(16)**

Early NMR work by Roberts and coworkers[51–53] showed that allyl Grignard reagents **(16)** are of the σ type in which the metal migrates rapidly from one terminus to the other. This result was confirmed by more recent high resolution ^{13}C NMR work of Schlosser and Stähle[54].

In the case of allylpotassium, the metal complex exists as a symmetric π structure. No temperature dependence was shown by either ^{13}C NMR for $\Delta\delta[C_{(1)}-C_{(3)}]$ or by ^{1}H NMR for substitution with deuterium at $C_{(3)}$. Thompson and Ford measured experimentally a variety of allylalkali metal compounds using variable-temperature NMR in THF-d_8[45]. Addends such as TMEDA, hexamethylphosphoric triamide (HMPA), 15-crown-5-ether, [2.1.1]cryptand and n-butyllithium showed either no change in the spectrum or rapid decomposition of the complexing agent. Measurement of the populations of E **(17)** and Z **(18)** isomers of 1-isopropylallylpotassium showed the Z isomer to be more stable (Table 11).



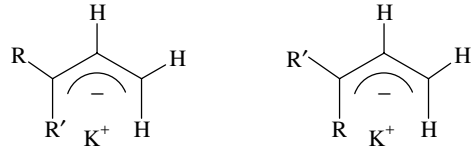
(17) **(18)**

Further investigation of allylpotassium complexes have shown that 2-isopropylallyl potassium does not show diastereotopism of the methyl groups at temperatures as low as $-155\,^{\circ}$C[54,59]. Therefore, the activation barrier for interconversion is on the order of 4 kcal mol^{-1} or lower. Both crotyl **(19)** and prenyl **(20)** potassium complexes are further examples of the preference for allylpotassium compounds to exist as symmetric π species. The potassium has the appropriate atomic radius to 'reach' both $C_{(1)}$ and $C_{(3)}$. No increase in stabilization is gained upon addition of solvent. Allylcesium behaves in the same manner. In general, the theoretically calculated rotational barriers (Table 9) are higher

TABLE 11. Experimental barriers to rotation

Compound		$\Delta G^{\neq}_c(T_c, {}^\circ C)$ (kcal mol^{-1})
Allyllithium		10.7 ± 0.2 (−51)
Allylpotassium		16.7 ± 0.2 (68)
Allylcesium		18.0 ± 0.3 (68)
2-Methylallylpotassium		15.9 ± 0.3 (51)
(*Z*)-1-Methylallylpotassium	$(C_{(1)}-C_{(2)})$	18–22[a]
	$(C_{(2)}-C_{(3)})$	17.0 ± 0.3 (68)
(*Z*)-1-Isopropylallylpotassium	$(C_{(1)}-C_{(2)})$	> 19.3 (68)
	$(C_{(2)}-C_{(3)})$	17.0 ± 0.3 (47)
(*E*)-1-Isopropylallylpotassium	$(C_{(2)}-C_{(3)})$	⩽ 14.0 (28)
2-Isopropylallylpotassium		< 4[b]
2-Isopropyl-1,3-diphenylallyl potassium		12.5[c]
(1,1,3,3-Tetramethylallyl)lithium		14[d]
exo-[1,1,3-Tris(trimethylsilyl)allyl]lithium		17[e]
1,3-Diphenylallylsodium		16.5 ± 0.2[f]

[a] Estimated; Reference 45.
[b] Reference 54.
[c] Reference 55.
[d] Reference 56.
[e] Reference 57.
[f] Reference 58.



(19) R = H, R′ = CH_3
(20) R = R′ = CH_3

than the experimentally determined ones. The discrepancy ranges from 0.9 kcal mol^{-1} for allylrubidium up to 7.8 kcal mol^{-1} for allyllithium.

Allyllithium is one of the most important complexes but is also more difficult to study. Schleyer and coworkers have shown recently that dynamic NMR studies of allyllithiums are complicated by aggregation[60]. As a result, the difference in the carbon signals from the isotopically labeled species is smaller than expected for two rapidly equilibrating nonsymmetric structures. The resulting variable-temperature NMR investigation also revealed that the lithium complex is unsymmetric with a low barrier to interconversion, but the disymmetry was attributed to aggregation. Allyllithium exists as a dimer at 165 K in tetrahydrofuran and becomes more aggregated at higher temperatures. Such aggregation also provides an explanation for the discrepancy between the calculated (17.7 kcal mol^{-1})[61] and experimental (10.7 ± 0.2[45] and 10.5 ± 0.2[62] kcal mol^{-1}) energies of activation for rotation of a terminal CH_2 group.

On substitution of allyllithium with methyl groups, the structures are distorted π complexes becoming more η^1-like. The previously described allyllithiums are contact ion pairs (CIP) whose dissociation is too low to permit study of the free carbanion. However, this is not the case for a more delocalized system such as 1,3-diphenylallyl whose lithium salts can exist as solvent separated ion pairs (SSIP) in ethereal solutions for which the organic moiety could be treated essentially as a free carbanion[55]; Boche and coworkers studied the effect of substitution at $C_{(2)}$ in their 1,3-diphenylallyl lithiums on the rotational barriers

and conformational preferences[55]. In the parent system, the more stable conformation of the allyl anion is the *exo,exo*-conformer. Upon substitution of larger groups such as phenyl and isopropyl at $C_{(2)}$, the *exo,endo*-conformer becomes more favorable. At the sterically demanding extreme where R = *tert*-butyl, the only conformer present is the *endo,endo*-structure. Therefore, the equilibrium of the interconversion is determined by the steric interaction between the R group at $C_{(2)}$ and the phenyl groups. The rotational energy barrier reflects the steric congestion upon substitution, increasing the ground-state energy conformation and decreasing the barrier, such as in the *tert*-butyl case (12.5 kcal mol^{-1}). The addition of HMPA has little effect and rules out ion pairing effects. In conclusion, these allyl anions are essentially SSIP or 'naked' in nature because there is little if no difference between the $\Delta G^{\ddagger}$ for 2-cyano-1,3-diphenylallyl anion in this study and of the lithium, sodium and potassium salts in DMSO[63,64]. In earlier experimental work of the rotational processes in these systems, Burley and Young found not only hindered rotation about the C−C bond of the allyl group in 2-methyl-1,3-diphenylallyl carbanion, but also about the C−ph bond in 2-methyl-1,3-diphenylallyl, 1,3-diphenylallyl and 1-methyl-1,3-diphenylallyl carbanions[65]. These interconversions are illustrated in Figure 3.

Streitwieser and Boerth studied the kinetic acidities of cycloalkenes with lithium cyclohexylamide (LiCHA) in cyclohexylamine for comparison with those of benzene and toluene[66]. The relative rates of deprotonation and the corresponding equilibrium p*K* values are tabulated in Table 12. These proton transfer transition states are stabilized by conjugation of the reacting C−H bond with the double bond.

In order to investigate the effect of chain length of alkenes upon acidity and aggregation, Thiele and Streitwieser probed the equilibrium acidity of a series of polyenes using UV VIS-spectroscopy in THF at 25 °C: Ph(CH=CH)$_n$CH$_2$Ph (n = 1, DP3; n = 2, DP5; n = 3, DP7; n = 4, DP9)[70]. The equilibrium acidity was determined using the transmetallation reaction of equation 3 with Cs^+ as the counterion. The results were consistent with

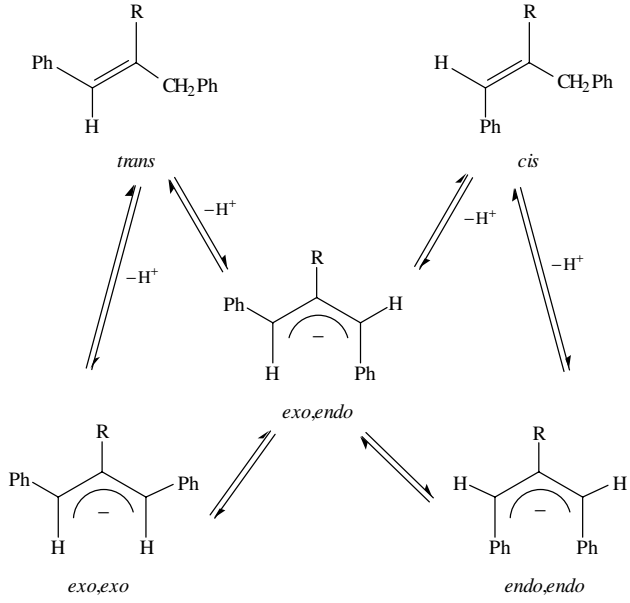


FIGURE 3. The proposed interconversion scheme for substituted 1,3-diphenylallyl anions

TABLE 12. Relative rates of deprotonation at 50 °C in cyclohexylamine, dihedral angle (C=C−C−H) as determined from force field calculations, and deduced equilibrium pK_{CsCHA} values for several carbon acids[a]

Compound	Relative rates	C=C−C−H[b]	pK_{CsCHA}
Cycloheptene	1	58.5°	
Cyclopentene	0.063	13.1°	44
Cyclohexene	0.193	123.5°	46
Cyclooctene	0.206	78.8°	
Benzene	0.505		43[c]
Toluene	119		41.2[d]

[a]Reference 66.
[b]Reference 67.
[c]Reference 68.
[d]Reference 69.

formation of monomers rather than higher-order aggregates. The increasing delocalization of charge was used to explain the decrease in pK_a with respect to chain length. These highly delocalized carbanions have less electrostatic attraction to cations and are more highly dissociated to the free ions in THF. The free anions have significantly different UV-VIS spectra and permitted the determination of the dissociation constants and the corresponding ionic pK values given in Table 13. These values are expected to apply to the DMSO solutions as well. The pK values correlate with various theoretical measures but also give a simple 'electron-in-a-box' type of correlation with the function $(n+8)^{-1}$, where n is the chain length and the '8' accounts for the effect of the phenyls on the size of the 'box'.

In the above work the available evidence suggests that the carbanions are in the fully extended conformation. Tolbert and Ogle[72] studied the same series of carbanions in DMSO solution by ^{13}C NMR spectroscopy and found only the fully extended conformations. This is the expected result on the basis of electron repulsion within the anions.

The unsubstituted pentadienyl anion also appears generally to be in the fully extended form, the so-called W-structure (Figure 4); examples are pentadienyllithium in THF[73]

TABLE 13. Compilation of the pK values for the cesium ion pair and free ion of polyenes in THF at 25 °C[a]

Compound	Cs ion pair pK	Free ion pK
DP3	27.85	26.17
DP5	25.62	23.79
DP7	24.14	21.91
DP9	23.01	20.46

[a]Reference 70.

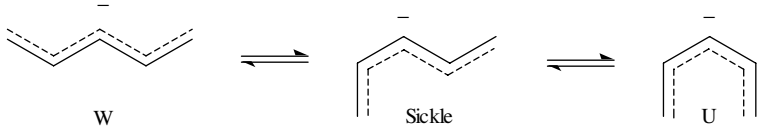


FIGURE 4. Stereoisomers of pentadienyl anion

and pentadienylpotassium in liquid ammonia[74]. In substituted pentadienyl systems, steric effects involving the substituents favor formation of the alternative S (Sickle) and U stereoisomers (Figure 4)[75].

IV. ACKNOWLEDGMENTS

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The Chemistry of Dienes and Polyenes. Volume 1
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CHAPTER **17**

The electrochemistry of dienes and polyenes

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I. INTRODUCTION

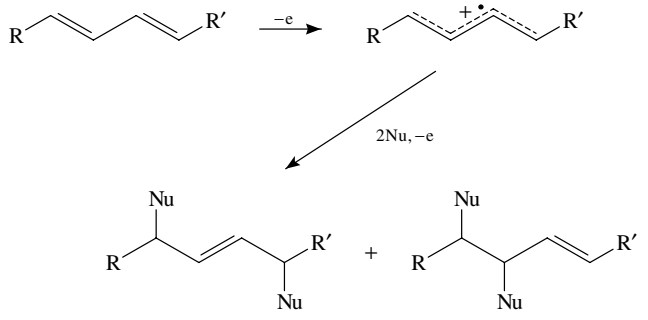
The electrochemical oxidation or reduction of dienes and polyenes is generally more useful than the corresponding reaction of monoolefins which is not substituted with activating groups, since the electrode potentials required in the reaction of dienes and polyenes are generally much lower than the potentials necessary in the reaction of monoolefins.

II. ANODIC OXIDATION

A. Conjugated Dienes

The anodic oxidation of conjugated dienes is much more easily achieved than the oxidation of monoolefins since the conjugation of the π-electron system lowers the oxidation potentials of the dienes. Several peak potentials for dienes are summarized in Table 1[1].

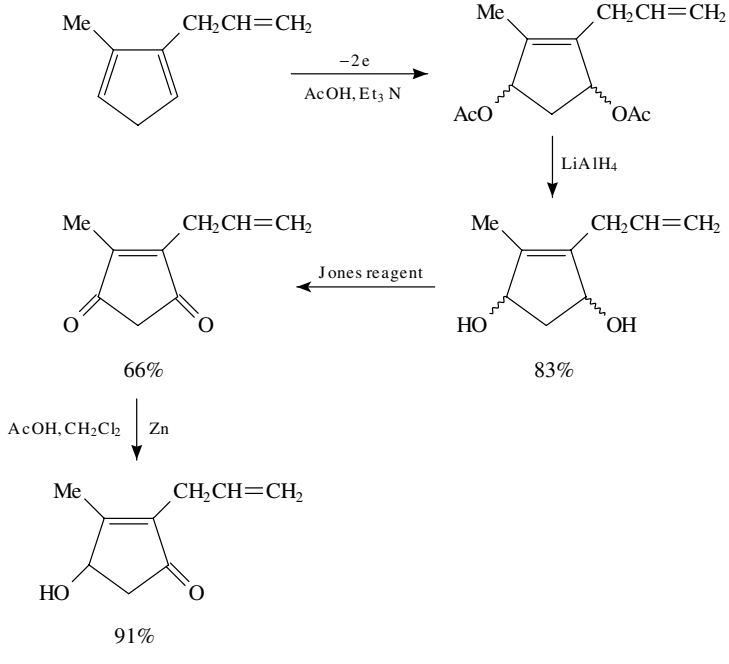
The typical pattern of anodic oxidation of conjugated dienes is oxidative 1,2- or 1,4-addition of nucleophiles, though the selectivity usually depends on the structure of the diene and the reaction conditions (equation 1).



(1)

Some typical results are shown in Table 2. The table shows that oxidation of conjugated dienes such as isoprene, piperylene (1,3-pentadiene), cyclopentadiene and 1,3-cyclohexadiene with a carbon anode in methanol or in acetic acid containing tetraethylammonium *p*-toluenesulfonate (Et_4NOTs) as the supporting electrolyte yields mainly 1,4-addition products[2]. 1,3-Cyclooctadiene yields a considerable amount of the allylically substituted product.

The product, 1,4-diacetoxy-2-allyl-3-methyl-2-cyclopentene, obtained (45% current efficiency) from 2-allyl-3-methyl-1,3-cyclopentadiene through anodic oxidation with carbon rod anode in acetic acid is successfully used as a starting compound in the synthesis of allethrolone as shown in equation 2[3].



(2)

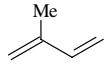
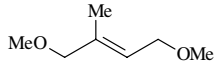
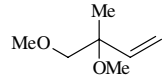
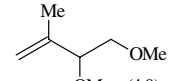
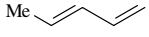
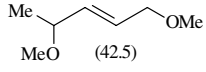
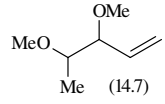
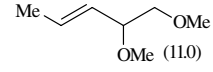
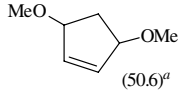
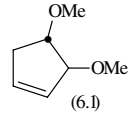
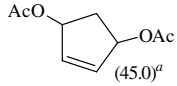
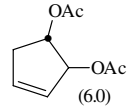
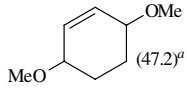
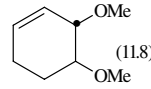
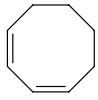
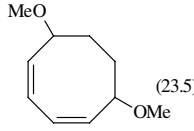
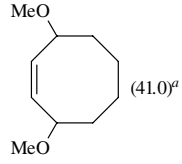
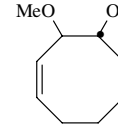
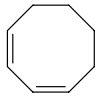
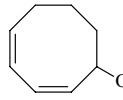
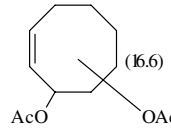
When a palladium(II)–hydroquinone system is used as the mediator[4] in the anodic oxidation of 1,3-cyclohexadiene in acetic acid, either *trans*- or *cis*-1,4-diacetoxy-2-cyclohexene is formed with rather high selectivity, though the possible formation of 1,2-diacetoxylated compound is not discussed.

TABLE 1. Peak oxidation potentials (E_p)[a] of dienes[b]

Diene	E_p	Diene	E_p
Butadiene	2.0	1,3-Cyclooctadiene	1.55; 1.70
Isoprene	1.75	1,3-Pentadiene	1.48
Cyclopentadiene	1.50	1,3-Cyclohexadiene	1.36

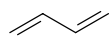
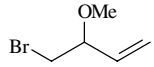
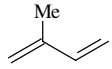
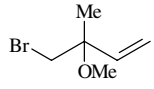
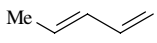
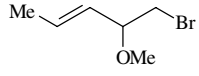
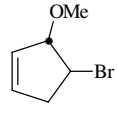
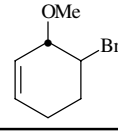
[a] V vs Ag/Ag^+.
[b] Glassy carbon; solvent, methanol; supporting electrolyte, 0.5 M $NaClO_4$

TABLE 2. Oxidation of conjugated dienes

1,3-Diene	Solvent	Product (current efficiency %)		
	MeOH	 (18.6)	 (12.5)	 (4.0)
	MeOH	 (42.5)	 (14.7)	 (11.0)
	MeOH	 (50.6)[a]	 (6.1)	
	AcOH	 (45.0)[a]	 (6.0)	
	MeOH	 (47.2)[a]	 (11.8)	 (2.8)
	MeOH	 (23.5)	 (41.0)[a]	 (8.2)
	AcOH	 (53.6)	 (16.6)	

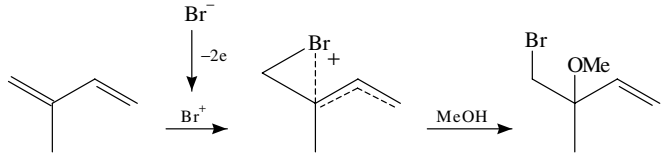
[a] Mixture (1:1) of *cis* and *trans* isomers

TABLE 3. Bromomethoxylation of 1,3-dienes

1,3-Diene	Products	Yield (%)
		40
		64
		66
		41
		45

In this reaction, the redox couple hydroquinone/benzoquinone promotes the second redox couple Pd(0) $\rightleftharpoons$ Pd(II) and Pd(II) causes the oxidative transformation of the diene to the 1,4-diacetoxylated compound. The most remarkable characteristic of this reaction
is that the oxidation takes place at anode potential lower than 1 V vs SCE. In a typical case, the yield of 1,4-diacetoxy-2-cyclohexene is 61% with a *trans*:*cis* ratio of 86:14. On the other hand, the ratio is 10:90 (34% yield) when the reaction is carried out in the presence of chloride anion[5].

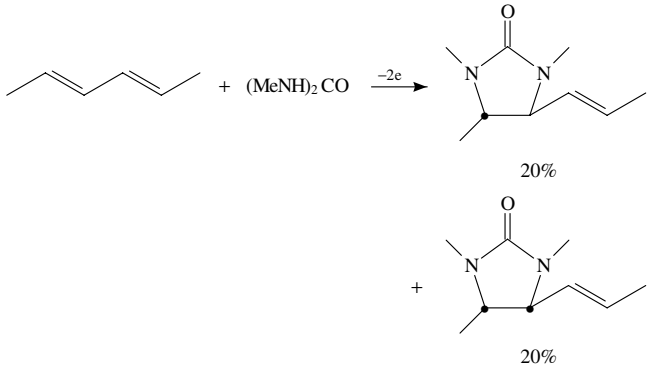
1,2-Addition takes place selectively when the reaction is carried out in methanol by using the redox couple of Br^-/Br^+ as the mediator as shown by some typical examples in Table 3[6]. The mechanism of this 1,2-addition may be as shown in equation 3 on the basis that it is regio- and stereoselective and follows the Markovnikov rule.



(3)

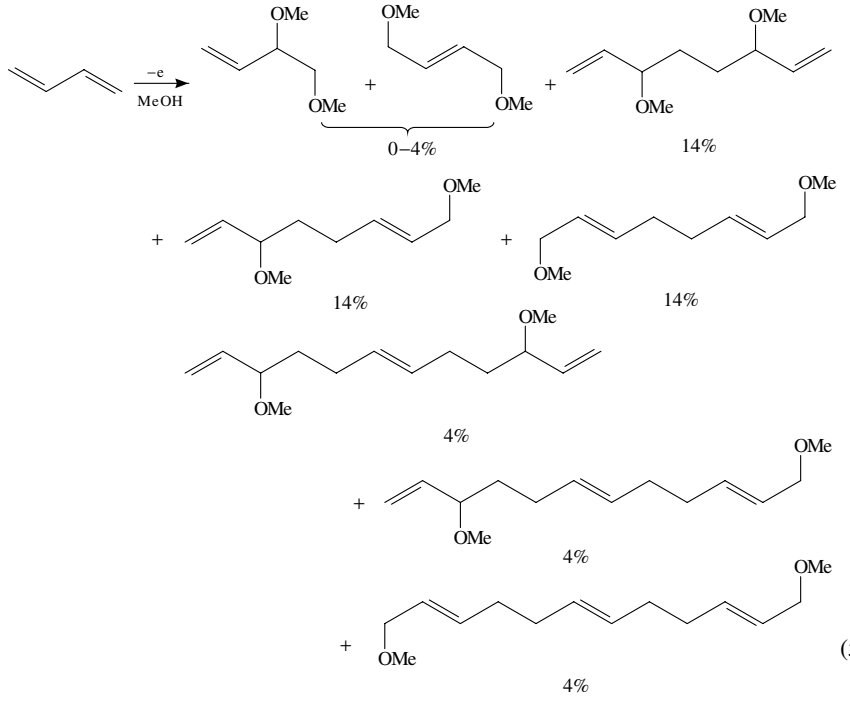
The electrophilic bromonium ion adds to the diene at the position which yields the most stable cationic intermediate and the stereochemical relation of the Br and the MeO group in the product is always *trans* when the diene system is cyclic. The fact that 1,2-addition takes place selectively but 1,4-addition does not occur is explained by the formation of the bridged bromonium ion as the intermediate.

When conjugated dienes are anodically oxidized with a graphite anode in MeCN in the presence of $NaClO_4$ and *N*,*N*′-dimethylurea, a variety of 2-imidazolidinones are formed though the yields are not always high as exemplified in equation 4[7].



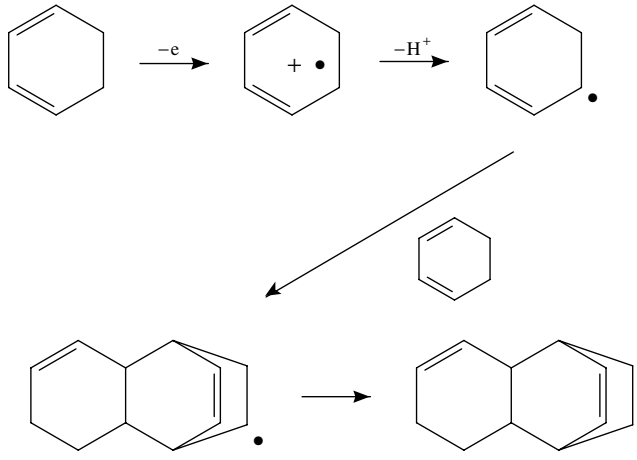
(4)

The products of electrochemical oxidation of conjugated dienes are considerably affected by the reaction conditions such as the material of the electrode, the supporting electrolyte and the solvent. The oxidation of butadiene with a graphite or carbon-cloth anode in 0.5 M methanolic solution of $NaClO_4$ mainly yields dimerized products along with small amounts of monomeric and trimeric compounds (equation 5)[1]. The use of platinum or glassy carbon mainly gives monomeric products. Other dienes such as isoprene, 1,3-cyclohexadiene, 2,4-hexadiene, 1,3-pentadiene and 2,3-dimethyl-1,3-butadiene yield complex mixtures of isomers of monomeric, dimeric and trimeric compounds, in which the dimeric products are the main products.



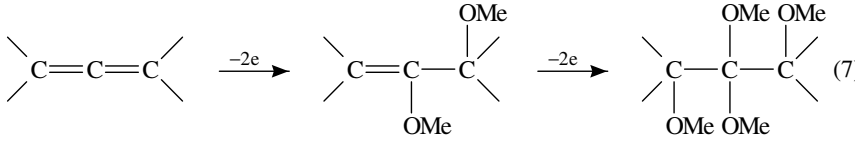
(5)

As mentioned above, the electrochemical oxidation of a diene yields 1,2- and 1,4-addition products when the reaction is carried out in the presence of a nucleophile such as methanol or acetic acid. When the oxidation is carried out in the absence of the nucleophile it usually yields a polymeric compound as the major product. The formation of a small amount of the Diels-Alder adduct is, however, observed when the reaction is carried out in CH_2Cl_2 with graphite anode. One of the proposed reaction pathways is shown in equation 6[8], though it is not clear whether the cyclohexadienyl radical serves as a diene (as shown in equation 6) or a dienophile in the Diels-Alder reaction.



(6)

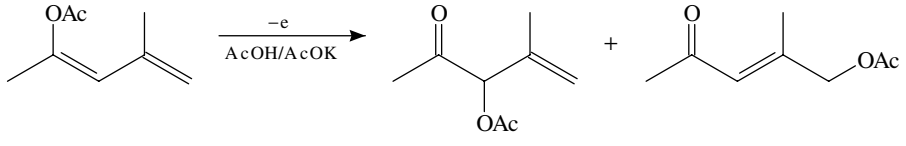
The anodic oxidation of 1,2-dienes in methanol takes place stepwise at each double bond yielding a tetramethoxylated compound as one of the products (equation 7)[9]. This result is reasonable since a 1,2-diene is not a conjugated diene.



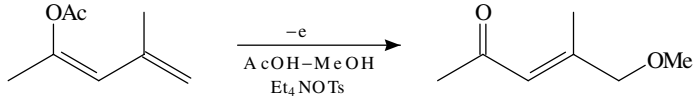
(7)

The electrochemical oxidation of monoolefins bearing electron-donating substituents such as alkoxy, acyloxy or dialkylamino group takes place more easily than that of simple monoolefins, and products formed by the addition of a nucleophile to the double bond are obtained with satisfactory yields[4].

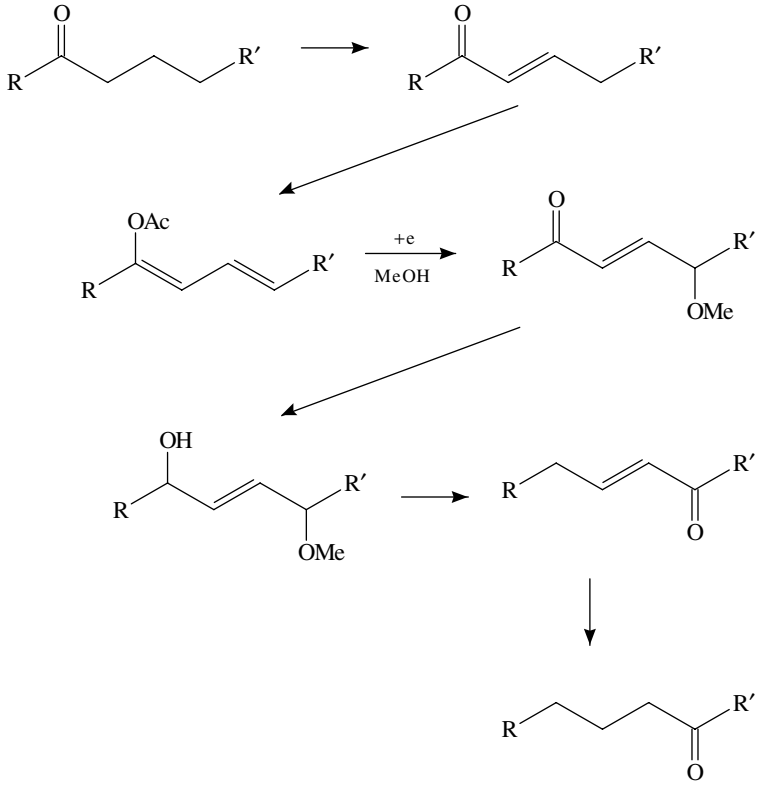
In the case of the anodic acetoxylation of a 1-acetoxy-1,3-diene, however, the addition of the acetoxyl group to the diene is usually not regioselective, and a mixture of the two positional isomers is yielded (equation 8). On the other hand, the anodic methoxylation of the same diene gives a 4-methoxy-enone with high regioselectivity when the reaction is carried out in methanol containing 10% acetic acid (equation 9)[10]. Some typical results are summarized in Table 4. This anodic and regioselective methoxylation is an effective key reaction for the transposition of a carbonyl group from the original position to the γ-position (1,4-transposition) as shown schematically in equation 10.



(8)



(9)

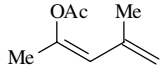
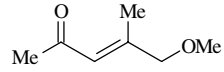
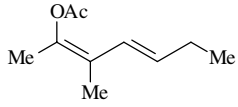
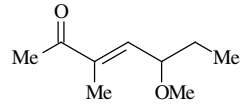
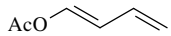
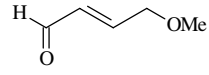
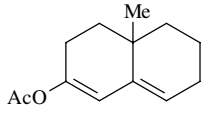
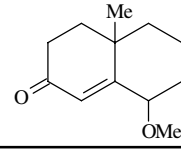


(10)

B. Nonconjugated Dienes

Compared with conjugated dienes, the electrochemistry of nonconjugated dienes is classified into two types, A and B[11,12]. In type A, the double bond of the diene behaves essentially the same as the double bond of a monoolefin in the anodic oxidation. A typical

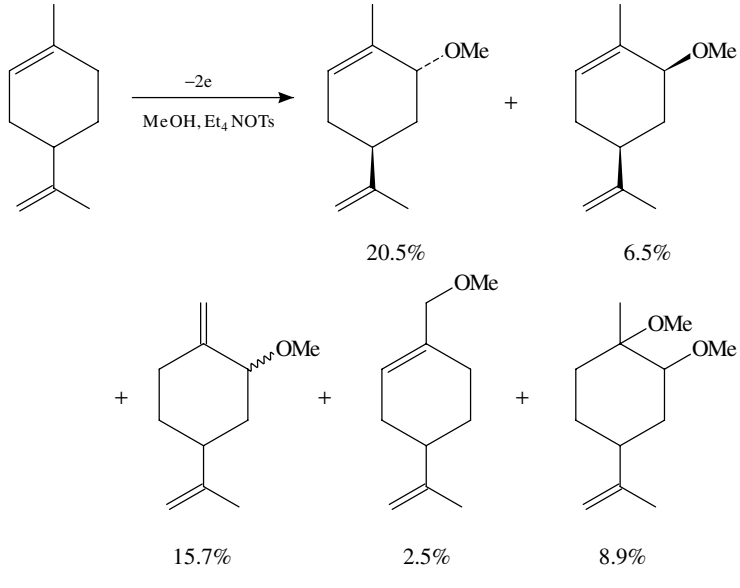
TABLE 4. Anodic oxidation of enol acetates

Dienol acetate	γ-Methoxy Carbonyl Product	Yield (%)[a, b]
		81
		74
		76
		66

[a] Isolated yields.

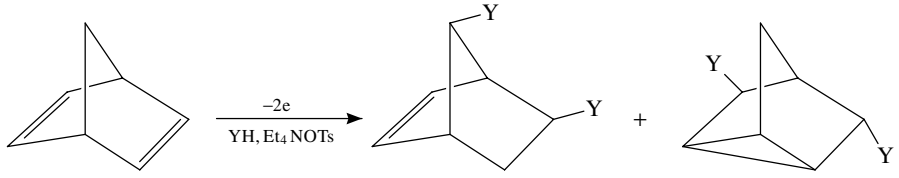
[b] The yields were obtained at the stage when 2 F/mol of electricity was passed.

example is the oxidation of limonene in methanol (equation 11) in which the reaction which actually takes place is the oxidation of the double bond located in the cyclohexene ring, followed by allylic substitution and ring contraction, whereas the isopropenyl group is retained intact. These patterns of reaction are similar to those observed in the anodic oxidation of monoolefins.



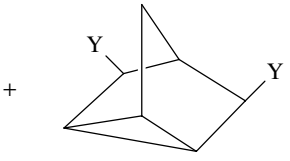
(11)

On the other hand, the electrooxidation of norbornadiene or bicyclo[2.2.2]octa-2,5-diene shows a different electrochemistry (type B) and yields a mixture of some unique products as shown in equations 12 and 13.

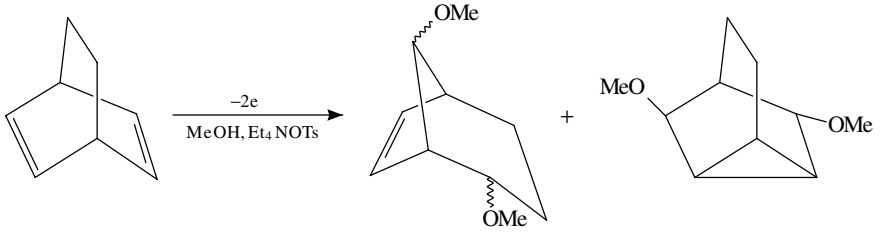


Y = OAc 6.2% 14.1%
Y = OMe 8.8% 16.5%

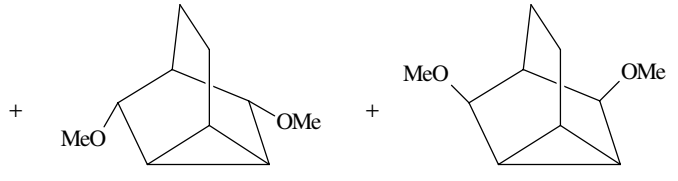
(12)



15.4%
18.4%

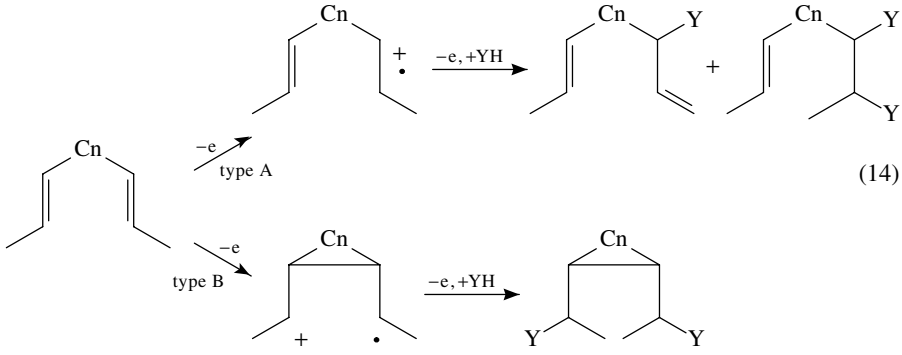


23.8% 22.5% (13)



9.1% 5.3%

These results clearly show that in type B reactions the electrooxidation pattern is remarkably different from that of the corresponding monoolefin. The types A and B are summarized schematically in equation 14.



(14)

In type A reactions one electron is removed from one of the two double bonds to form a cation radical, and allylic substitution and oxidative addition take place as the following reactions. On the other hand, in type B reactions the initial electron transfer from the double bond is accompanied by a transannular reaction between the two double bonds.

The difference between dienes reacting according to type A and those according to type B is clearly reflected in their oxidation potentials (Table 5).

Thus, the oxidation potential of the former type of diene (limonene) is substantially the same as that of the corresponding monoolefin (1-Me-cyclohexene), whereas norbornadiene and bicyclo[2.2.2]octadiene show much lower oxidation potentials than those of norbornene and cyclohexene.

This result suggests that in the anodic oxidation of type B, the cation radical formed from one of the two double bonds is stabilized through transannular interaction with another double bond.

As shown in Table 6 and Figure 1, the oxidation potentials of 2-substituted norbornadienes (1), 2-substituted bicyclo[2.2.2]octa-2,5-dienes (2) and 4-substituted [2.2]paracyclophanes (3) clearly indicate that the transannular interaction between two double bonds contributes already at the stage of the first electron transfer. Namely, in compounds 1−3, the electron is transferred from the unsaturated bond which is not substituted by the electron-withdrawing group, Figure 1 shows the

TABLE 5. Oxidation potentials of dienes and the corresponding monoolefins (V vs SCE)[a]

Norbornene	2.02	Cyclohexene	2.14	1-Me-Cyclohexene	1.70
Norbornadiene	1.54	Bicyclo[2.2.2]octadiene	1.82	Limonene	1.67

[a]Solvent: MeCN; supporting electrolyte, 0.1 M $LiClO_4$.

TABLE 6. Oxidation potentials of **1**, **2** and **3**

Substituent X	Oxidation potential (V vs. SCE)		
	1	**2**	**3**
H	1.54	1.82	1.47
CO_2Me			1.61
CO_2Et	1.85	2.11	
COMe	1.85	2.07	1.57
CN	1.99	2.22	1.65
NO_2			1.72

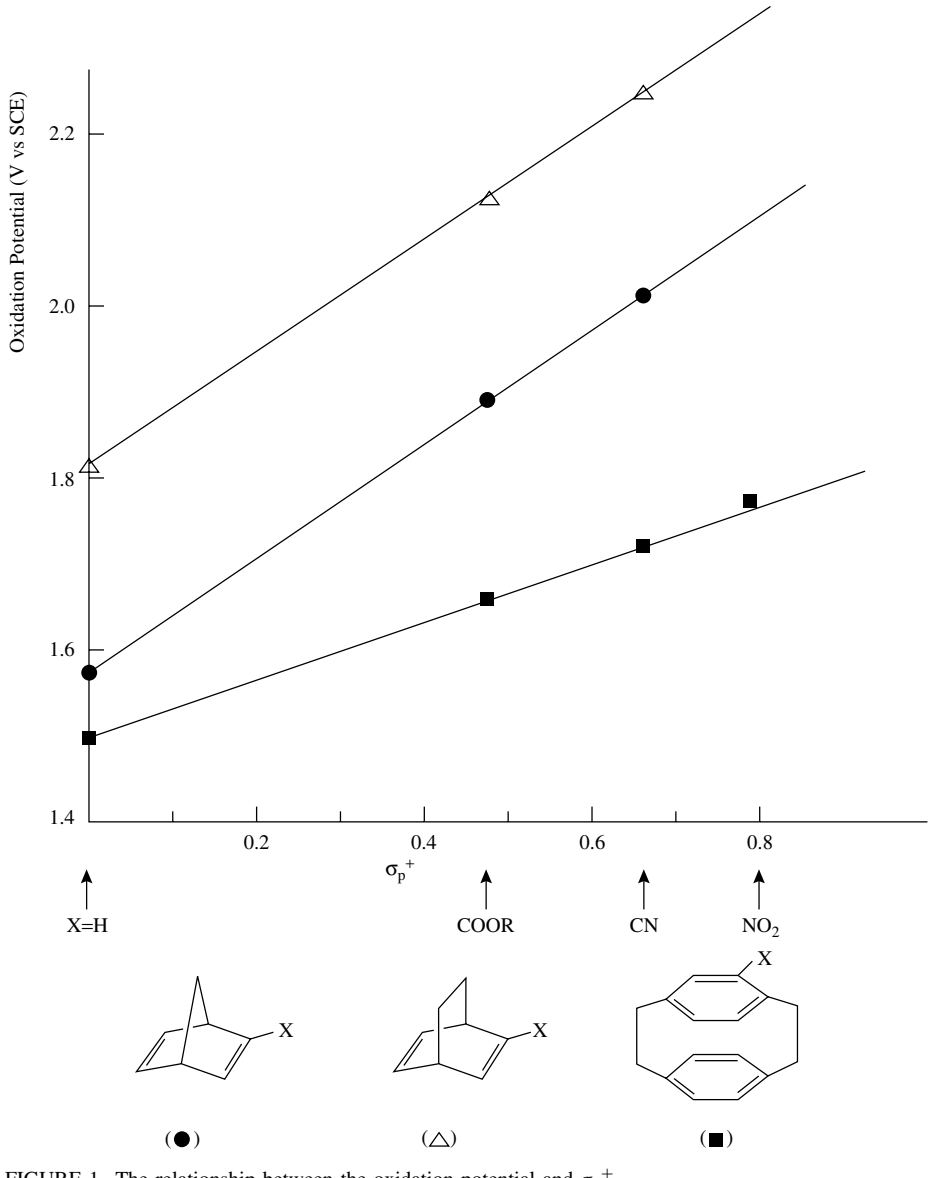


FIGURE 1. The relationship between the oxidation potential and σ_p^+

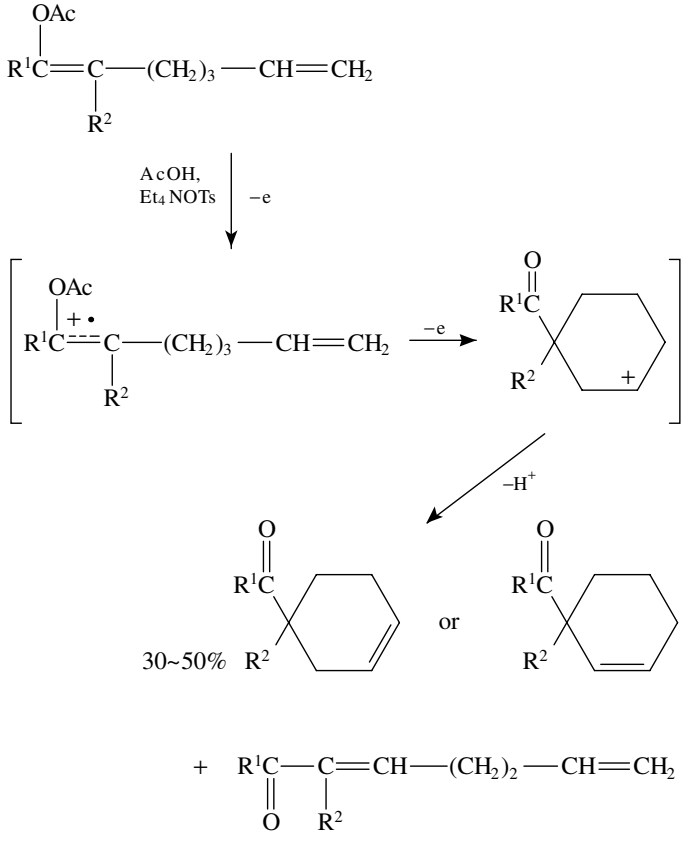
linear free energy correlations between the oxidation potentials which are required to remove an electron from the double bond not bearing the substituents and the σ_p^+ parameter.

This result indicates that the substituent located on one bond affects electronically the process of electron removal from the other double bond which is not bearing the substituent.

If the substituents are, however, electron-donating, the first electron transfer must take place at the double bond bearing the substituents. Hence, it is impossible to observe the transannular effect in this case.

Although it is unclear what type of σ value is the most suitable to use with a cation radical system, it is reasonable that the best linear relationship is given with σ^+, although for the substituents investigated $\sigma_p^+ \approx \sigma_p$.

Despite the fact that the electrochemical oxidation of most of the nonconjugated dienes generally does not give products which result from interaction of the double bonds with one another, the anodic oxidation 1-acetoxy-1,6-heptadienes gives intramolecularly cyclized products, that is, the cyclohexenyl ketones (equation 15)[13]. The cyclization takes place through the electrophilic attack of the cation generated from enol ester moiety to the double bond.



(15)

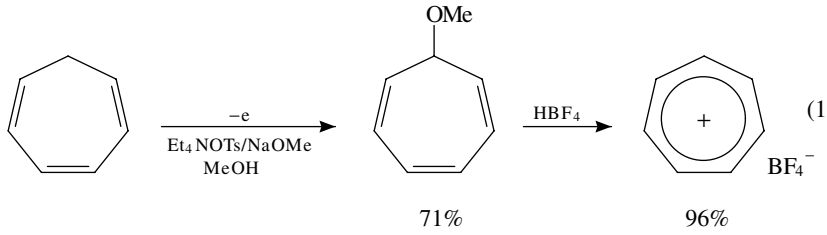
R^1=Me, R^2=Me, Et

C. Trienes

The anodic oxidation of acyclic polyenes is practically useless, since the control of the reaction site is usually difficult and hence the product is often a mixture of isomers which are not always easily isolable.

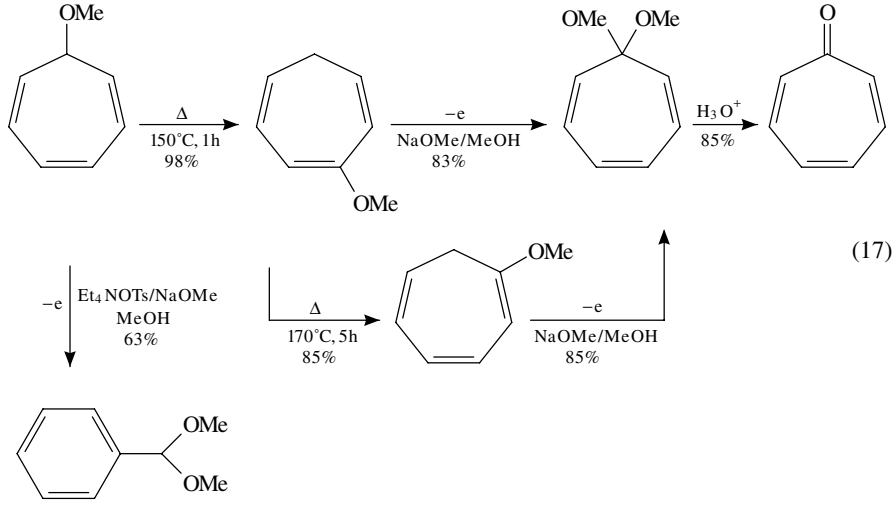
On the other hand, the anodic oxidation of 1,3,5-cycloheptatrienes is one of the most powerful key tools for the preparation of a variety of non-benzenoid aromatic compounds such as tropylium salts, tropones, tropolones, 2*H*-cyclohepta[*b*]furan-2-ones and azulenes[14].

The anodic oxidation of 1,3,5-cycloheptatriene in MeOH, however, gives the product 7-methoxy-1,3,5-cycloheptatriene (7-MeO-CHT) in a rather low yield when the reaction is carried out by using Et_4NOTs, NaOMe, Bu_4NBF_4 or H_2SO_4 as the supporting electrolyte. On the other hand, the use of a mixture of Et_4NOTs and NaOMe as the supporting electrolyte dramatically increases the yield (equation 16).



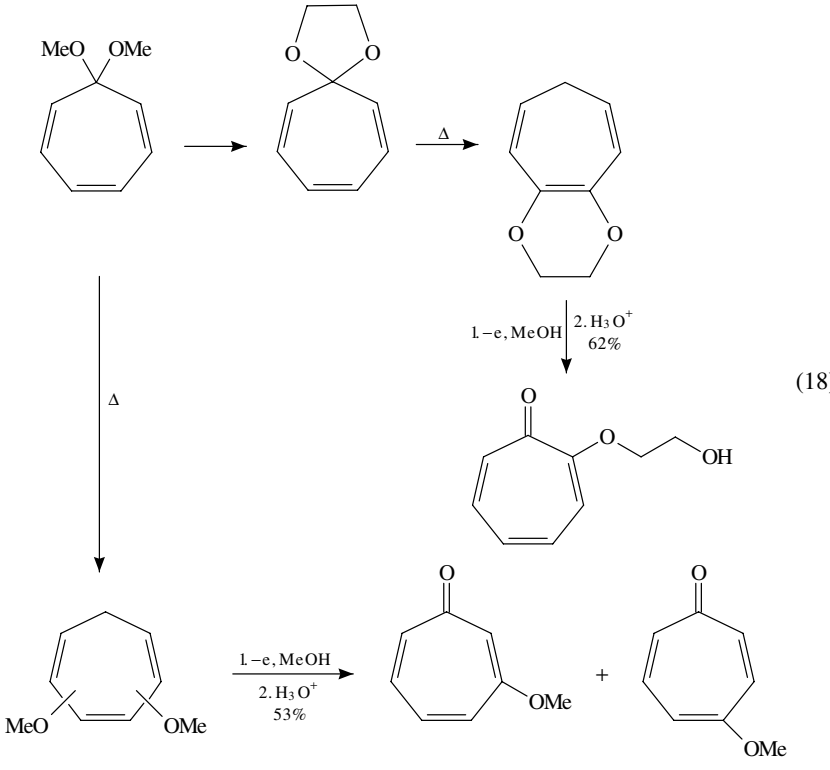
(16)

The anodic oxidation of 7-MeO-CHT in MeOH results in the formation of benzaldehyde dimethyl acetal through a ring contracting rearrangement, whereas 3-MeO-CHT and 1-MeO-CHT are prepared by thermal rearrangement of 7-MeO-CHT and afford 7,7-diMeO-CHT in 83% and 85% yields, respectively, upon the anodic oxidation. The hydrolysis of 7,7-diMeO-CHT in 5% aqueous H_2SO_4 gives tropone in 85% yield (equation 17).



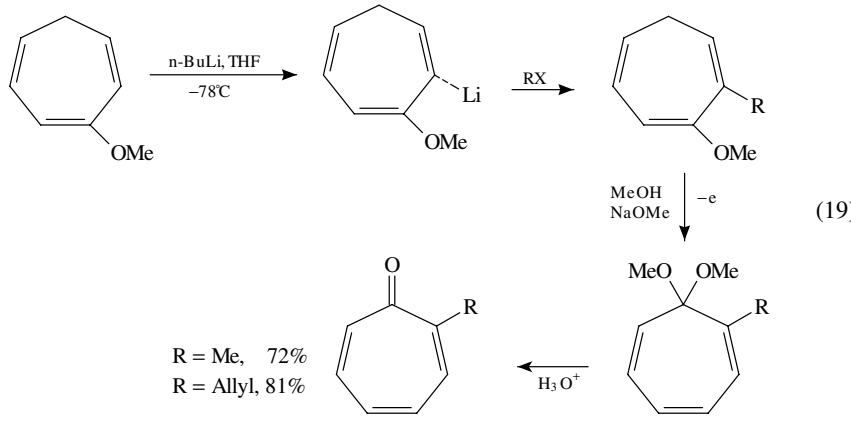
(17)

The transformation of 7,7-diMeO-CHT to α-, β- and γ-tropolones is also achievable by using anodic oxidation in the key step (equation 18), namely the electrochemical oxidation of an isomeric mixture of diMeO-CHTs prepared by the thermal rearrangement of 7,7-diMeO-CHT yields a mixture of methyl ethers of β- and γ-tropolones. On the other hand, the thermal rearrangement of the ethylene acetal of tropone gives 3,4-dioxyethylene-CHT as a single product due to the difficulty of formation of other isomers, and it yields the ether of α-tropolone upon anodic oxidation.

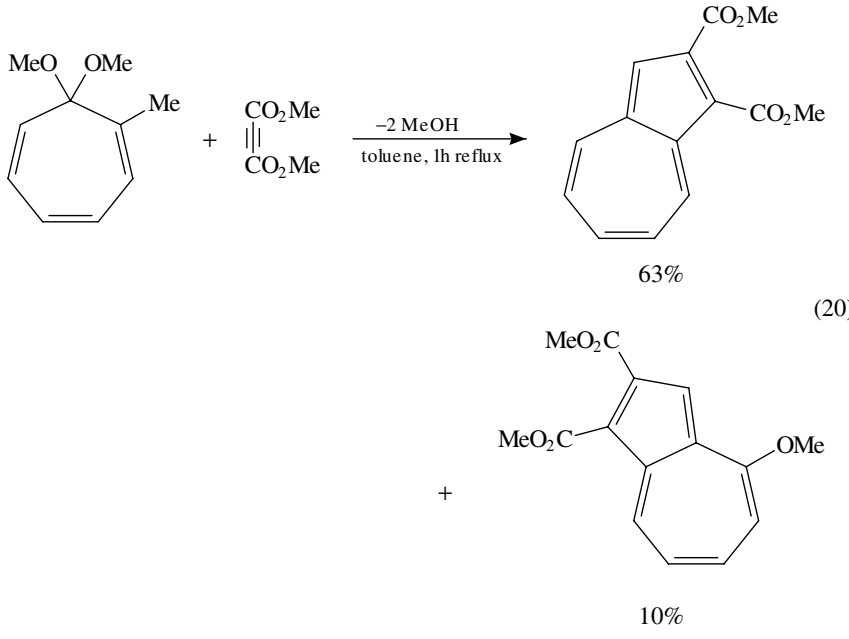


(18)

The anodic oxidation of 2-alkyl-3-MeO-CHT followed by hydrolysis of the intermediate 1-alkyl-7,7-diMeO-CHT gives 2-alkyltropones in high yields (equation 19). The precursor 2-alkyl-3-MeO-CHT is synthesized by the alkylation of 2-lithio-3-MeO-CHT prepared by the regioselective lithiation of 3-MeO-CHT with BuLi. The intermediate 1-alkyl-7,7-diMeO-CHT is highly useful for the synthesis of the azulene skeleton through its reaction with dimethyl acetylenedicarboxylate (equation 20).

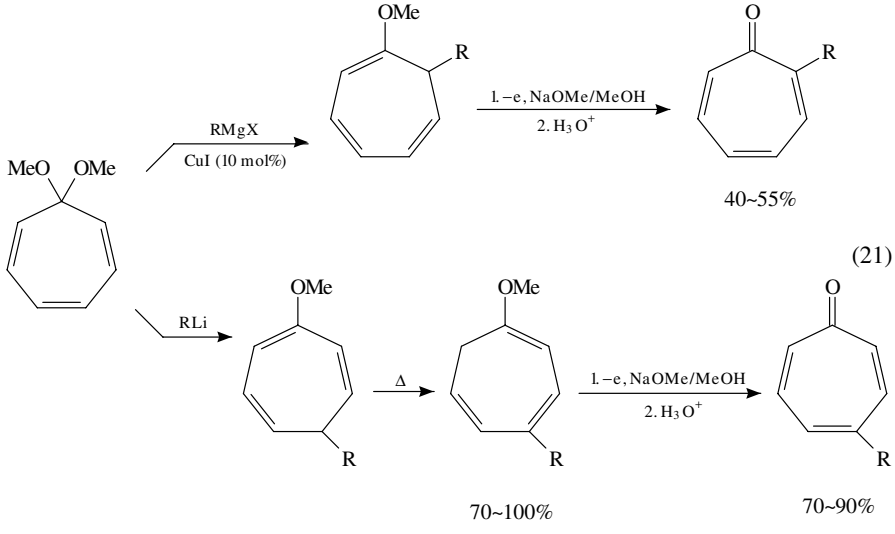


(19)



(20)

The electrochemical oxidation of 1-MeO-7-alkyl-CHT in MeOH yields 2-alkyltropones, while the thermal rearrangement of 3-MeO-7-alkyl-CHT to 1-MeO-4-alkyl-CHT followed by its anodic oxidation in MeOH affords 4-alkyltropones (equation 21). 1-MeO-7-alkyl-CHT is prepared by the regioselective alkylation of 7,7-diMeO-CHT with a Grignard reagent and CuI, while 3-MeO-7-alkyl-CHT is also regioselectively prepared by alkylation of 7,7-diMeO-CHT with an alkyl lithium.



(21)

III. CATHODIC REDUCTION

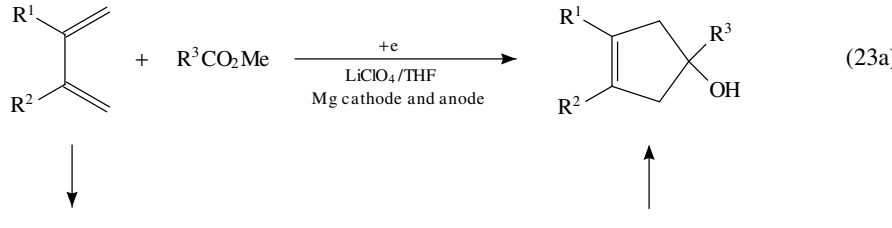
A. Dienes

Compared with the anodic oxidation of a 1,3-diene, the cathodic reduction of a 1,3-diene may be less interesting since the resulting simple transformation to monoolefin and alkane is more conveniently achieved by a chemical method than by the electrochemical method. So far, only few reactions which are synthetically interesting have been studied[15]. The typical pattern of the reaction is the formation of an anion radical from 1,3-diene followed by its reaction with two molecules of electrophile as exemplified by the formation of the dicarboxylic acid from butadiene (equation 22)[16].

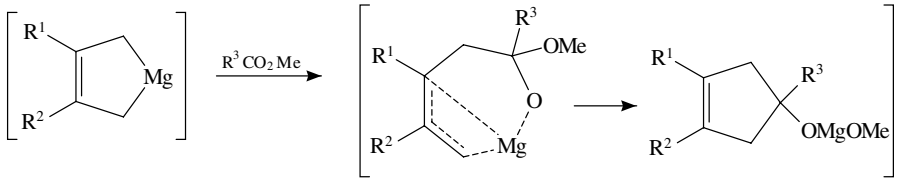
$$CH_2{=}CH{-}CH{=}CH_2 \xrightarrow[CO_2]{+e} \xrightarrow{H^+} HO_2C{-}CH_2{-}CH{=}CH{-}CH_2CO_2H \quad (22)$$

50%

On the other hand, it has been found that the electrochemical reduction is a very unique and useful tool in synthetic organic chemistry when magnesium is used as the material of the electrode. The cathodic reduction of 1,3-dienes with magnesium electrode gives very unique products, i.e. 3-cyclopentenol derivatives when it is carried out in the presence of a carboxylic acid ester (equation 23)[17].



(23a)



(23b)

This novel electroreductive cyclocoupling corresponds to a 1,4-addition of a one-carbon unit to the 1,3-diene, and does not take place without using magnesium electrode. The first step in this coupling reaction is the cathodic reduction of 1,3-diene to an anion radical, and the second step is the formation of a Mg-diene complex, which thereafter reacts with the ester to yield the coupling product as shown in equation 23b.

The intermediary formation of the Mg-diene complex is confirmed by a two-step reaction method, namely in the first step a solution of 1,3-diene is electrochemically reduced with magnesium electrode in the absence of the ester. After a sufficient amount of electricity is passed, the current is terminated and the ester is added to the solution. The fact that the coupling product is also formed by this two-step method strongly supports the formation of the intermediate Mg-diene complex.

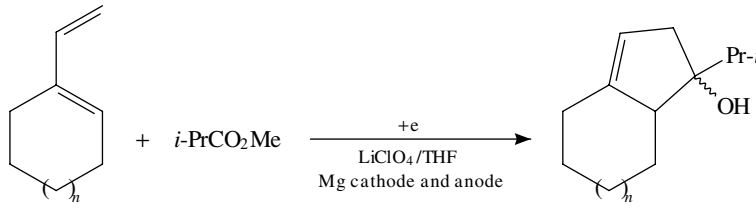
Some of the typical results are shown in Table 7. The aromatic ester does not give the cyclized product but other products were not identified.

This cyclocoupling reaction is not limited to acyclic dienes. Both 1-vinylcyclohexene and 1-vinylcycloheptene give the cyclized products in good yields (equation 24).

TABLE 7. Cathodic coupling of 1,3-dienes with esters

Diene		Ester	Product
R^1	R^2	R^3	Yield (%)[a]
Me	H	*n*-Bu	76
Me	H	*i*-Pr	71
Me	H	$PhCH_2CH_2$	56
$(CH_3)_2C{=}CHCH_2CH_2$	H	Et	63
Me	Me	*i*-Pr	88
Me	H	Ph	0

[a]Isolated yields.

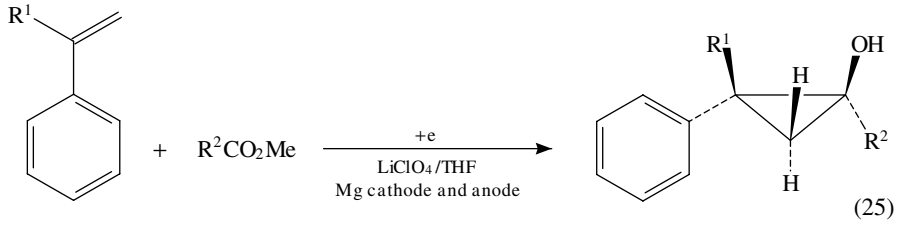


(24)

($n = 1$)
($n = 2$)

($n = 1$) 62%
($n = 2$) 72%

Although styrene is not a 1,3-diene, the cathodic reduction of a solution containing styrene and an ester with magnesium electrode interestingly affords a single stereoisomer of 2-phenylcyclopropanol derivative in which the phenyl and the alkyl (R^2) groups are stereoselectively located in a *cis* relationship on the cyclopropane ring (equation 25).



(25)

$R^1 = H$
$R^1 = Me$

Yield (%)

$R^1 = H$, $R^2 = Me$	71	
$R^1 = H$, $R^2 = Et$	67	*cis*
$R^1 = H$, $R^2 = i$-Pr	55	
$R^1 = R^2 = Me$	94	

Although a 1,2-diene is not a conjugated diene, it is also electrochemically reducible with platinized platinum electrode in acidic solution to the monoolefin and a saturated alkane[18].

In contrast with oxidation, clear reduction wave is not observed in the electrochemical reduction of cyclopentadiene[19].

B. Trienes and Polyenes

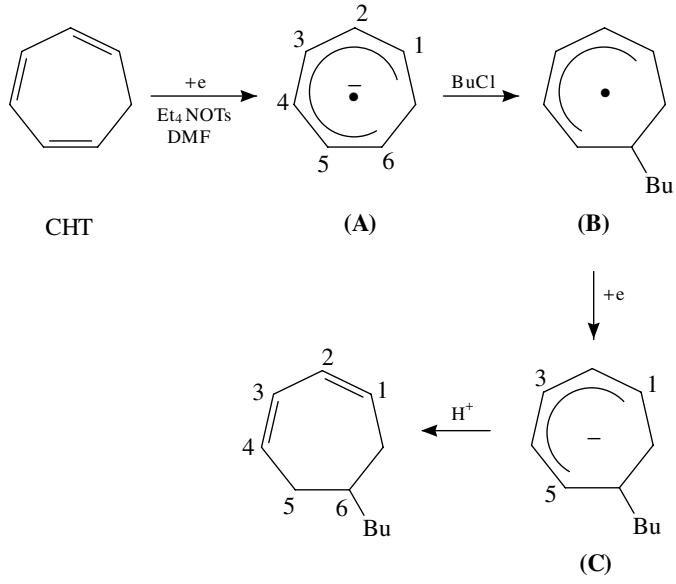
The electrochemical reduction of cycloheptatriene (CHT) in liquid ammonia takes place at about −2.5 V vs SCE and forms the radical anion of CHT. The radical anion is stable in ammonia on the voltammetric time scale but decays slowly by disproportionation and coupling reaction pathways to give respectively 1,3- and 1,4-cycloheptadienes (total yield 34–39%) and $C_{14}H_{18}$ (in yields of 55–58%) isomers which incorporate the bitropyl carbon skeleta[20].

The anionic intermediates generated by the cathodic reduction of CHT and some of its derivatives such as 1-MeO- and 3-MeO-CHTs are regioselectively alkylated with alkyl halides to give 6-alkyl-1,3-cycloheptadiene and 1-MeO-6-alkyl-1,3-cycloheptadiene as the main products, respectively[21].

The electroreduction of CHT in DMF in the presence of *n*-butyl chloride gives, for example, 6-butyl-1,3-cycloheptadiene as the main product (equation 26). This selectivity in alkylation is interesting, since it is also known that the reductive butylation of CHT using Li/NH_3 as the reducing agent gives a mixture of 5-butyl-1,3-cycloheptadiene and 3-butyl-1,4-cycloheptadiene in which the latter is the main product[22,23].

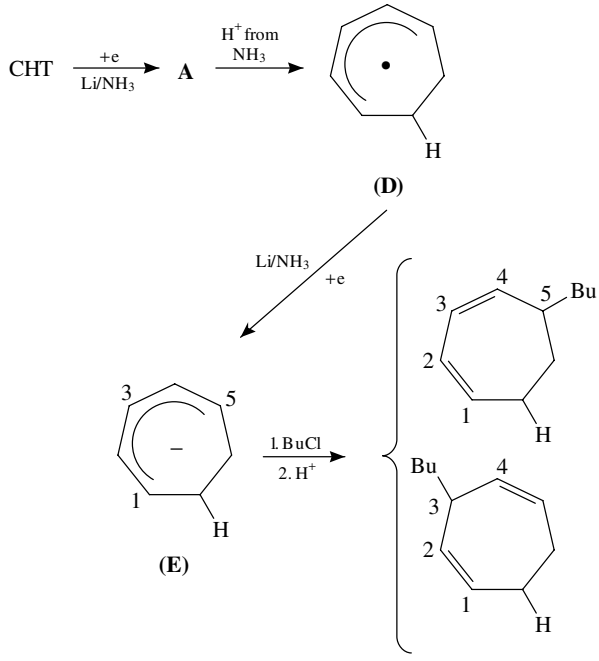
This difference of regioselectivity in alkylation of CHT is explained by the difference of the electrophile which reacts with the first active intermediate formed from CHT. Thus, the first active intermediate formed by one-electron transfer to CHT is an anion radical species **(A)** in both the electrochemical and the Li-metal reduction.

Since the electroreduction is carried out in the presence of BuCl in aprotic solvent (DMF), **A** reacts with BuCl before it is protonated by the solvent to give a radical species **(B)** as the second intermediate. It is reasonable that **A** reacts with BuCl at its 1- and 6-positions since the negative charge density is the highest at these two positions. In the third intermediate **C**, formed by one-electron reduction of **B**, the negative charge is mainly located at the 1-, 3- and 5-positions. The counter cation of the anion **C** is, however, the bulky Et_4N^+. Hence, anion **C** is most reactive at its 5-position and gives the 6-butyl derivative upon protonation at the 5-position[21] (equation 26).



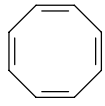
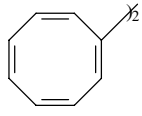
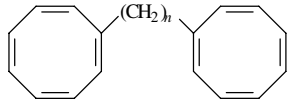
(26)

On the other hand, in the reduction of CHT with Li/NH_3, butyl chloride is absent when **A** is formed and hence **A** is protonated by NH_3 at its 1- and 6-positions to yield a radical intermediate **D**. In the anionic intermediate **(E)**, formed by one-electron reduction of **D**, the negative charge is mostly located at the 1-, 3- and 5-positions. Hence, the butylation takes place at these positions to give 5-butyl-1,3-cycloheptadiene and 3-butyl-1,4-cycloheptadiene as the final products (equation 27).



(27)

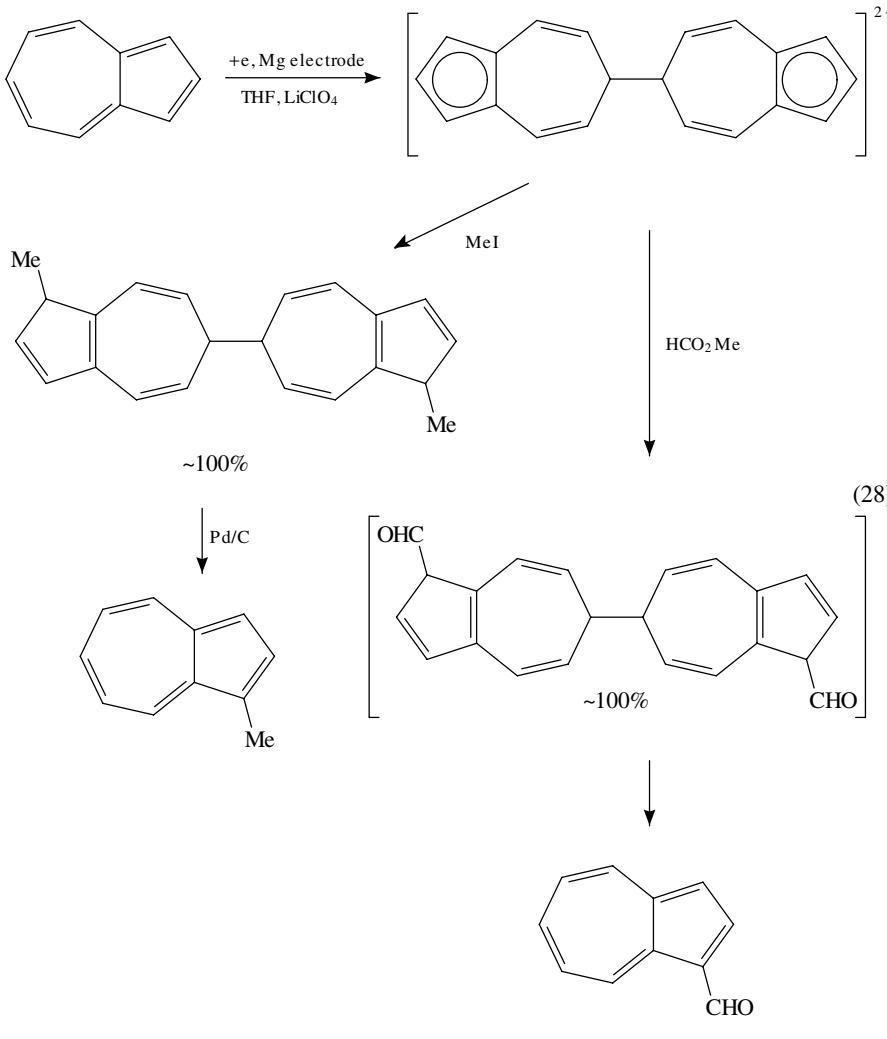
TABLE 8. Reduction peak potentials for some derivatives of cyclooctatetraene

		Ep (V vs SCE)
		−1.62
		−1.66
	$n=1$	−1.62
	$n=2$	−1.66
	$n=3$	−1.68

This electroreductive alkylation is successfully applied to the synthesis of β-thujaplicin.

Cyclooctatetraene and some of its derivatives are electrochemically reducible in dry degassed DMF containing Bu_4NClO_4 as the supporting electrolyte. The first reduction peak potentials which are required to form the corresponding anion radical are shown in Table 8[24], though a further reaction of the intermediates is not known.

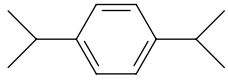
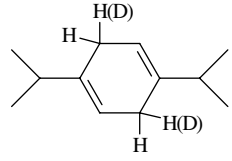
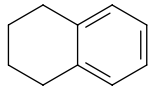
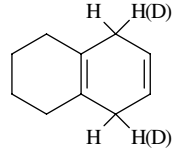
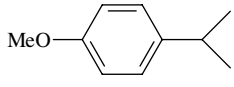
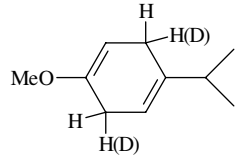
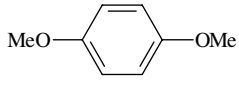
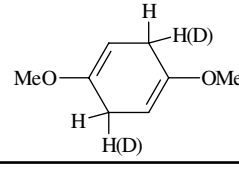
The electrochemical reduction of azulene with carbon, platinum, lead or zinc cathode does not give any product, whereas that with magnesium electrode yields a dimeric compound as the only reduction product, though the dimeric compound is easily transformed to the corresponding monomeric compound by a mild oxidation as shown in equation 28[25].



(28)

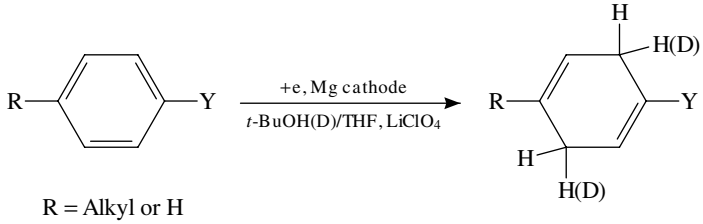
Although benzene is not a triene and its electrochemical reduction is not always practically facile, the benzenoid ring has been found to be easily reduced by the electrochemical method when magnesium is used as cathode[26] (equation 29). As some of the typical

TABLE 9. Electroreductive synthesis of dienes from benzenoid compounds

Benzenoid compound	Diene	Yield (%)[a]
		83 (80)
		94 (70)
		91(79)
		80 (67)

[a] Yields shown in parentheses are those for deuteriated products.

results summarized in Table 9 show, this electrochemical method is practically useful for the synthesis of dienes and especially of deuteriated dienes.



(29)

R = Alkyl or H
Y = Alkyl or MeO

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CHAPTER **18**

Syntheses and uses of isotopically labelled dienes and polyenes

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I. INTRODUCTION

Sections I–V of this chapter deal with the syntheses of unsaturated organic compounds playing an essential role in biochemical processes of life. Numerous polyunsaturated compounds have been synthesized in order to elucidate their physiological role, for instance in brain. However, the main impact on permanent searches for new improved methods of synthesis of isotopically labelled dienes and polyenes comes from nuclear medicine and nuclear pharmacy. The deuterium and carbon-13 labelled polyunsaturated compounds are needed as internal standards in mass spectral determinations of very low concentrations of biologically active substances in biological fluids.

The mechanism of protective action of some unsaturated compounds against cancer and the mechanism of reactions of compounds possessing cytoprotective activity, of compounds needed for treatment of cardiovascular diseases, of gastrointestinal ulcers in man, of neonatal hyperbilirubinemia, or of breast carcinoma, unsaturated inducers of colon cancer, receptor interactions in biological membranes, etc, are the frequent topics addressed by the isotopic chemical synthetic papers reviewed in Sections II–V of this chapter. Sections III and IV deal with isotopically labelled prostaglandins which are the object of synthetic studies and with the impressive progress which has been made in the synthesis of ^{11}C-labelled compounds of very high specific activity, applied in non-invasive PET methods in diagnosis and treatment.

A large number of papers are published annually on isotopic studies of the mechanisms of chemical reactions of unsaturated compounds. In spite of the large efforts of theoretical chemists and isotope physical chemists the mechanism of two important classes of organic reactions, namely Diels-Alder addition reactions and thermal aliphatic Claisen rearrangements, opening the route to the synthesis of unsaturated carbonyl compounds, has not been clarified satisfactorily. Experimental studies of the elementary acts in these organic reactions by the methodology of carbon and hydrogen isotope effects are difficult, time consuming and expensive and the examples presented in Section VI of kinetic isotope effect (KIE) investigations are very fragmentary. In many cases one can consider them rather as a more or less important introduction, but not a complete solution of the problem. They inform the reader about the contemporary state of fundamental studies in this field.

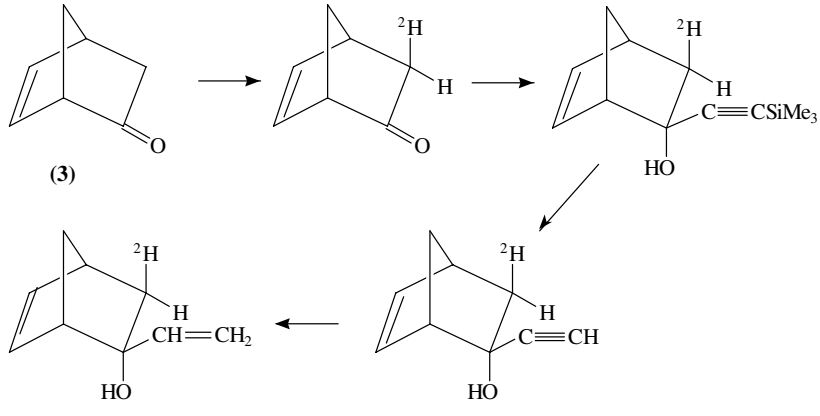
II. SYNTHESIS OF DIENES AND POLYENES LABELLED WITH STABLE ISOTOPES

A. Synthesis of Deuterium-labelled Compounds

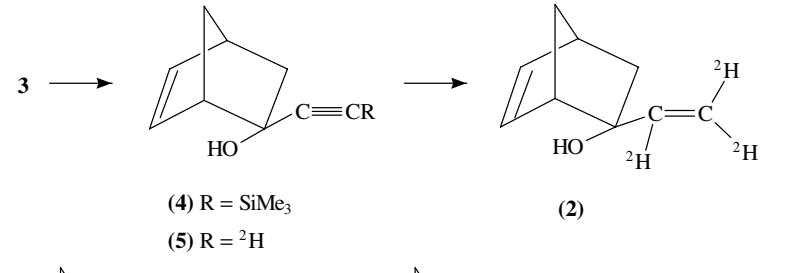
1. Synthesis of the deuterium-labelled 2-exo-vinylbicyclo[2.2.1]hept-5-en-2-ols

The title compound has been deuterium labelled[1] with ^{2}H at $C_{(3)}$ **(1)**, and in the vinyl group **(2)** by deuterium exchange of the enolizable hydrogen atoms in **3** followed by

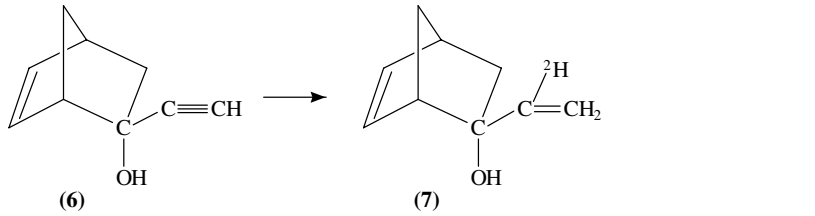
the reaction sequence shown in equation 1, and by desilylation of the intermediate **4** with NaO^2H in MeO^2H followed by reduction of the labelled alcohol **5** with lithium aluminium deuteride in THF, respectively (equation 2). The reduction of **6** with $LiAl^2H_4$, followed by quenching with a protic solvent, gave mainly (in 89% yield) the labelled alcohol **7** (equation 3). These deuteriated compounds were needed for elucidating the mechanism of the mass spectral fragmentation of the 2-hydroxy-1,3-butadiene formed upon electron-impact ionization.



(1)



(2)

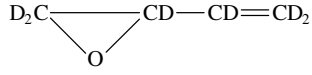


(3)

2. Synthesis of [D_6]-butadiene monoepoxide

[D_6]-butadiene monoepoxide, **8**, has been synthesized[2] by treating the water solution (pH 5.5) of magnesium monoperoxyphthalate hexahydrate at room temperature with [D_6]-1,3-butadiene at 1 atmosphere in 94% yield after 50 min reaction time. Under these conditions less than 1% of butadiene diepoxide has been formed as determined by GC/MS. The concentration of the [D_6]-butadiene monoepoxide in the aqueous reaction mixture at various reaction times has been determined by selective ion monitoring of ions with m/z

of 42, 48 and 74 for [D_6]-butadiene monooxide and of ions with m/z of 30, 58 and 90 for [D_6]-butadiene diepoxide, respectively.

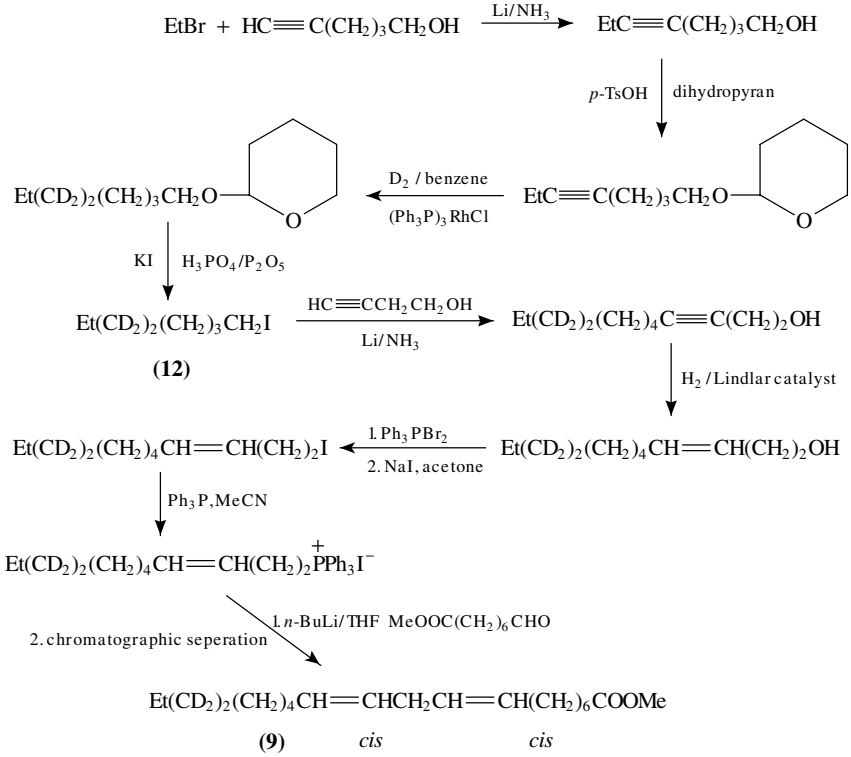


(8)

The epoxide metabolites of inhaled 1,3-butadiene, used in industry[3], are reported to be carcinogenic and mutagenic in rodents, and their *in vivo* concentration following inhalation exposure to butadiene has to be determined[4] by gas chromatography/mass spectroscopy, the isotope dilution method utilizing **8** as an internal standard. Commercially available [D_6]-propylene oxide has been used previously as an internal standard to monitor *in vivo* blood propylene oxide levels following inhalation exposure to propylene[5].

*3. Synthesis of methyl 8c,11c-eicosadienoate-17,17,18,18-D_4, **9**, methyl 8c,11c,14c-eicosatrienoate-17,17,18,18-D_4, **10** and methyl 5c,8c,11c-eicosatrienoate-17,17,18,18-D_4, **11***

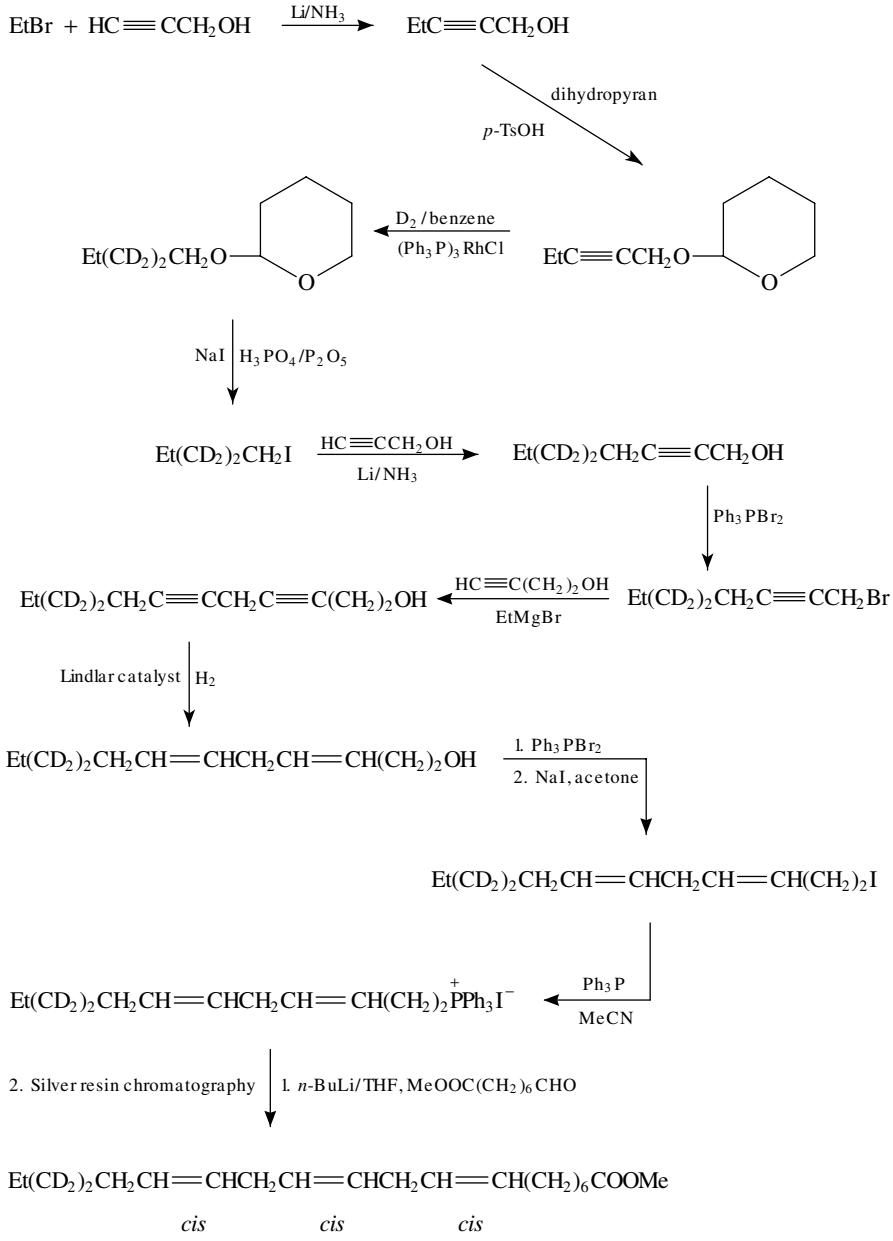
The deuteriated title compounds **9**, **10** and **11** have been synthesized[6] in multigram quantities in order to investigate the fatty acid metabolism in humans[7–9] (equations 4–6).



41% total combined yields, step yields 82–96%

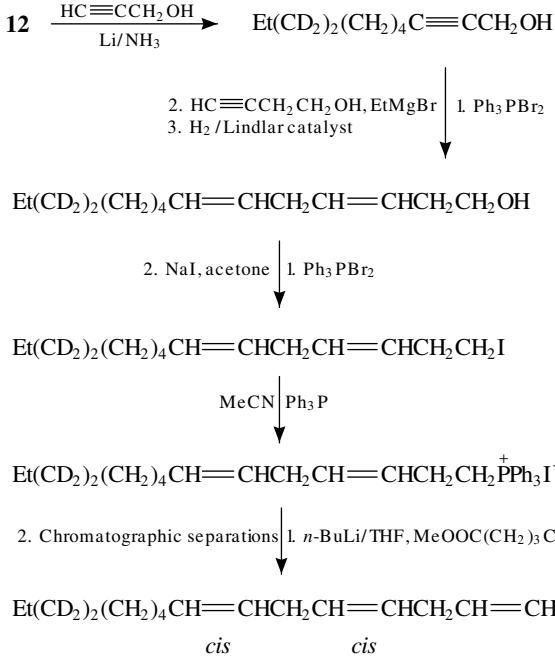
(4)

The reaction sequences shown in equations 4 and 5 involve the reduction of the appropriate acetylenic tetrahydropyranyl (THP) ethers with $(Ph_3P)_3RhCl$ and deuterium gas.



(10) 25% combined yield

(5)

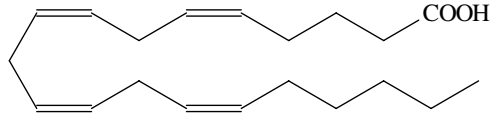


(6)

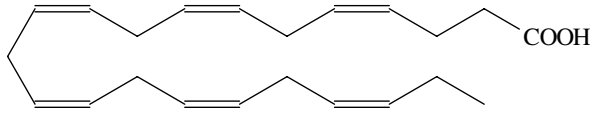
(11) 40% combined yield

4. Synthesis of ethyl ω-$^2H_5$-decosa-4,7,10,13,16,19-hexaenoate, ***16***

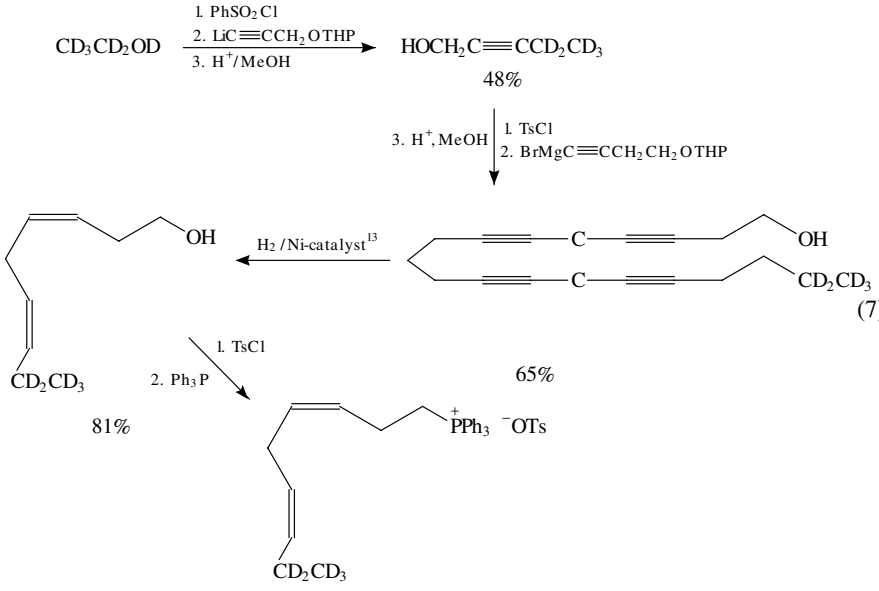
Elucidation of the physiological role of arachidonic acid **13** and other polyunsaturated fatty acids, particularly the role of all *Z*-4,7,10,13,16,19-decosahexaenoic acid **14**, found in brain, required the corresponding stable-isotope labelled material[10,11]. The deuteriated phosphonium salt **15**, the key intermediate used in the synthesis of title compound **16** (equation 8), has been prepared in 19% overall yield[12] starting with ethanol-D_6 (equation 7).



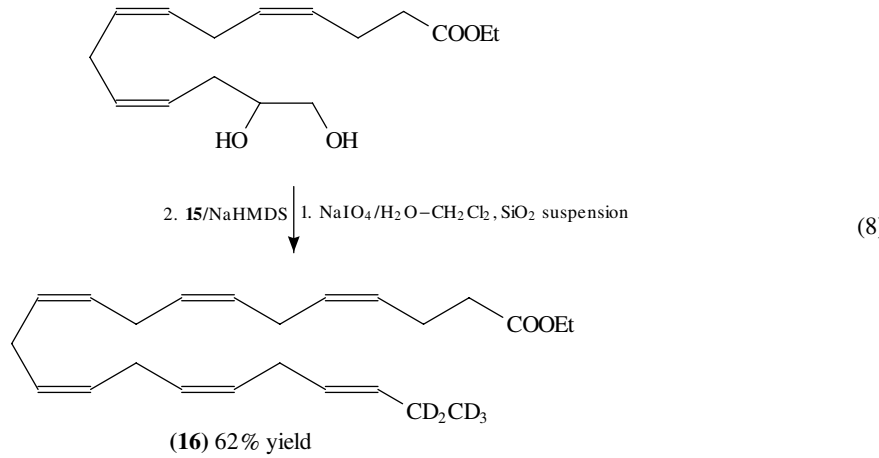
(13)



(14)



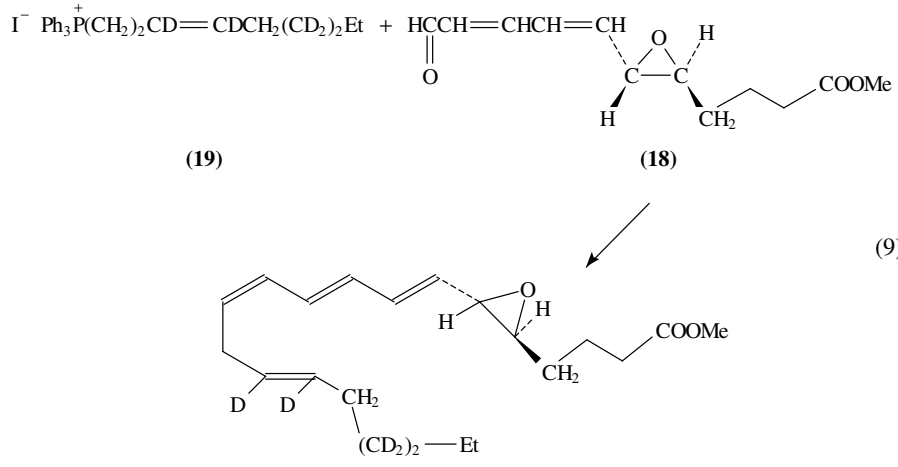
(15) 76% step yield, 19% overall yield



(16) 62% yield

5. Synthesis of deuteriated leukotriene A_4 methyl ester

14,15,17,17,18,18-[$^2H_6$]-Leukotriene A_4 methyl ester, **17**, has been synthesized[14] by Wittig olefination of epoxy dienal **18** with the key reagent 3,4,6,6,7,7-[$^2H_6$]-(*Z*)-(3-nonen-1-yl)triphenylphosphonium iodide, **19** (equation 9). **17** is employed as stable isotope internal standard for the MS trace analysis of eicosanoids[15–17].

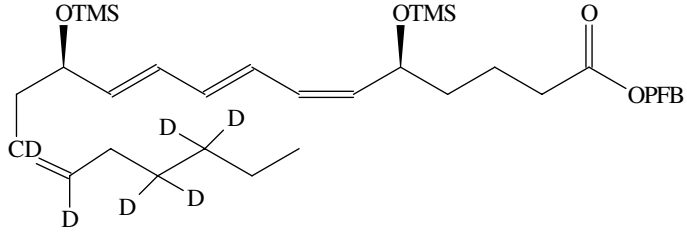


(9)

(17) [$^2H_6$]-LTA$_4$ methyl ester, 78%

6. Synthesis of [14,15,17,17,18,18-$^2H_6$]-leukotriene-B$_4$

The deuteriated title compound **20**, needed for quantitative determination of endogenous LTB$_4$ in various biological fluids by GC/MS[18,19], has been obtained[20] by enzymatic hydration with human monocytes of D$_6$-LTA$_4$ precursor[14,21]. Leukotriene D$_6$-LTB$_4$ has been separated from its *trans* isomers, 6-*trans*-D$_6$-LTB$_4$ and 12-epi-6-*trans*-D$_6$-LTB$_4$, in high isotopic purity (99.4%) by reversed-phase HPLC and identified by GC/MS. Leukotrienes B$_4$ and C$_4$ are potent inflammatory mediators[22].

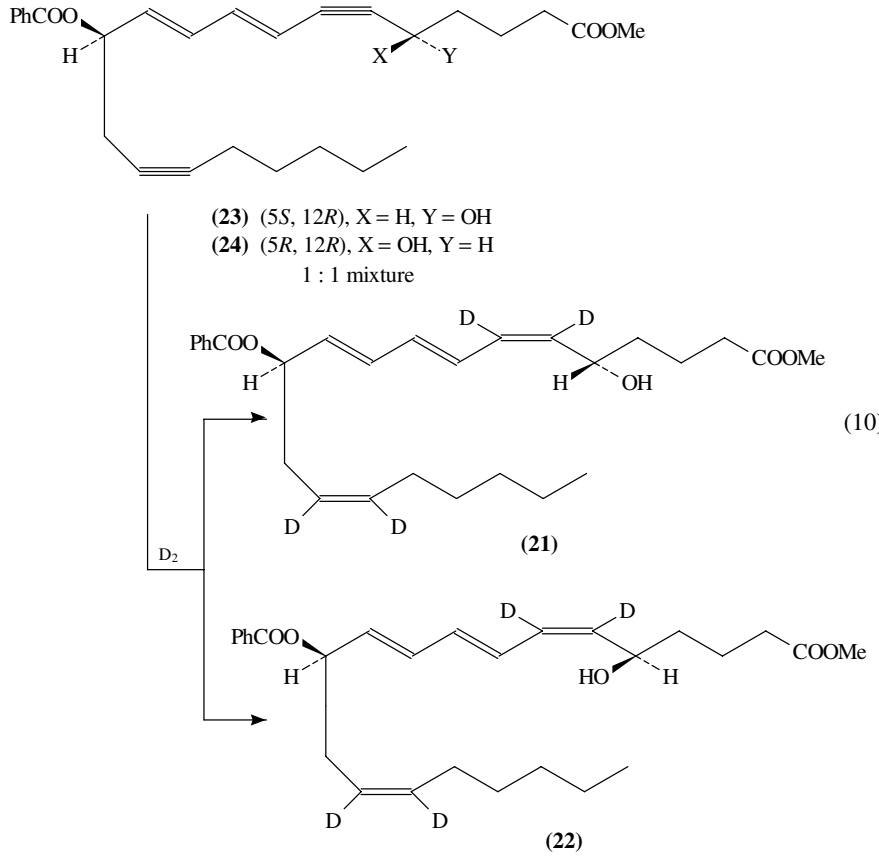


(20) pentafluorobenzyl (PFB) - TMS derivative of the enzymatic product used in SIM (selected ion monitoring) GC/MS analysis of the title compound

7. Synthesis of [6,7,14,15-$^2H_4$]-leukotriene B$_4$ methyl ester

The title compounds LTB$_4$, **21** (*Z*) and **22** (*Z*), have been synthesized[23] by stereoselective reduction with deuterium gas of a 1:1 mixture of the suitable diacetylenic precursors **23** and **24** using Lindlar catalyst or palladium on barium sulphate catalyst (equation 10). Leukotriene B$_4$, a 5-lipoxygenase metabolite of arachidonic acid, playing

a major role in allergic, inflammatory and immunological states[24], had to be deuterium labelled for its quantification in biological samples[25,26] and for defining its physiological role.



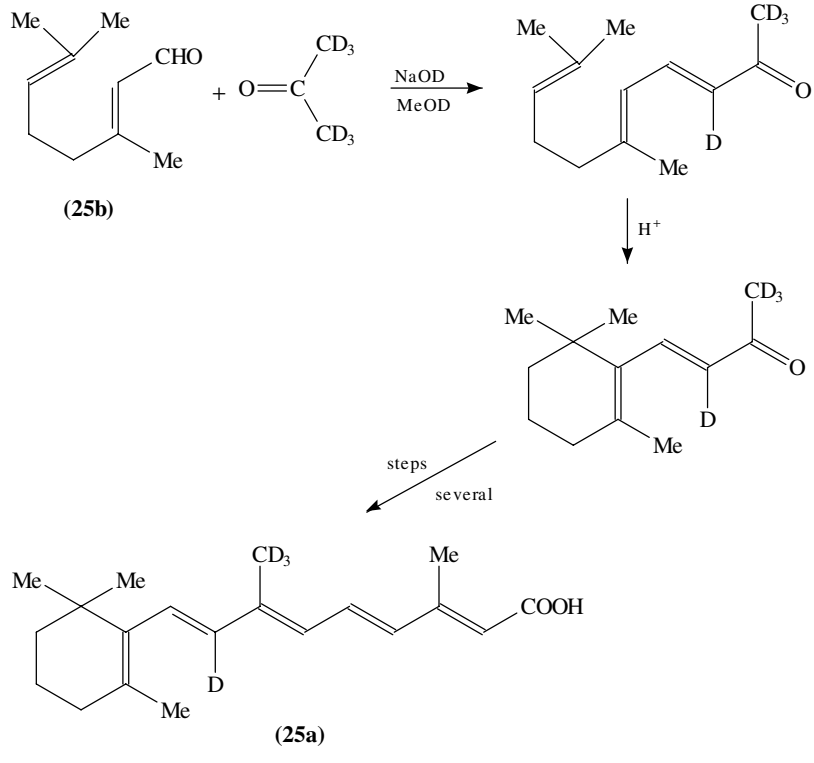
(10)

8. Synthesis of 13-cis-retinoic 8,(9,9,9-methyl)-D_4 acid

The D_4 acid **25a**, which according to MS had 94% of D_4, has been prepared[27] from citral **25b** and acetone-D_6 as before[28] (equation 11).

9. Synthesis of tri-, tetra- and penta-deuteriated forms of vitamin A

Four deuteriated retinols, **26–29**, with 3 to 5 deuterium atoms have been synthesized[29] for metabolism of vitamin A studies in humans[30]. Deuterium has been introduced into appropriate intermediates, used in the reaction scheme shown in equation 12, by base-catalysed exchange with ^2H_2O or perdeuterioacetone. The numbering system for retinol (vitamin A alcohol) is shown in equation 12.



(11)

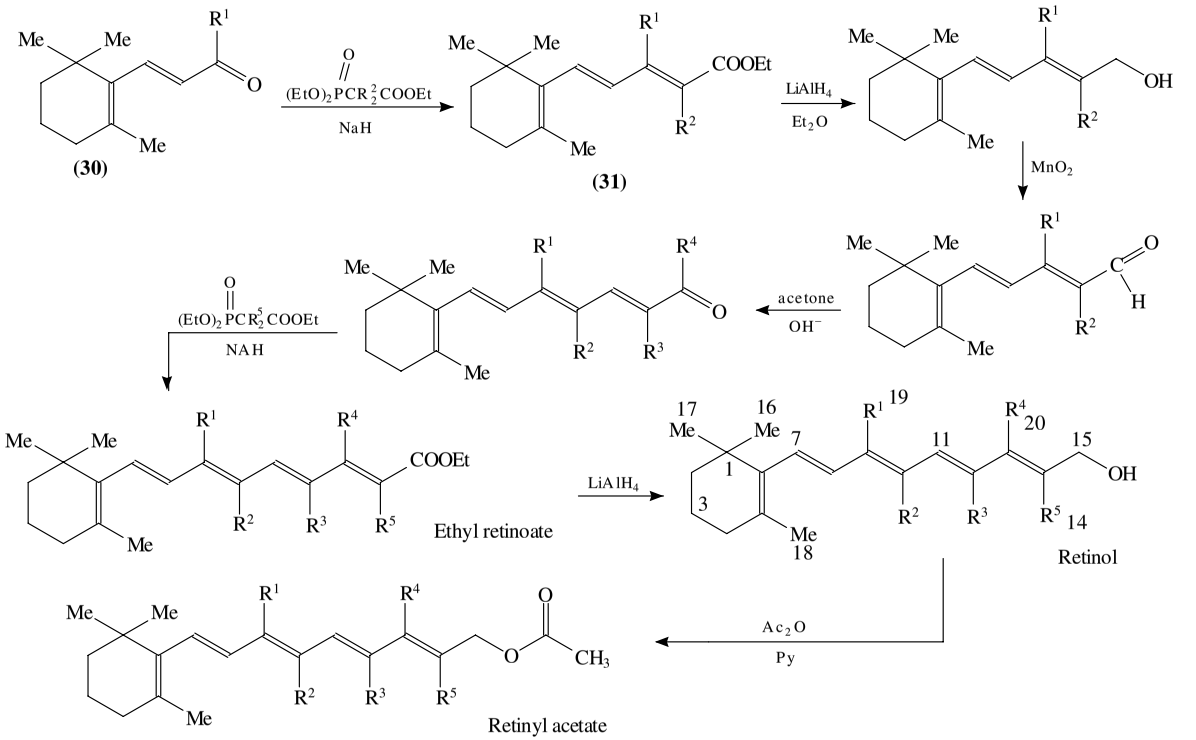
In the case of the synthesis of 10,19,19,19-$^2H_4$-vitamin A, the most useful for biological studies, three deuterium atoms were incorporated into β-ionone **30**, in >98% by deuterium exchange with excess D_2O in the presence of NaO^2H (and pyridine). The tri-deuteriated **30**, utilized in Wittig–Horner reaction with dideuterio triethyl phosphonate, provided tetradeuteriated ethyl β-ionilidene acetate **31** with more than 98% $^2H_4$ (by NMR). No deuterium loss in the subsequent synthetic steps was observed as evidenced by MS and NMR analysis.

10. Synthesis of deuteriated $^2H_8$-β-carotene

Dietary β-carotene, a nutritionally important source of vitamin A, exhibits a protective effect against cancer risk[31,32]. The deuteriated compound, 10,10′,19,19,19,19′,19′,19′-$^2H_8$-β-carotene, **32**, has been obtained[33] by double condensation of the C-15 Wittig salt **33** with the symmetrical C_{10} dial 2,7-dimethyl-2,4,6-octatrienedial, **34** (equation 13) for the study of β-carotene metabolism in humans.

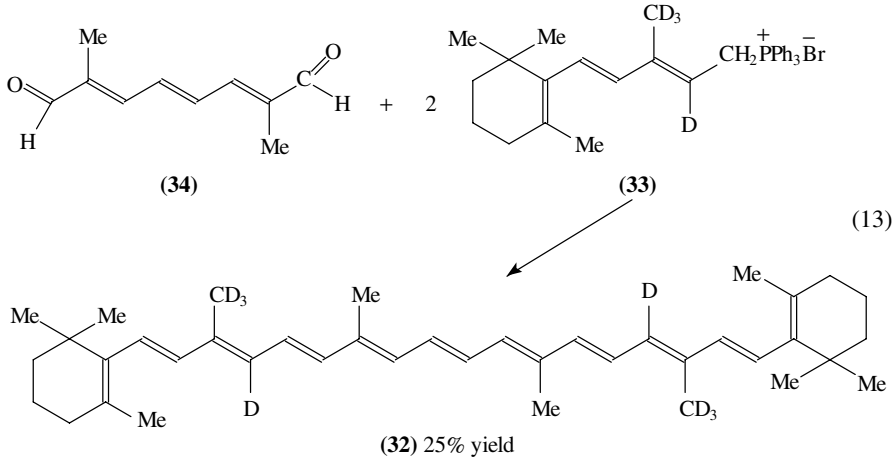
*11. Synthesis of (±)-16,17,18,19-[$^2H_4$]-prostaglandin D_2, **35***

Using dimethyl 3,4,5,6-[$^2H_4$]-2-oxoheptylphosphonate, **36**, prepared in two steps as shown in equation 14, the title prostaglandin D_2, **35**, has been synthesized[34] in thirteen steps (equation 15).

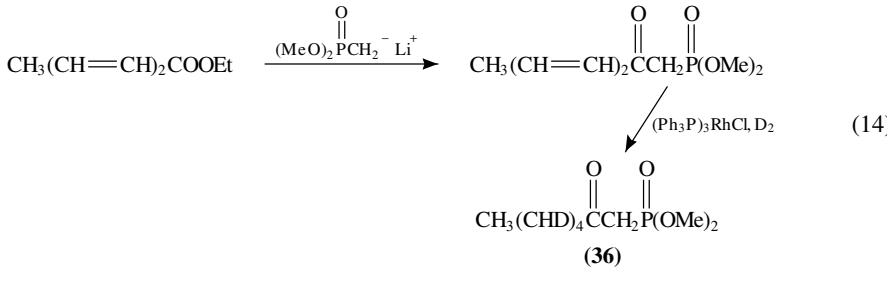


(12)

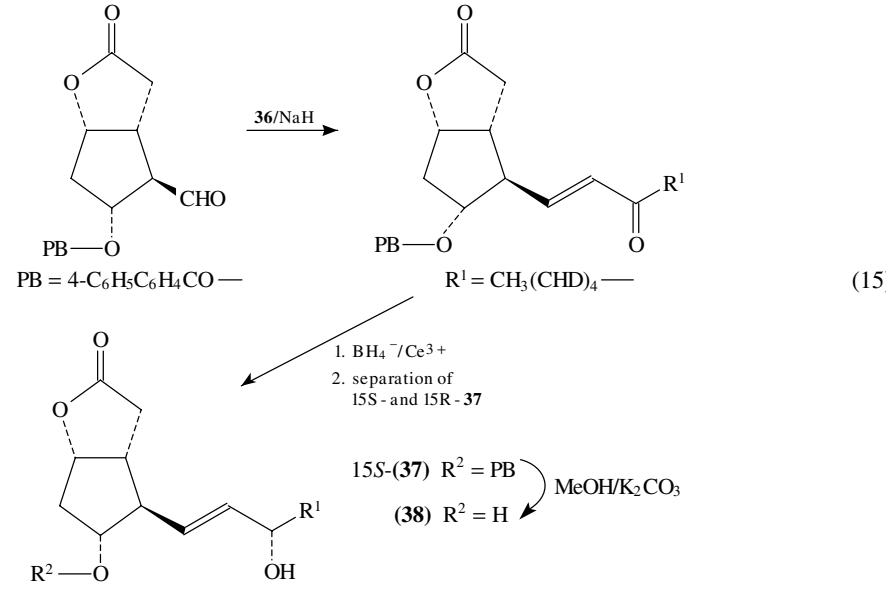
(26) 20, 20, 20- $^2H_3$ -retinoic acid ethyl ester (R^1 = Me, R^4 = C^2H_3)
(27) 14, 20, 20, 20 - $^2H_4$-retinoic acid ethyl ester (R^1 = Me, R^4 = C^2H_3, R^5 = ^2H)
(28) 12, 14, 20, 20, 20 - $^2H_5$-retinyl acetate (R^1 = Me, R^3 = R^5 = ^2H, R^4 = C^2H_3)
(29) 10, 19, 19, 19 - $^2H_4$-retinyl acetate (R^1 = C^2H_3, R^2 = ^2H, R^4 = Me)



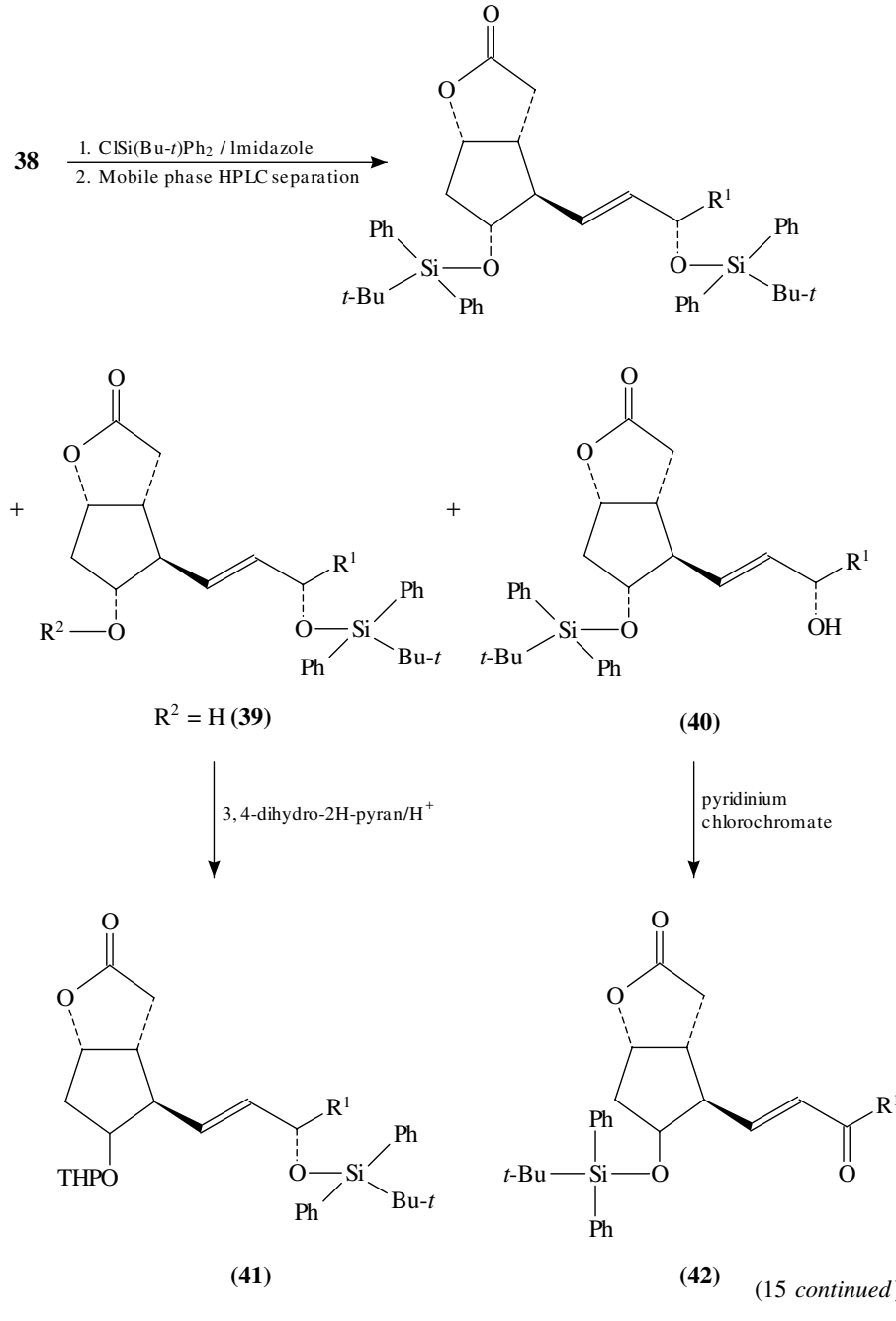
(34) **(33)** **(32)** 25% yield (13)



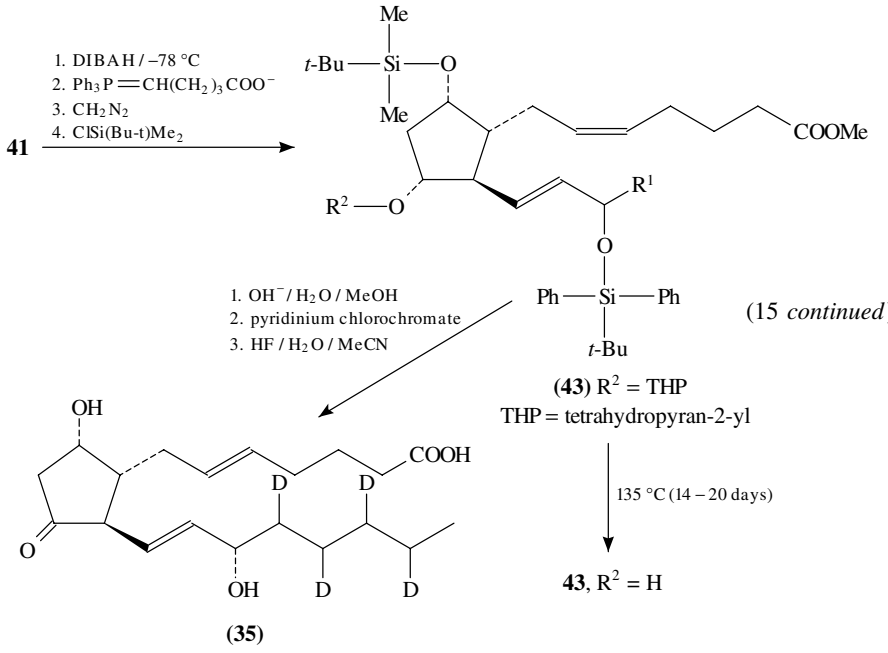
(36) (14)



(15)



(15 *continued*)



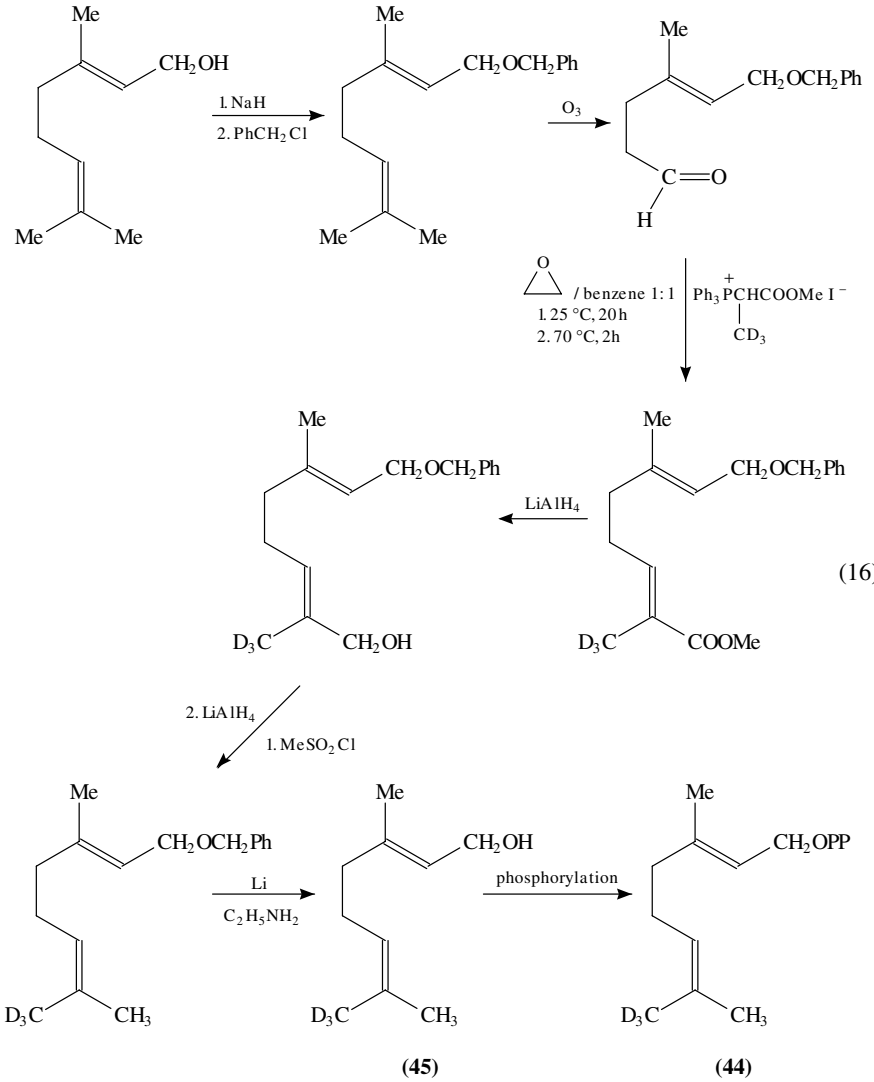
12. Synthesis of [10,10,10-$^2H_3$]-geranyl diphosphate

The title compound **44**, [10,10,10-$^2H_3$]-3,7-dimethyl-2(*E*)-6-octadienyl diphosphate, has been obtained[35] as in equation 16, in order to investigate the mechanism of biosynthesis of limonene[36]. In the last step the diphosphate ester **44** was obtained as the trilithium salt in 47% yield by converting [10,10,10-$^2H_3$]-geraniol **45** into [10,10,10-$^2H_3$]-geranyl chloride with *N*-chlorosuccinimide, treating the chloride with tris(tetra-*n*-butyl)ammonium hydrogen diphosphate, and converting the product into the ammonium salt with cation exchange resin. The resulting triammonium salt of the diphosphate ester was converted into the trilithium salt with lithium chloride.

13. Synthesis of 4- and 10-deuteriated neryl and geranyl-β-D-glucosides and their use in tandem MS studies

a. The title compounds, **46** (*Z*) and **47** (*E*), have been synthesized[37] starting with the deuteriated ketone **48**, prepared in >99% isotopic abundance by base-catalysed exchange with [$^2H_2$]-water. Reaction of **48** under Wittig–Horner conditions furnished the unsaturated esters **49** and **50** which, after chromatographic separation, have been reduced selectively with diisobutyl aluminium hydride (DIBAH), avoiding the reduction of C=C double bond. Modifying the published procedure[38] for the β-D-glucosidation of alcohols, **46** and **47** have been obtained under optimized reaction conditions[37] (equation 17).

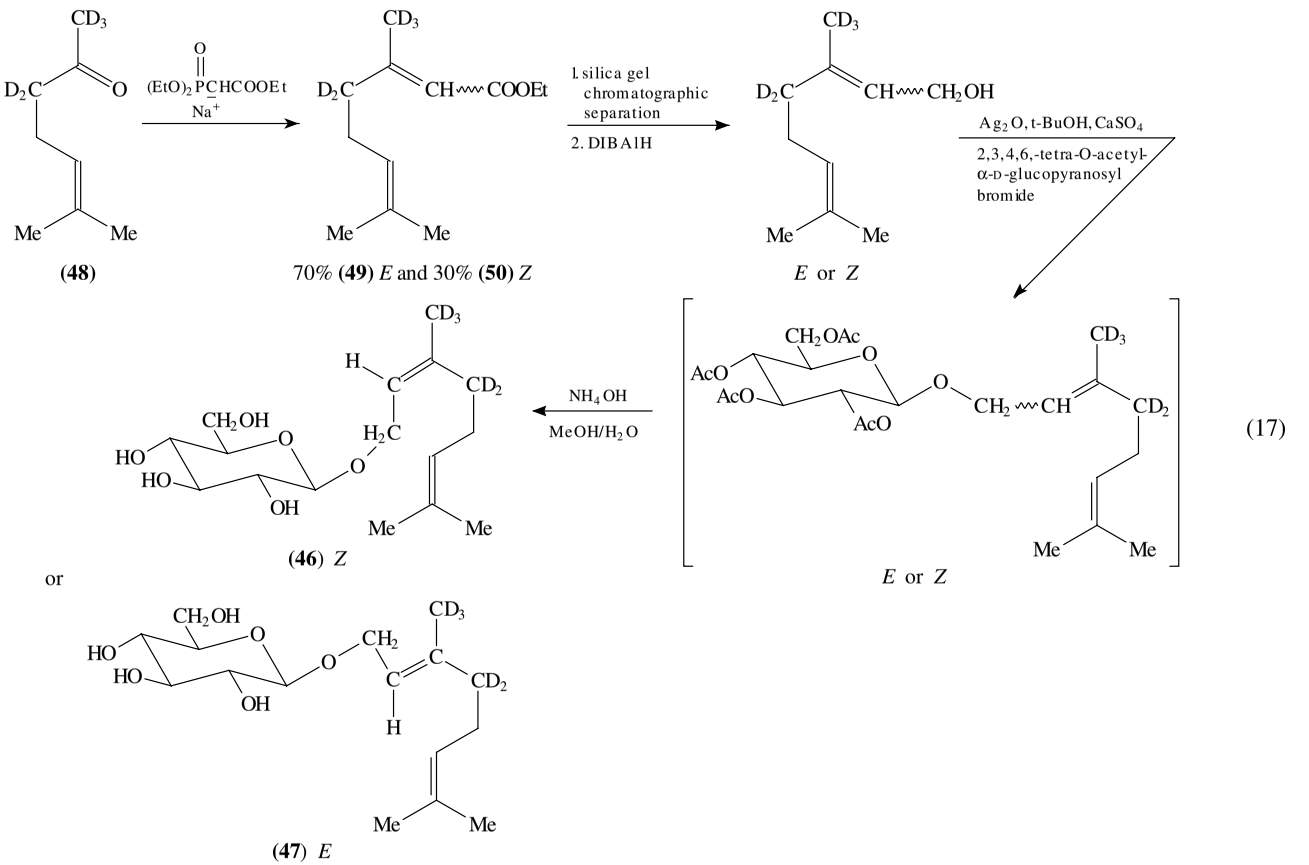
b. Tandem MS comparison of the low-energy CAD collision spectra of (M − H) ion, generated in ammonia NICl (triple quadrupole MS[37]) from geranyl, 4-[$^2H_2$]-10-[$^2H_3$]-geranyl, neryl and 4-[$^2H_2$]-10-[$^2H_3$]-neryl-β-D-glucosides, revealed the formation of the



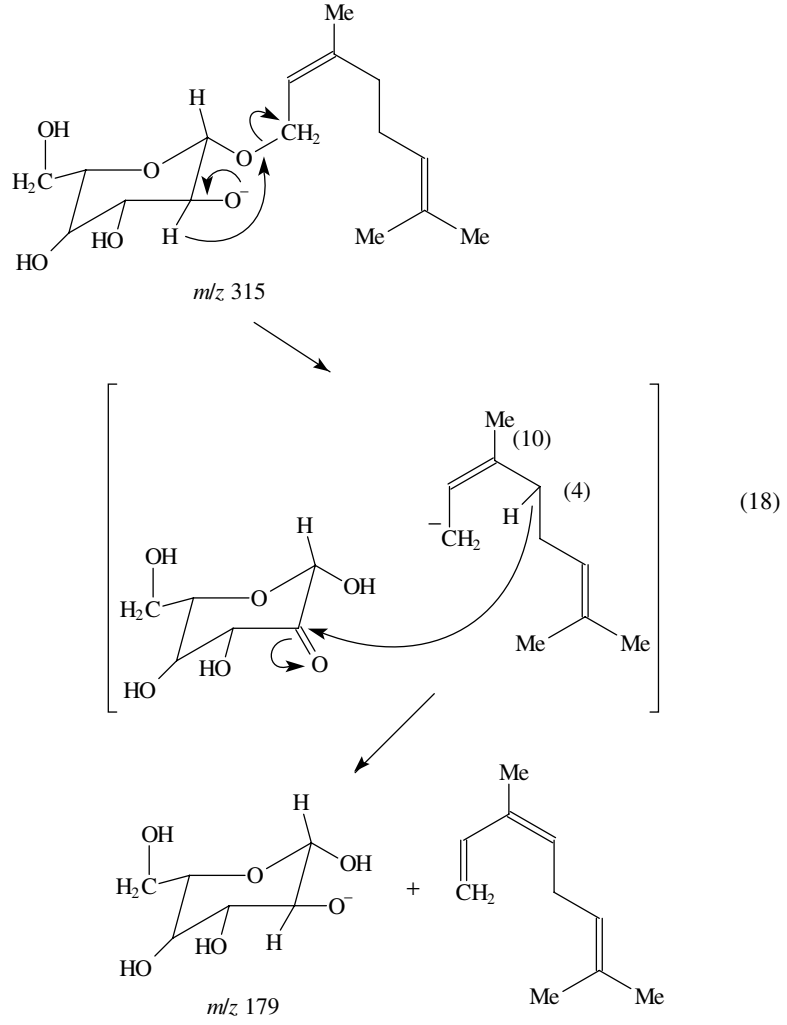
(16)

99.4% deuterium enrichment at C-10
20% overall yield

daughter m/z 179 $(C_6H_{11}O_6)^-$ ion and m/z 180 $(C_6H_{10}{}^2H_1O_6)^-$ ion from parent 315 $(M-H)^-$ and parent 320 $(M-H)^-$ ion, respectively, of the above glucosides. This confirmed the mechanism of the fragmentation of **46** and **47**, exemplified for decomposition of m/z 315 $(M-H)^-$ ion of neryl-β-D-glucoside. The formation of the m/z 179 ion is the result of hydride migration from position 4 (and 10) of the aglycone unit to the osidic part taking place in the intermediate 'anionic ketonic complex' (equation 18). The molecular ion $(M-H)^-$ arises from the osidic part, whereas the aglycone is eliminated as a neutral fragment.


CD3
D2C
O
Me
Me
(48)
(EtO)2PCHCOOEt
Na+
70% (49) E and 30% (50) Z
1. silica gel chromatographic separation
2. DIBAlH
CH CH2OH
E or Z
Ag2O, t-BuOH, CaSO4
2,3,4,6,-tetra-O-acetyl-α-D-glucopyranosyl bromide
CH2OAc
AcO
CH2 CH
CD2
NH4OH
MeOH/H2O
(46) Z
or
(47) E

(17)



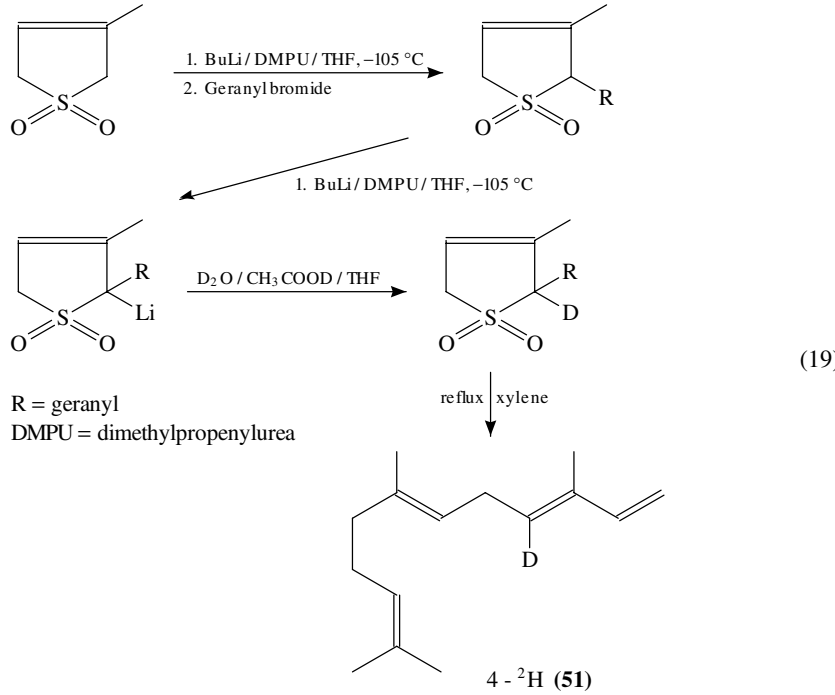
(18)

14. Synthesis of 4-^{2}H-α-farnesene and 1-^{2}H-α-farnesene

The sesquiterpene α-farnesene, **51**, a primary aroma component which occurs in the skin of apples[39] and other fruits[40], attractant and oviposition stimulant to *Laspeyresia pomonella*[41,42], has been deuteriated at $C_{(1)}$ and at $C_{(4)}$ (equations 19 and 20), for study of the induction of superficial scald of apples[43].

15. Synthesis of D_6-α-farnesene

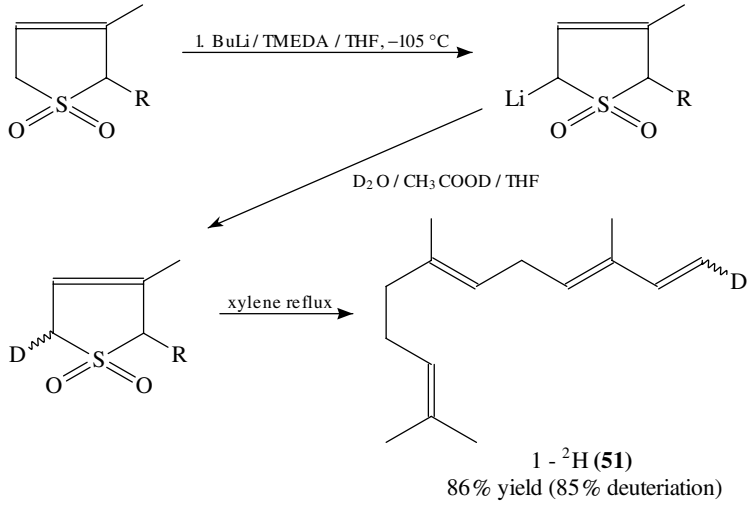
The title compound, **52**, 3,7-dimethyl-11-$^2H_3$-methyl-12,12,12-$^2H_3$-dodeca-1,3*E*,6*E*,10-tetraene, bearing a higher proportion of deuterium, was needed for continuing studies of the induction of superficial scald of apples. It has been synthesized[44] by two parallel



(19)

R = geranyl
DMPU = dimethylpropenylurea

4 - ^{2}H **(51)**
85% yield (60% deuteration)



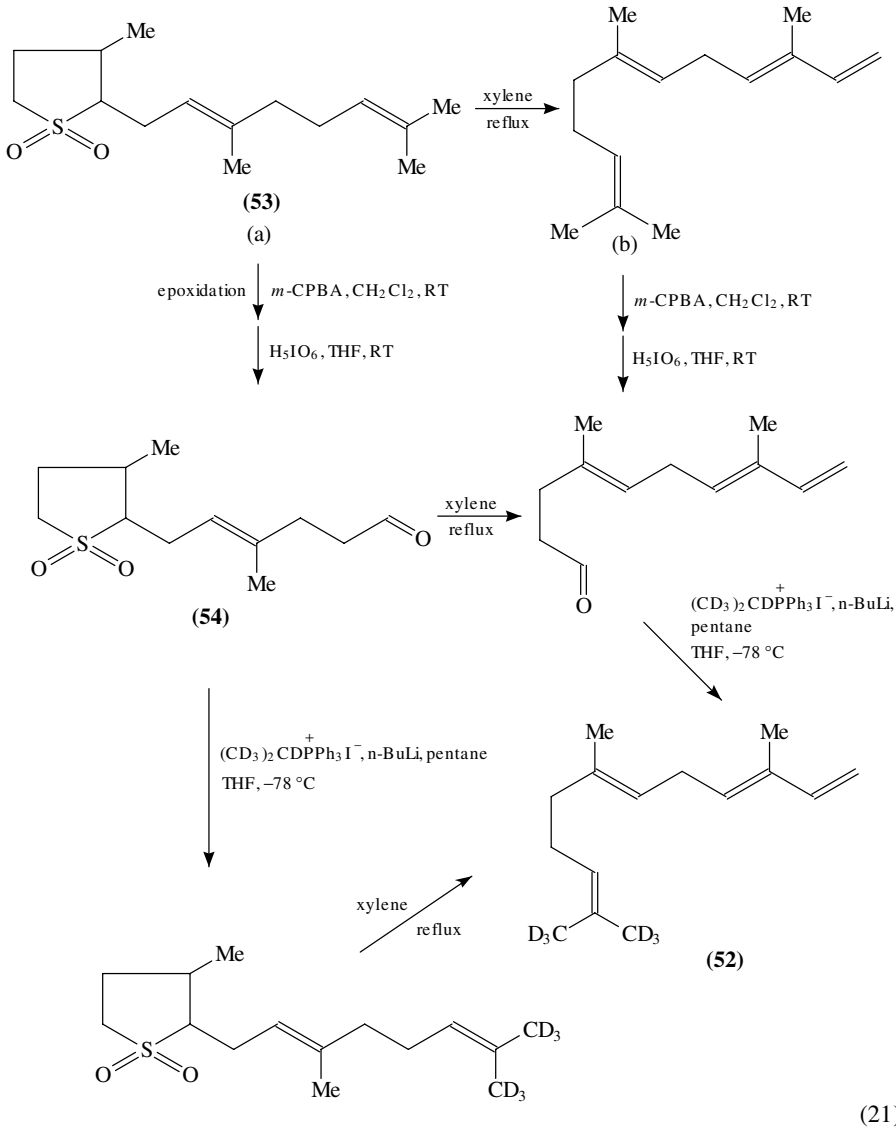
(20)

1 - ^{2}H **(51)**
86% yield (85% deuteration)

TMEDA = *N*, *N*, *N*′, *N*′ - tetramethylethylenediamine

routes a and b (equation 21), starting from the common substrate 2-geranyl-methyl-sulpholene, **53**. Route b gave product **52** in only 9% yield. The overall yield in the synthesis

carried out according to route a, which involves the Wittig reaction of aldehyde **54** with $^2H_7$-isopropyl triphenylphosphonium iodide, followed by thermal elimination of sulphur dioxide, was better (23%).

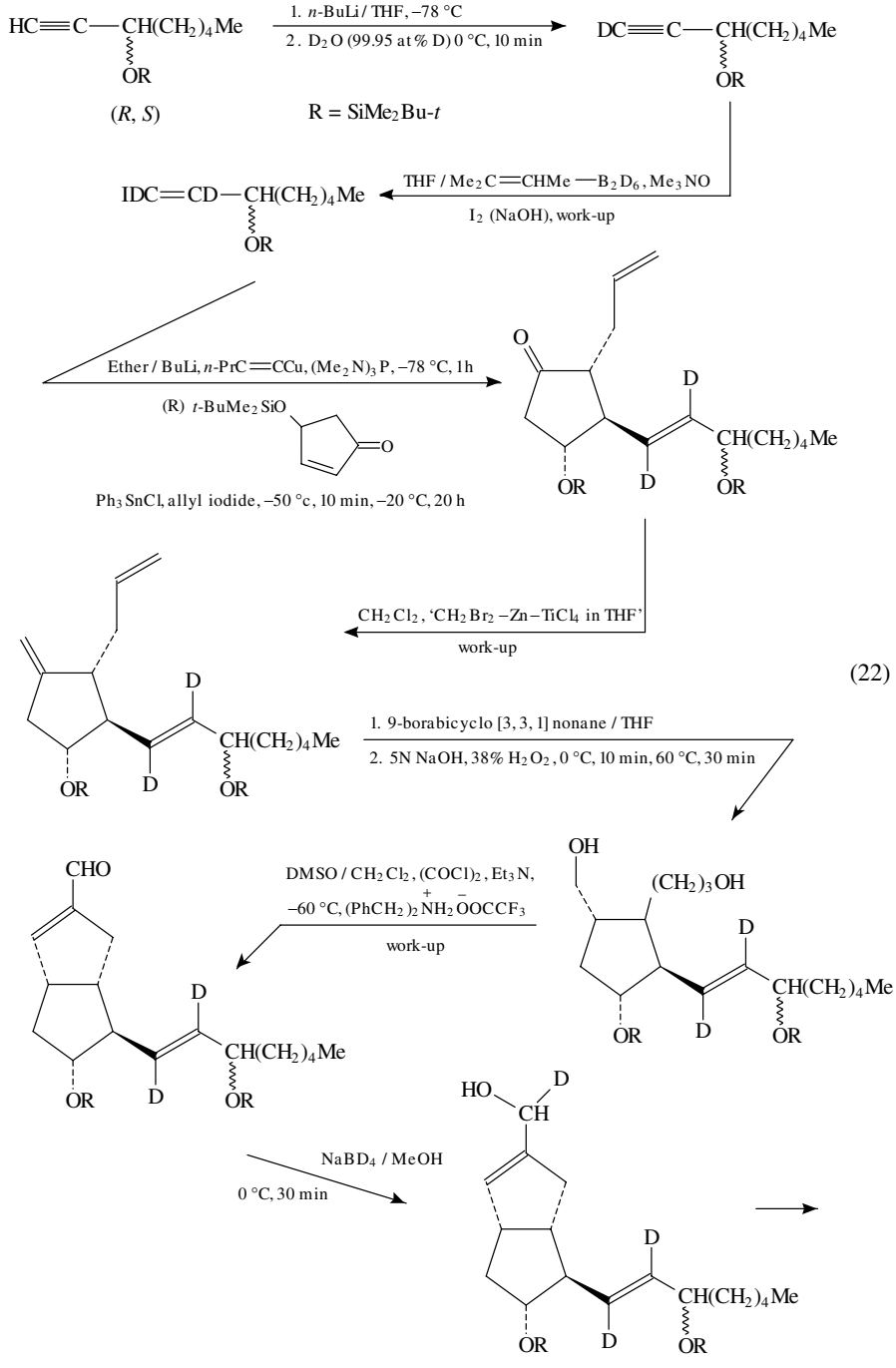


(21)

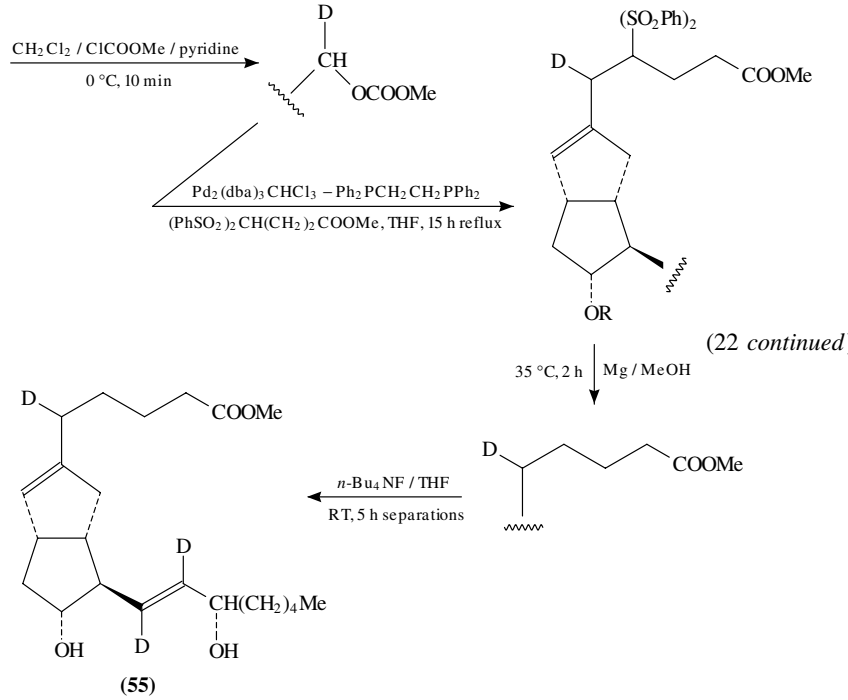
16. Synthesis of polydeuteriated 9 (O)-methano-$\Delta^{6(9\alpha)}$-prostaglandin I_1 methyl esters

a. Synthesis of [5,13,14)-$^2H_3$], of the title derivative, **55**, a promising therapeutic agent for cardiovascular diseases[45–47], has been carried out via H/D exchange, deuterioboration

and sodium borodeuteride reduction[48] as shown in equation 22.

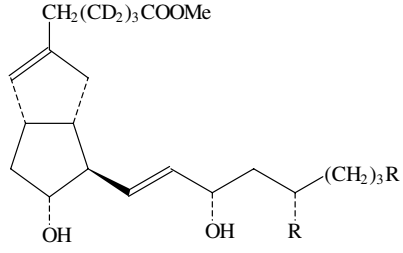


(22)

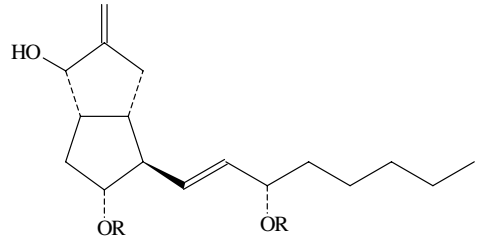


(55)

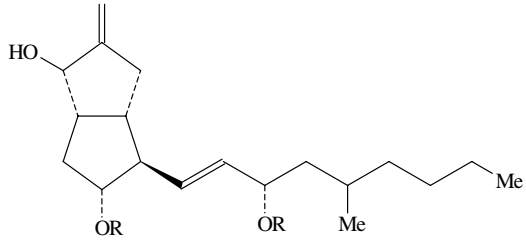
b. The [2,2,3,3,4,4-$^{2}H_6$] derivative **56** has been prepared[48] starting with tetrahydrofuran-D_8 (equation 23). Similarly, the derivatives **57** and **60** have been prepared as shown in



(56) R = H, **(57)** R = Me

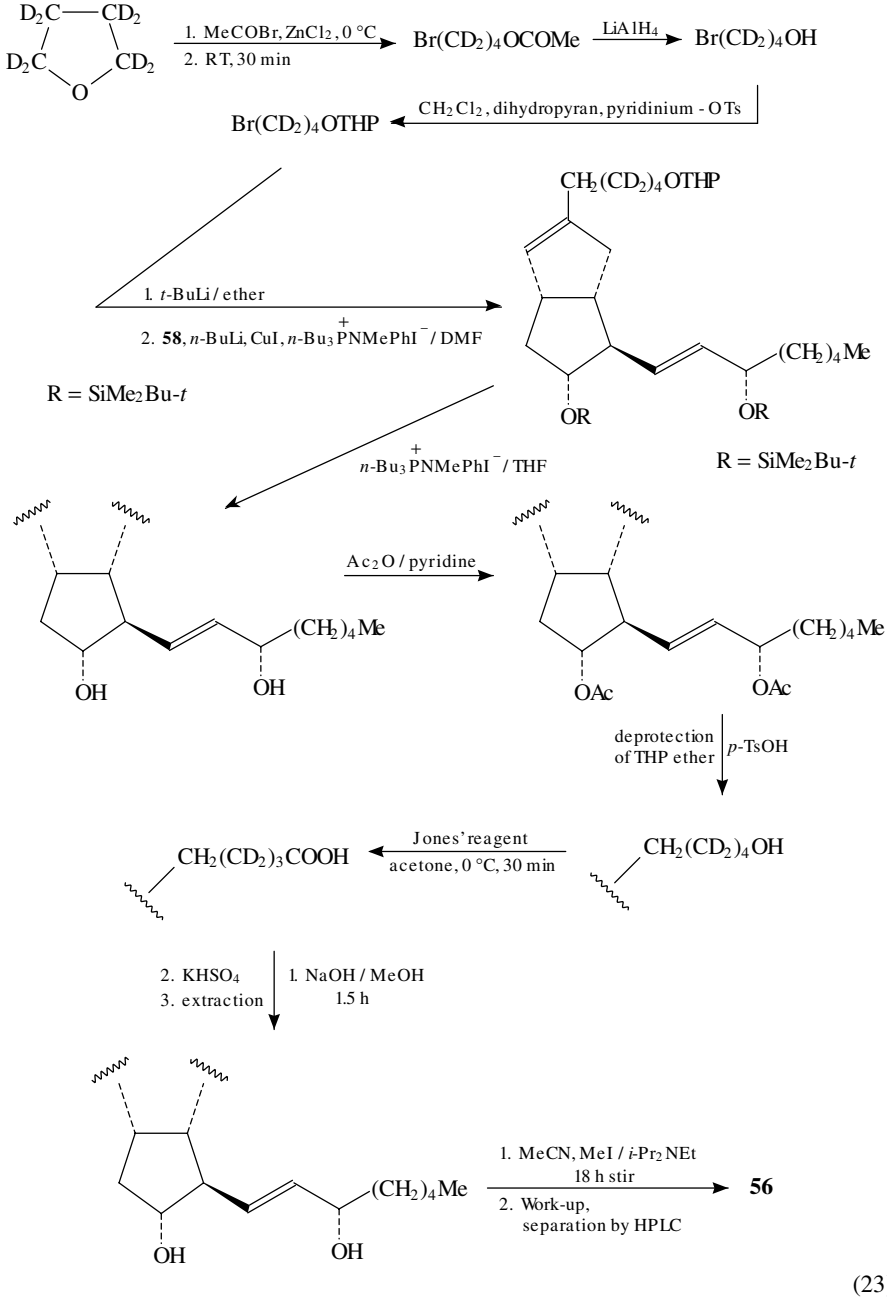


(58) R = $SiMe_2Bu$-*t*

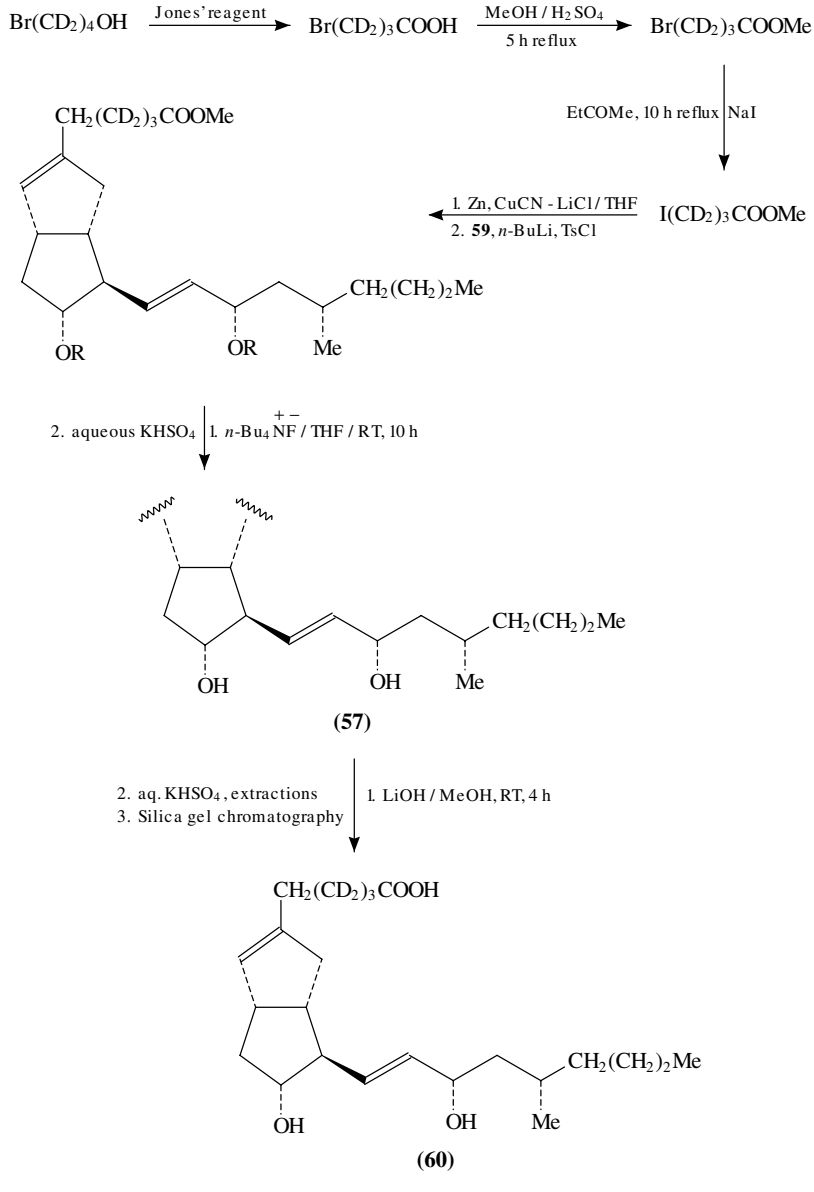


(59)

equation 24. The polydeuteriated isocarbacyclin derivatives **55**, **56** and **57** have been obtained for use as internal standards in GC/MS quantitative analysis and for use as substrates in metabolic studies.



(23)

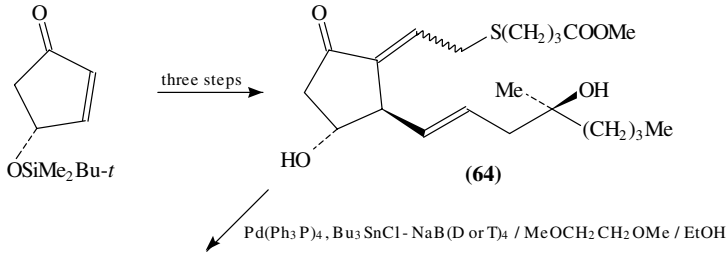


(24)

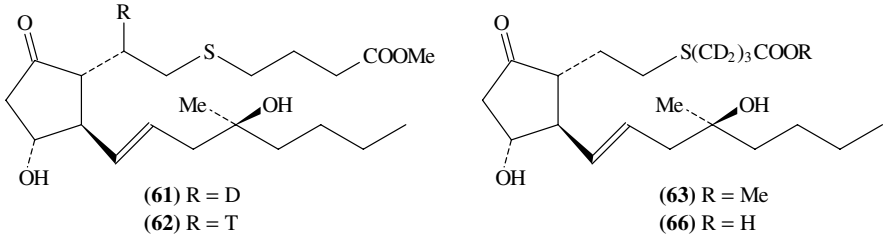
17. Synthesis of [7-^{2}H]-, [7-^{3}H]- and [2,2,3,3,4,4-$^2H_6$]-(16S)-15-deoxy-16-hydroxy-16-methyl-5-thiaprostaglandin E_1 methyl ester, ***61****,* ***62*** *and* ***63***

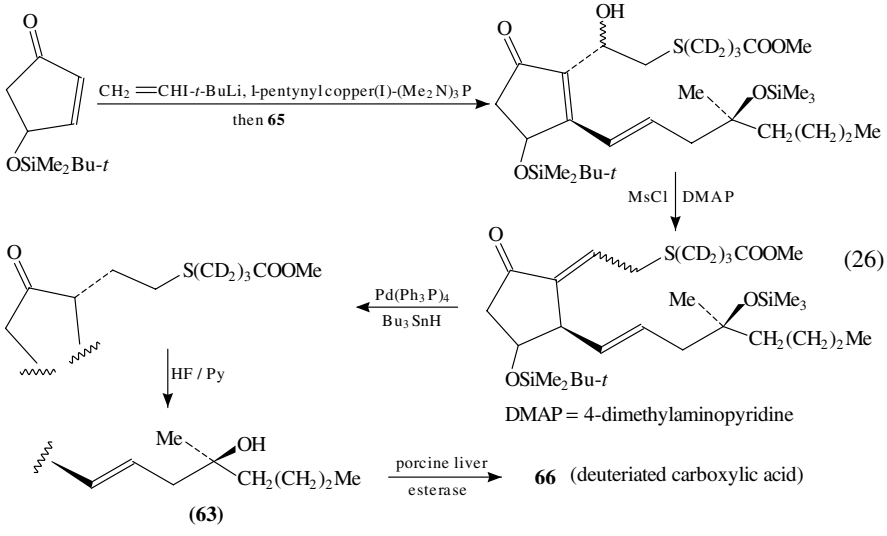
The prostaglandin E_1 and E_2 analogues showing antisecretory and cytoprotective activities[49,50] had to be deuterium or tritium labelled for preclinical studies. The tritiated or deuteriated title compounds **61**, **62** and **63** have been synthesized[51] by the methods outlined in equations 25, 26 and 27. Compounds **61** and **62**, with hydrogen at 7-position

substituted by deuterium or tritium atoms, have been obtained by conjugate reduction of the enone function of the Δ^7 olefinic precursor **64** with *in situ* generated tributyltin[^{2}H]- or [^{3}H]hydride in the presence of palladium(0) catalyst (equation 25). Compound **63** with hydrogen atoms at the 2,3,4-positions substituted by deuterium atoms has been synthesized[51] as shown in equation 26, using the hexadeuteriated aldehyde **65** prepared in three steps (equation 27). Compound **63** has been used[51] as internal standard in GC/MS analysis.

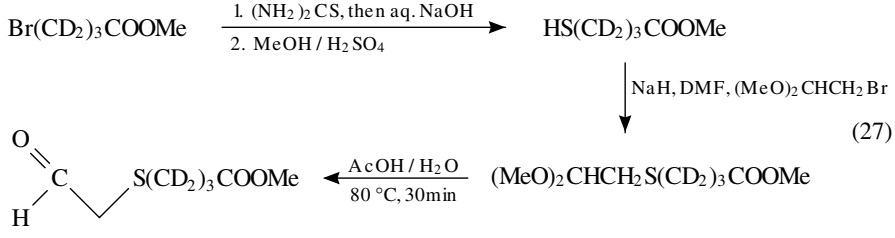


61, 85% deuterium (by MS)
62, 146.8 mCi, 15% yield, specific activity 13.8 mCi/mmol, 95% radiochemical purity (25)





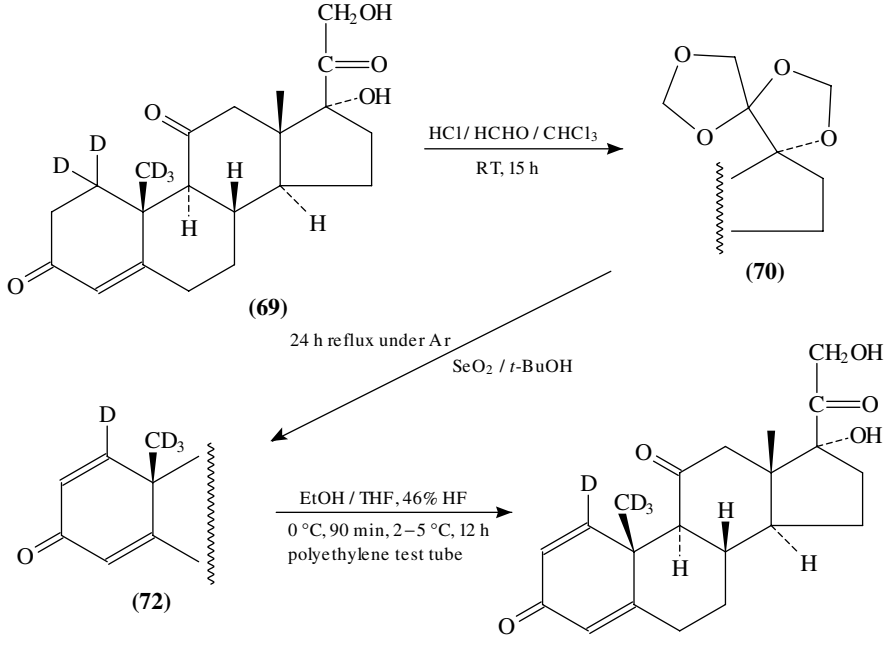
(26)



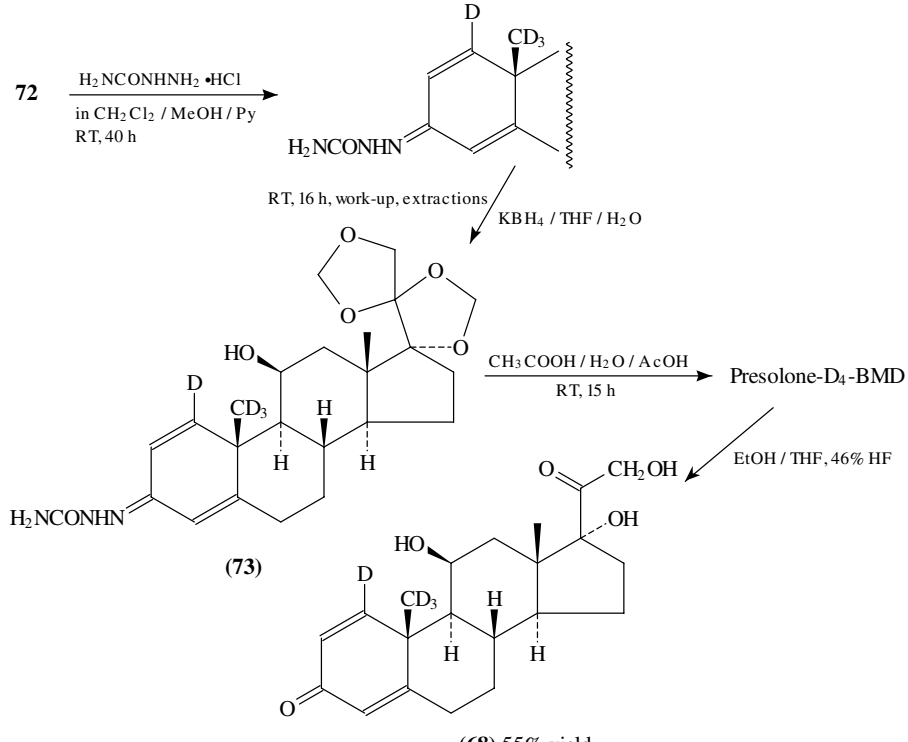
(27)

18. Synthesis of multiply deuterium labelled prednisone and prednisolone

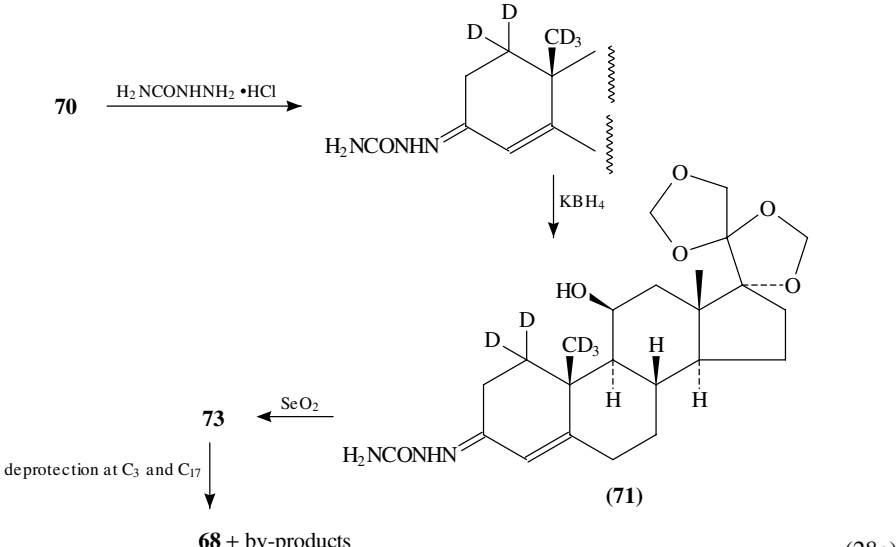
[1,19,19,19-$^2H_4$]Prednisone, **67**, and [1,19,19,19-$^2H_4$]prednisolone, **68**, containing four deuterium atoms at chemically stable sites, have been synthesized[52] starting from [1,1,19,19,19-$^2H_5$]cortisone, **69** (equations 28a, 28b and 28c). No loss of deuterium from the $C_{(19)}$ and $C_{(1)}$ positions has been observed in the course of a synthetic sequence which involved the oxidation of the intermediates **70** and **71** with selenium dioxide in *t*-butanol. Route 28c has been less satisfactory because of the formation of by-products, especially in the oxidation of **71**. Compounds **67** and **68** with ^2H-label in chemically and biologically stable $C_{(1)}$ and $C_{(19)}$ positions are suitable for use in stable isotope methodology (coupled with GC/MS[53,54]) of investigations on steroid hormones in humans[55].



(67) [1, 19, 19, 19 - $^2H_4$]-17α, 21-Dihydroxypregna-1,4-diene-3,11,20-trione (prednisone-D_4) (28a)


72
H2NCONHNH2 •HCl
in CH2Cl2 / MeOH / Py
RT, 40 h
RT, 16 h, work-up, extractions
KBH4 / THF / H2O
CH3COOH / H2O / AcOH
RT, 15 h
Presolone-D4-BMD
EtOH / THF, 46% HF
(73)
(68) 55% yield

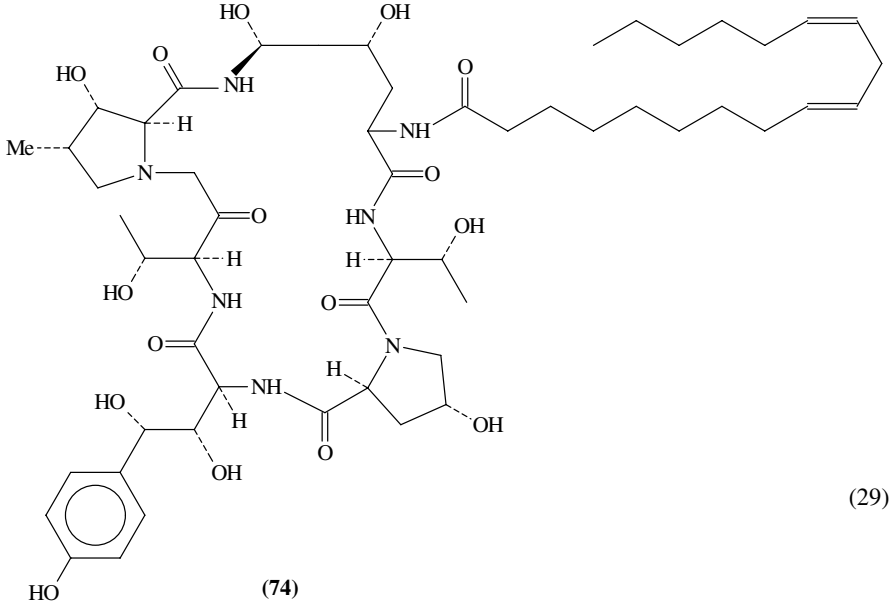
(28b)


70
H2NCONHNH2 •HCl
KBH4
(71)
SeO2
73
deprotection at C3 and C17
68 + by-products

(28c)

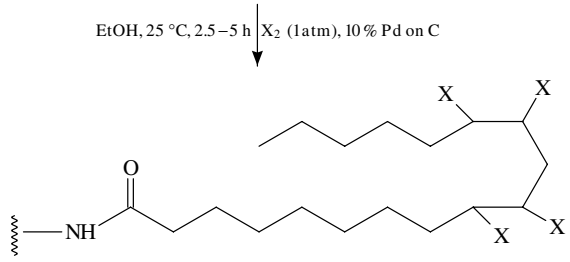
19. Synthesis of deuteriated and tritiated echinocandin B and anilinostearamide and the problem of HPLC isotope effects

Echinocandin B, **74**, a macrocyclic peptide possessing antibiotic and antifungal properties[56], has been catalytically reduced with hydrogen, deuterium or tritium[57] (equation 29). The proton NMR and mass spectra of the reduction product **76** indicated that incorporation of deuterium exceeded saturation of double bonds. Four to ten deuterium atoms (with eight predominating) had been incorporated. This means that under the experimental conditions employed allylic labelling took place and a double-bond isomerization occurred during the reaction. Hydrogen–deuterium exchange might be also occurring[58].



(74)

(29)



(75) tetrahydroechinocandin B, 20% yield (in EtOH, 2.5 h reaction time)

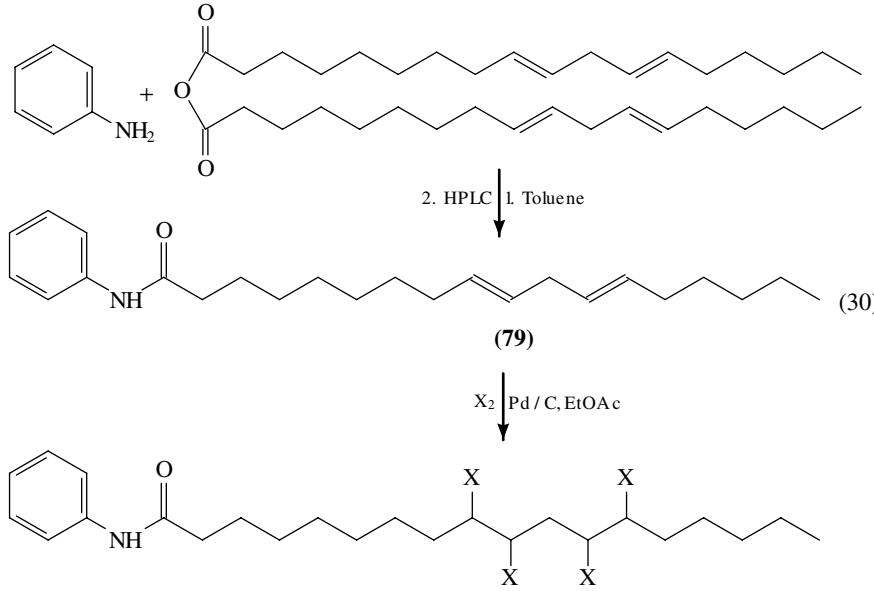
(76) X = ^{2}H, 30% yield (5 h reaction time in DMF)

(77) X = ^{3}H, 5.41 mCi, specific activity 129.0 Ci mmol^{-1}, 97.6% radiochemical purity by HPLC

During the reversed phase HPLC analysis of the tritiated echinocandin **77** it has been observed that the radioactivity of **77** has been detected prior to the UV absorbance of the

reference compound. This chromatographic isotope effect has been also observed in the case of deuteriated analogue and the elution order tritiated < deuteriated < hydrogenated has been established.

The model compound anilinostearamide **78**, labelled in the aliphatic chain only, prepared subsequently by the reduction of linoleic precursor **79** with hydrogen or deuterium (equation 30), exhibited a chromatographic isotope effect of similar magnitude. The labelled compound elutes on the reversed-phase HPLC prior to the unlabelled one.



(78) X = H (100% yield); X = ^{2}H (100% yield)

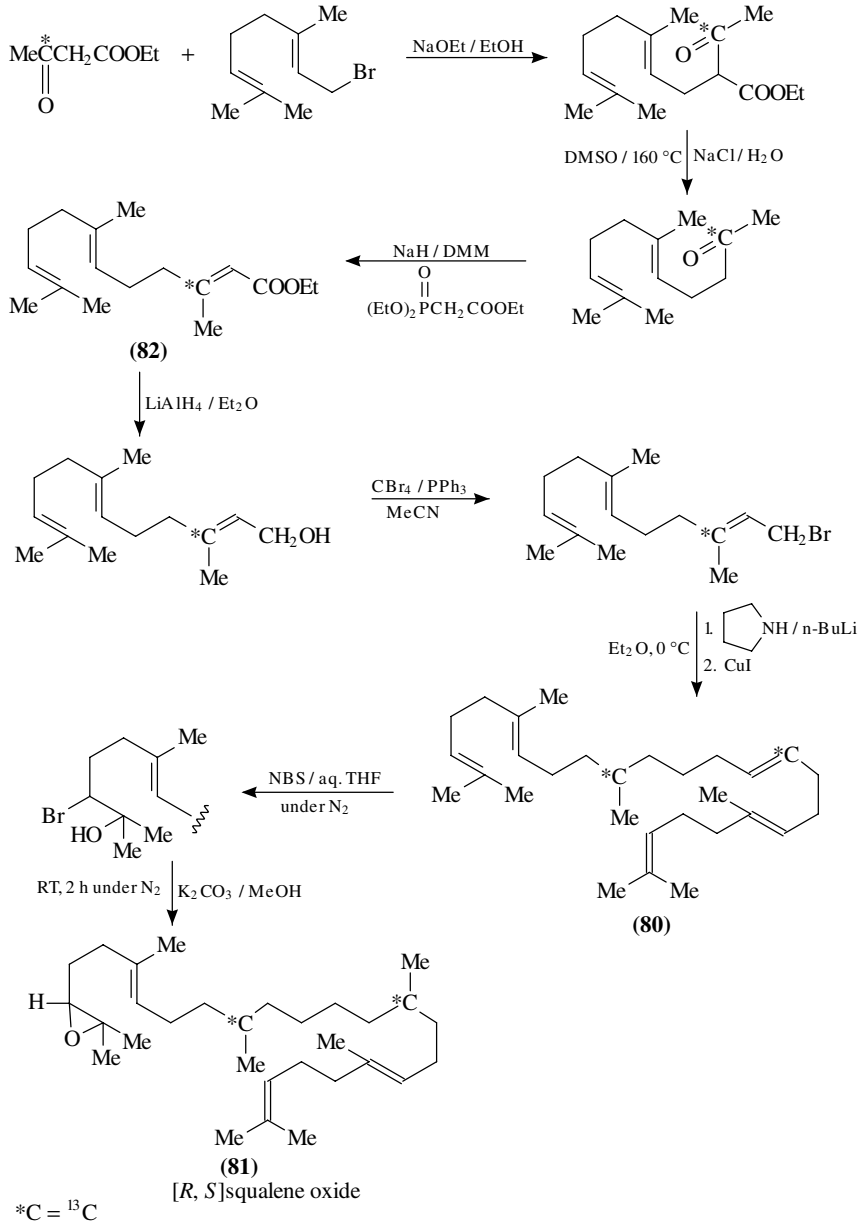
It has been suggested[57] that the observed isotope effect arises from the differences in interaction between the C−H and C−D bonds and the stationary phase. The deuteriated compounds are less lipophilic than the unlabelled ones. The C−D bonds are shorter, exhibit lower polarizabilities and have lower vibrational frequencies. The deuterium atoms behave as being smaller than hydrogen atoms. The C−D bonds do not have as strong an attractive force to the stationary phase as do the C−H bonds and therefore the deuteriated species are eluted faster on reversed-phase HPLC than the hydrogenated species[59−64]. The rigorous treatment of Vapour Pressure Isotope Effects (VPIE) and Chromatographic Isotope Effects developed by Bigeleisen[65], van Hook[66] and Devyatykh[67] is presented in review articles and monograph chapters[68−70].

B. Synthesis of Carbon-13-labelled Compounds

*1. Synthesis of 10,15-[$^{13}C_2$]-Squalene, **80**, and -DL-squalene oxide **81***

10,15-[$^{13}C_2$]-Squalene, **80**, has been produced[71] in the reaction sequence shown in equation 31 which involves alkylation of 3-^{13}C-ethyl acetoacetate with geranyl bromide, followed by hydrolysis, decarboxylation and treatment with triethyl phosphonoacetate and then reduction of the ester **82** with $LiAlH_4$, bromination with CBr_4/PPh_3 and coupling the farnesyl bromide with CuI/Li-pyrrolidine. Epoxidation of **80** has been effected by

treatment with NBS in aqueous THF followed by elimination of HBr with K_2CO_3.



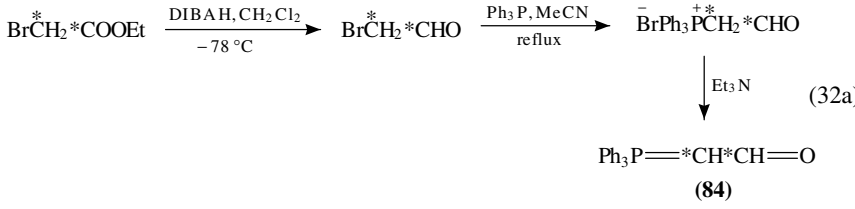
(31)

The ^{13}C-labelled squalene has been used[71] to study the mechanism of its enzymatic conversion to lanosterol (3-β-hydroxy-8,24-lanostadiene[72]) by yeast squalene-oxide lanosterol

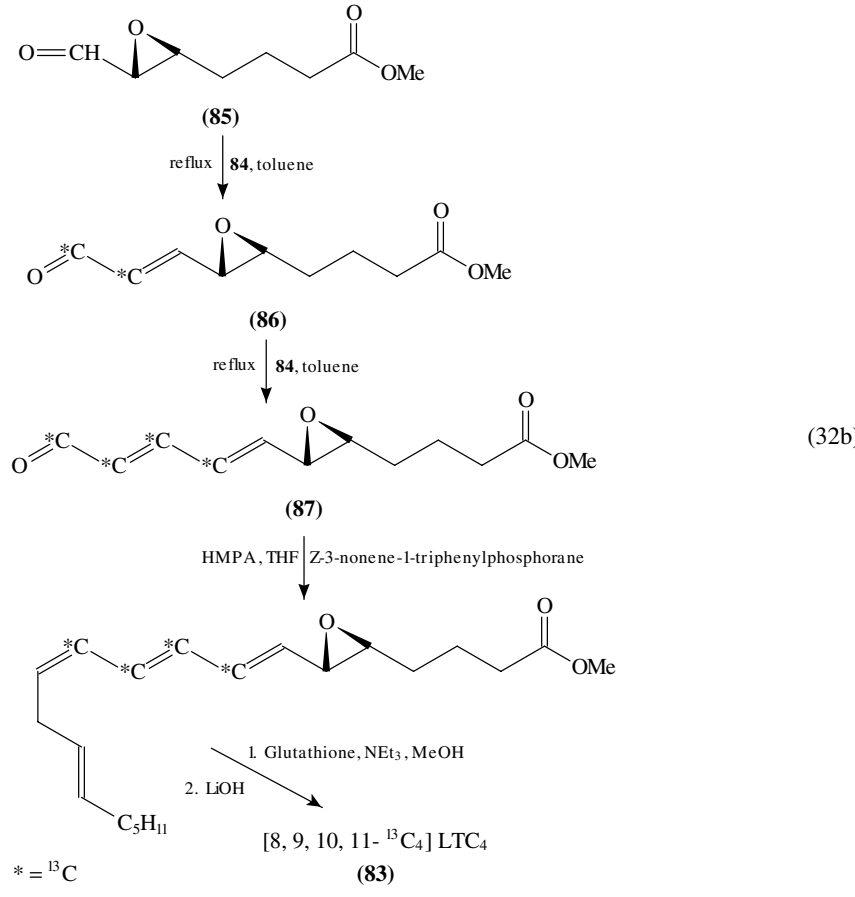
cyclase and it will be utilized in the future for preparations of labelled steroid analogues commercially unavailable.

2. Synthesis of [8,9,10,11-$^{13}C_4$]leukotriene C_4

The title compound, [8,9,10,11-$^{13}C_4$]LTC_4, **83**, an ideal internal standard for GC/MS and other MS determinations of cysteine containing leukotrienes which show biological effects at very low concentration, such as smooth muscle contraction and hypersensitivity reactions[73], has been obtained[74] in a reaction sequence shown in equations 32a and b.



(32a)

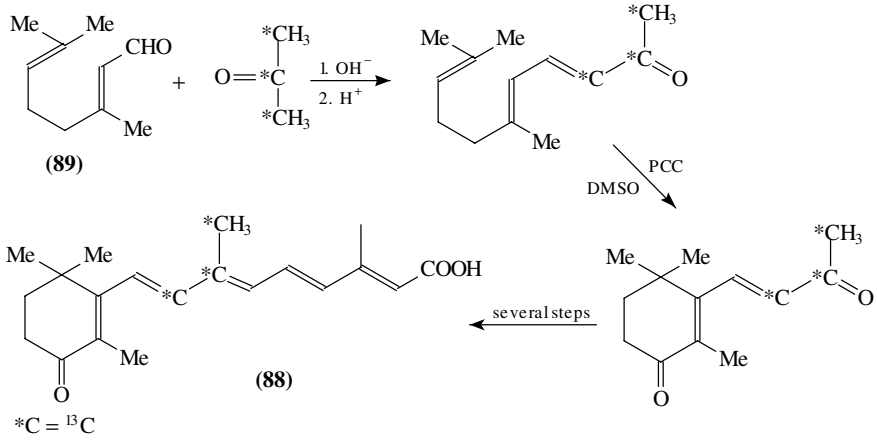


(32b)

Wittig reaction of [1,2-$^{13}C_2$]formylmethylenetriphenylphosphorane, **84**, with **85** and subsequent Wittig reaction of **86** with **84** yielded [8,9,10,11-$^{13}C_4$]LTA$_4$ methyl ester, **87**, which in the last step was converted to **83** in 12% yield.

3. Synthesis of 4-oxo-13-cis-retinoic-8,9,19-$^{13}C_3$ acid

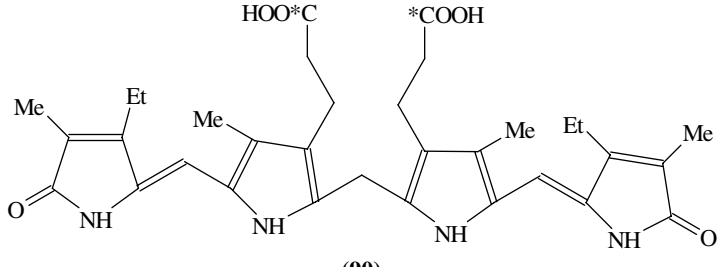
The title compound, **88**, the main metabolite of 13-*cis*-retinoic acid in mammals, has been synthesized[27] as before via condensation of acetone-1,2,3-$^{13}C_3$ with 3,7-dimethyl-2,6-octadienal (citral), **89** (equation 33).



(33)

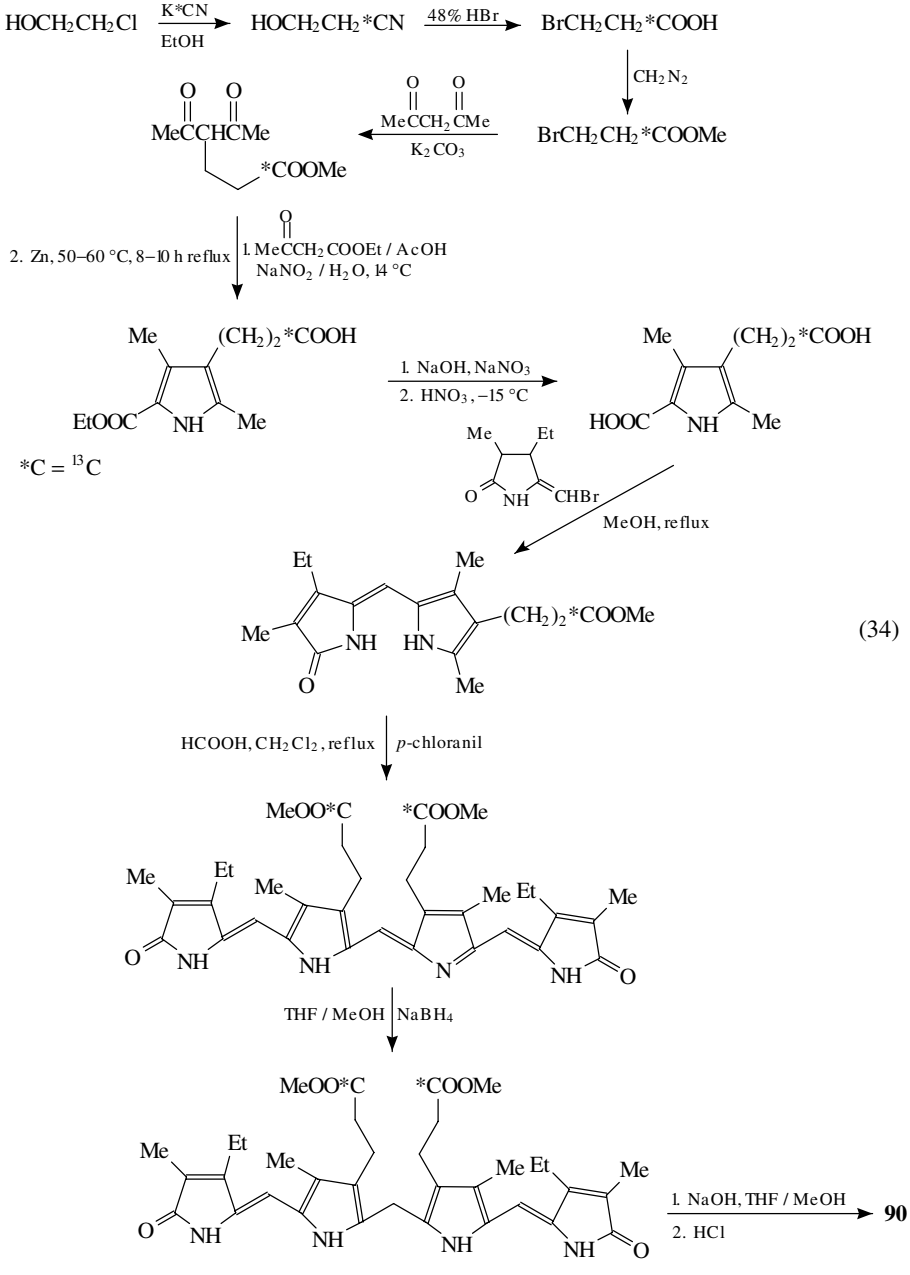
4. Synthesis of bis-[^{13}COOH]-mesobilirubin-XIIIα

Mesobilirubin-XIIIα labelled with ^{13}C in two propionic acid ^{13}COOH groups, **90**, has been synthesized[75] in 11% overall yield from K^{13}CN in 10 steps shown in equation 34. **90**, a model compound not found in nature, is to be used to study the conformation of bilirubin in solution[76] or when bound to proteins or in membranes to understand its ability to cross several selective physiological barriers such as placenta and blood–brain barrier



(90)

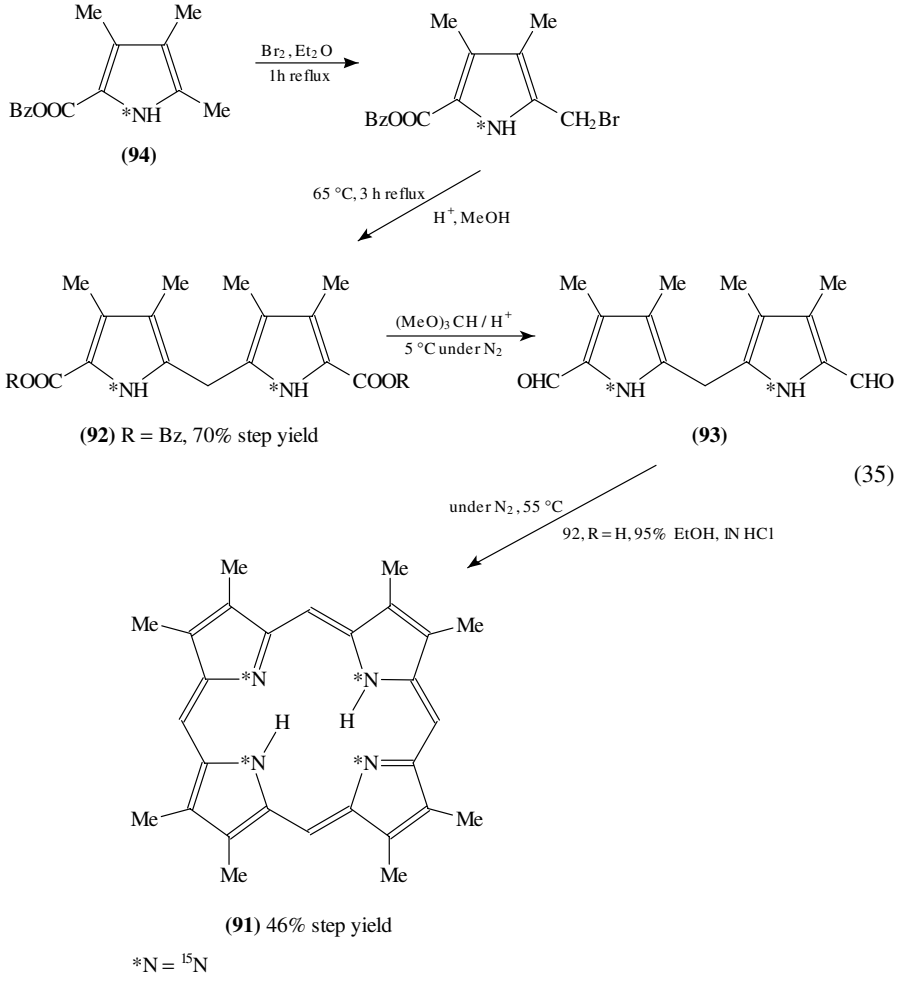
(BBB). It is suggested[75] that conformation-stabilizing intramolecularly hydrogen-bonded bilirubin is involved in transport of **90**.



C. Synthesis of Nitrogen-15-labelled Compounds

1. Synthesis of [$^{15}N_4$]-octamethylporphyrin

[$^{15}N_4$]-octamethylporphyrin **91** has been synthesized[77] for solid state NMR studies by condensation of [$^{15}N_2$]-5,5′-dicarboxy-3,4,3′,4′-tetramethyldipyrrylmethane **92** with [$^{15}N_2$]-5,5′-diformyl-3,4,3′,4′-tetramethyldipyrrylmethane, **93**, in 46% yield as outlined in equation 35, which follows from the previously described synthetic procedure[78,79].



(35)

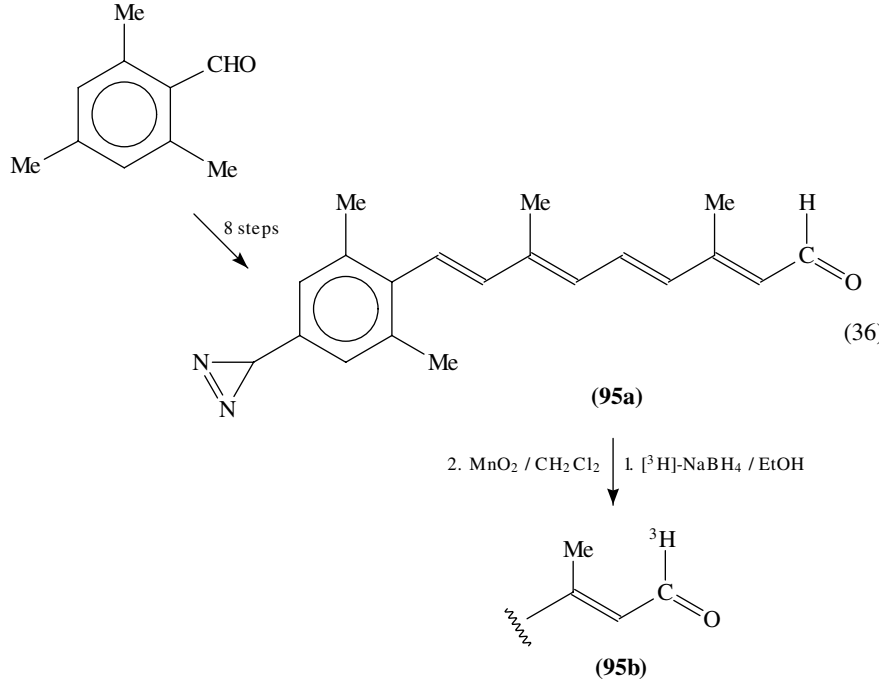
Benzyl [^{15}N]-3,4,5-trimethylpyrrol-2-carboxylate, **94**, has been obtained[77,79] in 38% yield in the reaction of [^{15}N]-sodium nitrite with benzyl acetoacetate in AcOH at 10–5 °C, during 18 h, followed by addition of 3-methyl-2,4-pentanedione, AcONa, powdered zinc in AcOH, heating the suspension at 60 °C during 1 h, pouring the suspension over ice-water (5 °C, 18 h) and recrystallization (MeOH–H_2O).

III. SYNTHESIS AND USES OF DIENES AND POLYENES LABELLED WITH TRITIUM

A. Synthesis of Tritium-labelled Retinol and Retinoic Acid Analogues

1. Synthesis of 3,7-dimethyl-9-[4′-(3H-diazirinyl)-2′,6′-dimethylphenyl]-2E,4E,6E,8E-nonatetraenal-1-^{3}H, ***95b***

This photoaffinity labelling analogue of all-*trans*-retinal, **95b**, has been tritium labelled[80] by reduction of unlabelled aldehyde **95a** with [^{3}H]-$NaBH_4$ and subsequent oxidation of the obtained tritium-labelled retinol with activated manganese dioxide. The product **95b** (specific activity 38.3 mCi mmol^{-1}) has been isolated by preparative TLC (equation 36).

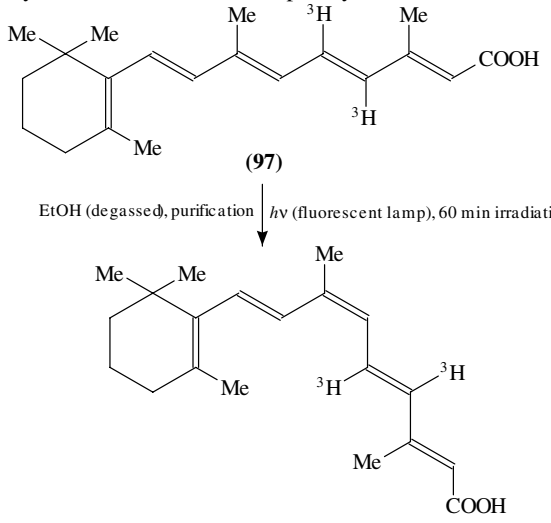


(36)

95b has been used to investigate the mechanism of the light-driven proton pumping activity taking place in purple membranes[81,82] of halobacteria living in water of very high salt concentration, which they utilize as energy transducers. The purple membrane contains a single protein *bacteriorhodopsin*, folded into its lipid bilayer. The colour is caused by the presence of one equivalent of retinal, 3,7-dimethyl-9-(2,6,6-trimethyl-1-cyclohexen-1-yl)-2,4,6,8-nonatetraenal covalently bound to the protein through the protonated Schiff base linkage[81,82].

2. Synthesis of 9-cis-retinoic acid [11,12-$^3H_2$(N)] by photochemical isomerization

The tritium-labelled 9-*cis*-retinoic acid [11,12-$^3H_2$], **96**, the natural ligand for retinoid X receptor (RXR)[83], has been produced[84] by small-scale photoisomerization of all-*trans*-retinoic acid [11,12-$^3H_2$(N)], **97**, followed by HPLC purification (equation 37).



(37)

(96) specific activity of 48.7 Ci mmol^{-1}, radiochemical purity > 96%

3. Synthesis of isotopically labelled retinoids

a. Synthesis of tritium-labelled retinyl acetate. Retinyl acetate, **98**, labelled with tritium at the $C_{(11)}$ and $C_{(12)}$ positions, has been obtained[27] by partial reduction of oxenin **99** with tritium gas to hydroxenin [11,12-$^3H_2$], **100**, and subsequent acetylation and rearrangement (equation 38). The phase transfer 'rearrangement solvent' is 10 mg of acetyl trimethylammonium bromide (CETAB) + 10 μL pyridine in 100 mL of CH_2Cl_2.

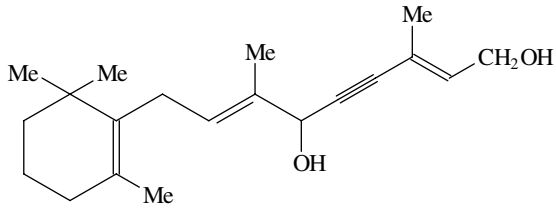
*b. Synthesis of tritium-labelled [11,12-$^3H_2$] retinol, **101**, retinyl ester, **102**, and all-trans retinoic acid, **103***. Retinol-[11,12-$^3H_2$], **101**, was obtained[27] by alkaline hydrolysis of **98**, retinoic-[11,12-$^3H_2$] acid, **103**, was obtained by oxidation of **101** with manganese dioxide and silver oxide, retinyl-[11,12-$^3H_2$] propionate, **102a**, retinyl [11,12-$^3H_2$]-myristate, **102b**, and retinyl-[11,12-$^3H_2$] palmitate, **102c**, have been obtained by treatment of **101** with propionic anhydride and myristoyl chloride or palmitoyl chloride, respectively (equation 39).

Retinyl esters **102a–c** (1 mCi ml^{-1}) stored under argon at $-60\,^{\circ}$C in toluene containing 40 μg of 2-*t*-butyl-4-methoxyphenol and 4 μL of pyridine are quite stable. After 1 year about 60% decomposition was noted, due to radiolysis in the case of **102c**. Retinoic acid **103** under similar conditions is also radiochemically stable, but after 4 months the material has to be repurified[85]. Specific activities of tritium-labelled retinoids in the 10–40 Ci mmol^{-1} range have been found necessary in view of the discovery and use of cellular retinoid binding proteins[86].

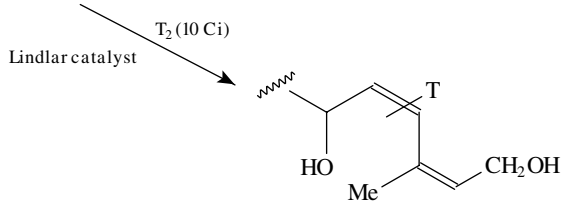
B. Synthesis of Tritium-labelled Analogues of Juvenile Insect Hormones

1. Synthesis of tritium-labelled photoaffinity analogues of natural hormones

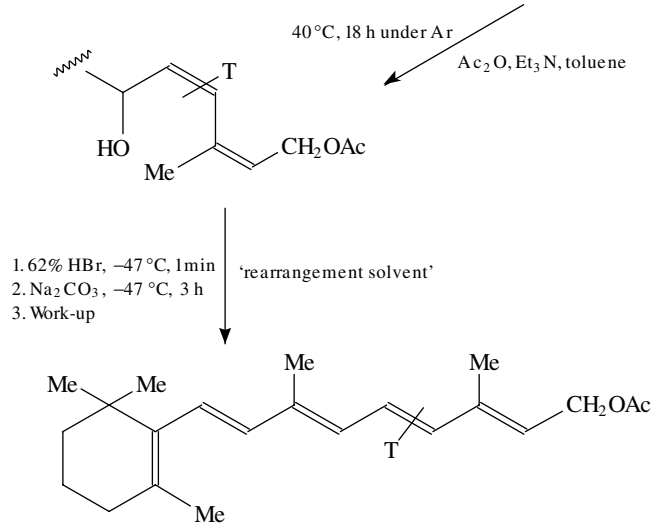
The tritium-labelled diazoacetates **107**, **108** and **109** have been obtained[87a] from the corresponding tritiated[87b] juvenile hormones (JH), JHI, JHII and JHIII (**104–106**), by



(99)



(100) 40% yield, radiation purity of 90%, specific activity 40–50 Ci mmol^{-1}



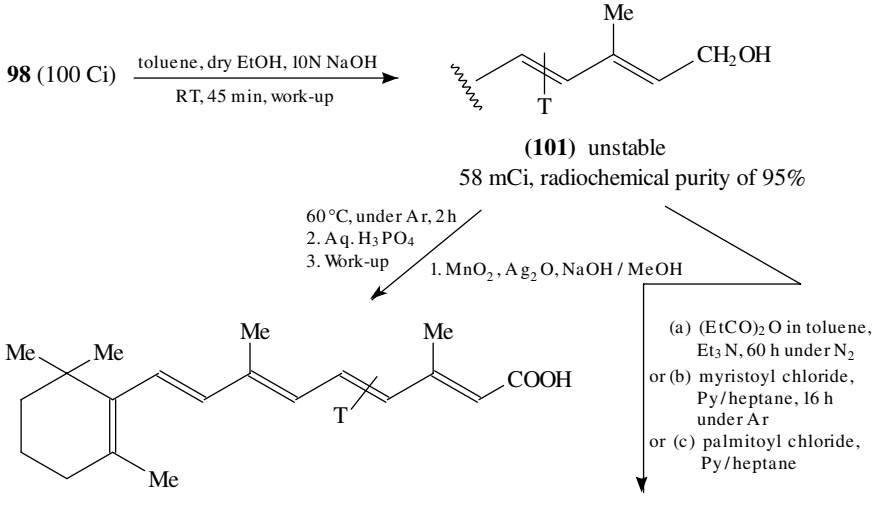
(38)

(98) specific activity 22.7 Ci mmol^{-1}, 69 mCi mg^{-1}; radiochemical purity of 91%

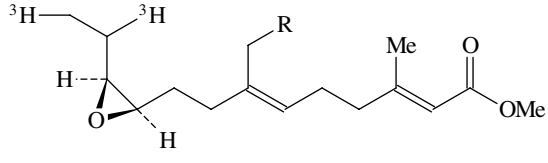
selective reduction of the ester group, followed by acylation of the corresponding alcohols with glyoxylic acid chloride tosylhydrazone **110**[88] and subsequent treatment with *N*,*N*-dimethylaniline and triethylamine[89] (equations 40 and 41). **107**, **108** and **109** are used for photoaffinity labelling of extracellular and cellular JH binding proteins[87].

2. Synthesis of [12-^{3}H]-farnesoic acid and [13-^{3}H]-farnesyl diazomethyl ketone

The tritium-labelled farnesoic acid [^{3}H]-MF, **111**, and its diazomethyl ketone analogue, [^{3}H]-FDK, **112**, which can be used for the photoaffinity labelling of MF binding

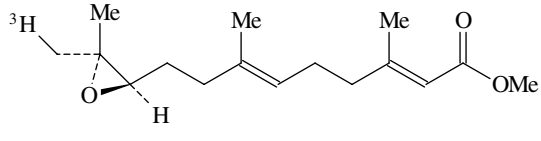


(39)

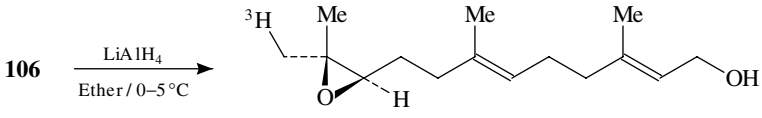


(104) JHI; R = Me
specific activity 58 Ci mmol^{-1}

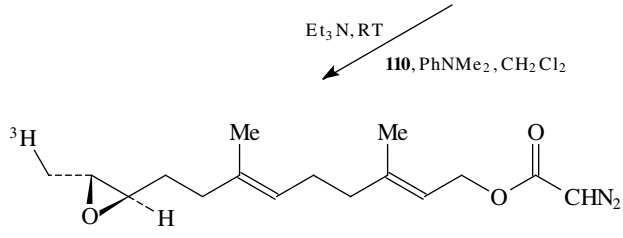
(105) JHII; R = H
specific activity 58 Ci mmol^{-1}



(106) JHIII, specific activity 15 Ci mmol^{-1}

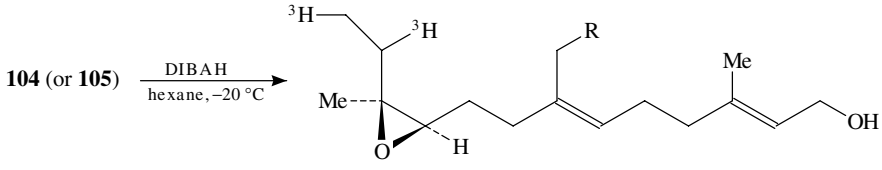


43% radiochemical yield

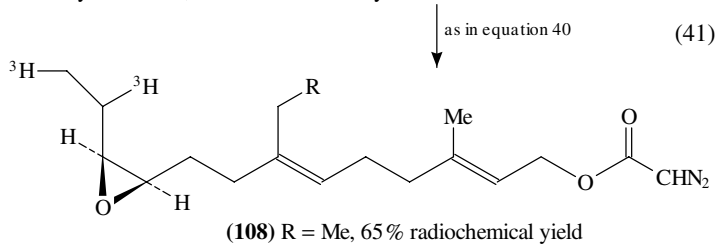


(40)

(107) 52% radiochemical yield



R = Me, 72% radiochemical yield R = H; 62% radiochemical yield



(41)

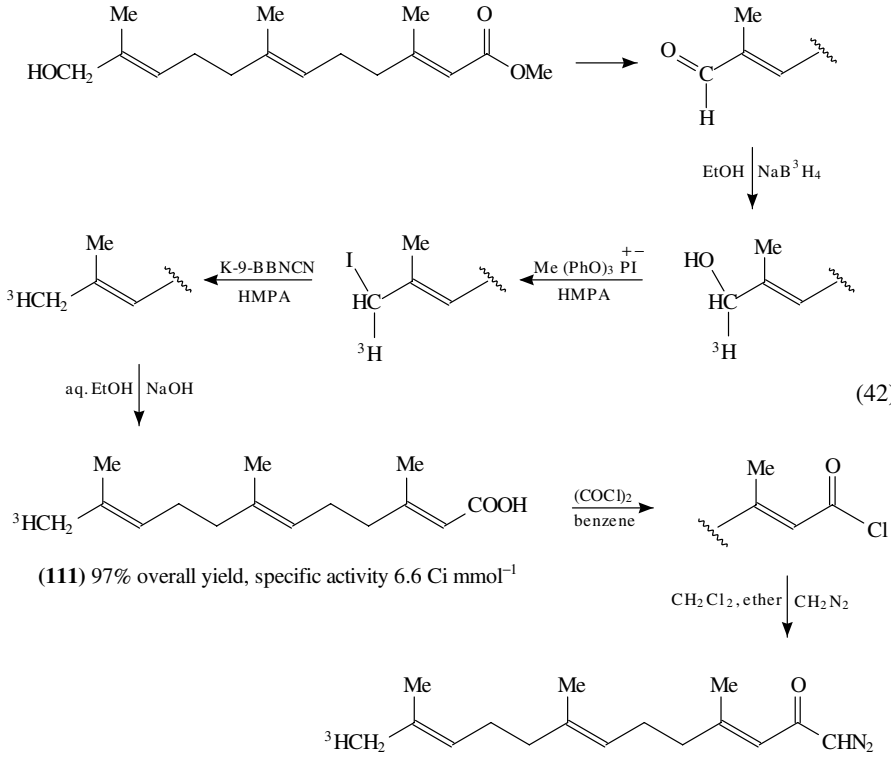
(108) R = Me, 65% radiochemical yield
(109) R = H, 58% radiochemical yield

proteins, have been synthesized[90] in the procedure presented in equation 42, to examine the biochemical role of MF in crustacean physiology[91].

C. Synthesis of Tritium-labelled Prostaglandin Analogues

1. Synthesis of enprostil-[13,14-^{3}H]

Enprostil, **113**, antisecretory prostaglandin (PG) analogue, containing tritium in the metabolically stable 13,14-positions and having a high specific activity of 41 Ci mmol^{-1}, has been prepared[92] in a fifteen-step microscale synthesis (equation 43). The tritium-labelled **113** was required for use in absorption, distribution, metabolism and excretion studies before the development of this substance for treatment of gastrointestinal ulcers in man[93]. Labelled prostaglandins having specific activity in excess of 100 Ci mmol^{-1} are to be developed[92].



(42)

(111) 97% overall yield, specific activity 6.6 Ci mmol^{-1}

(112) specific activity 6.6 Ci mmol^{-1} (24% radiochemical yield) + **(111)** 72% radiochemical yield

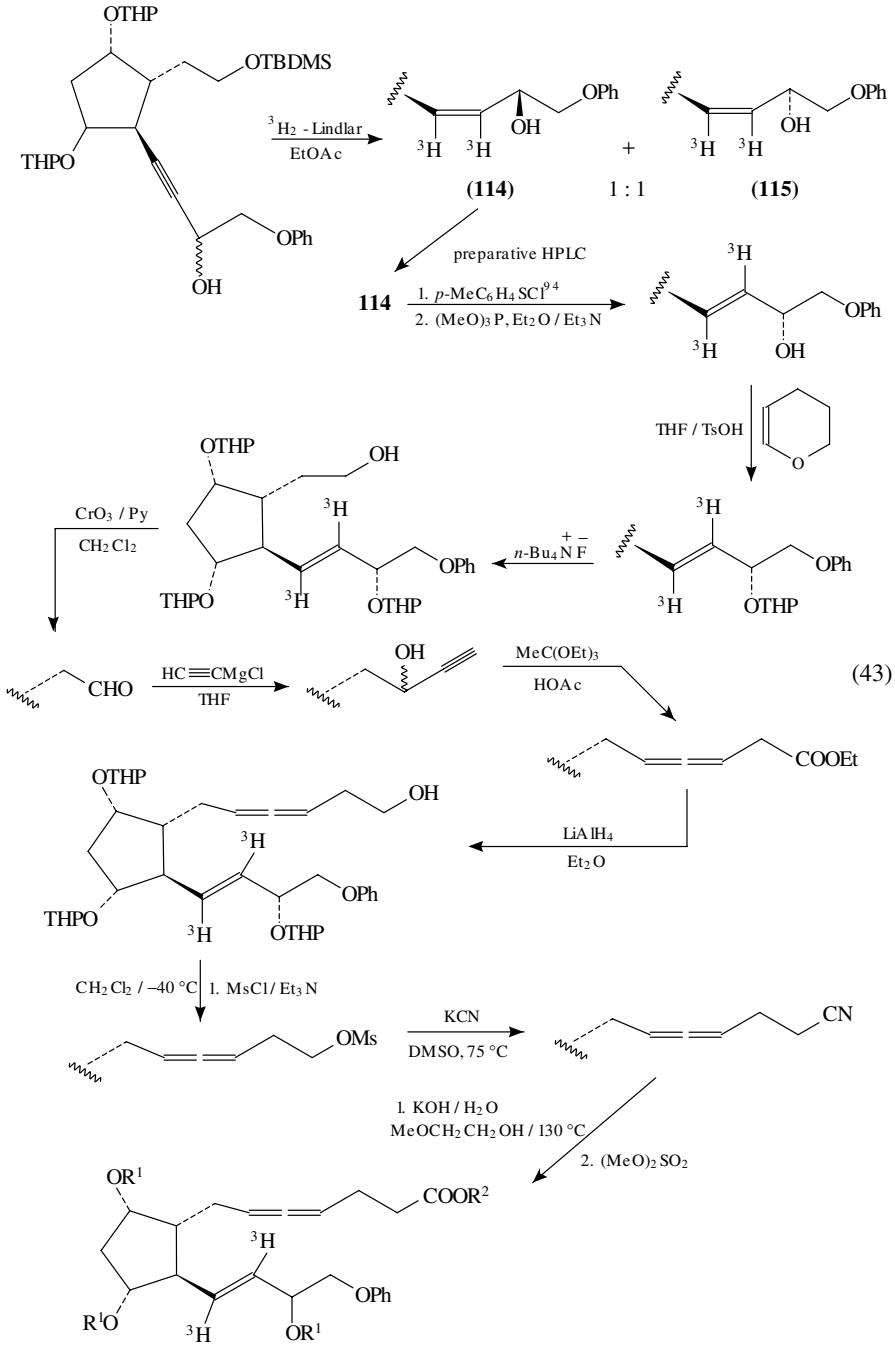
2. Synthesis of di-tritiated 9-(O)-methano-$\Delta^{6(9\alpha)}$-prostaglandin I_1 methyl esters

Two di-tritiated isocarbacyclin methyl esters **116** and **117** in the title have been synthesized[95] from (*Z*)-olefinic precursors **118** and **119** at the ω-side chain by catalytic hydrogenation with tritium gas (equations 44 and 45). The therapeutic candidates for cardiovascular deseases[96], **116** and **117**, were required for preclinical studies and for use in RIA analysis.

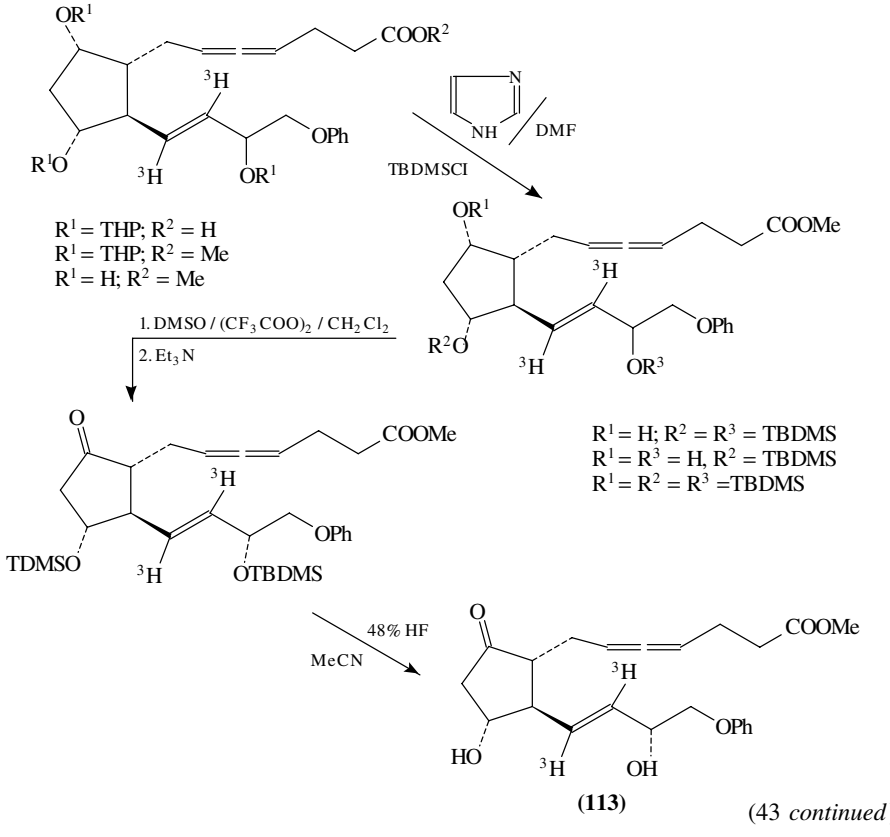
3. Enzymatic synthesis of tritium-labelled prostaglandin D_2 and other prostaglandins

Tritium-labelled [5,6,8,9,12,14,15(*n*)-^{3}H]PGD$_2$ **120**, prepared in one-stage enzymatic synthesis, using PGH-synthetase/PGH-PGD-isomerase[97], from tritium-labelled [5,6,8,9,11,12,14,15(*n*)]arachidonic acid, produced previously[98], has been converted[97] by enzymatic and chemical transformations into 15-keto-13, 14-dihydro-[^{3}H]PGD$_2$, **121**, 9α, 11β-[^{3}H]PGF$_2$, **122**, 9-deoxy-Δ^9-[^{3}H]PGD$_2${[^{3}H]PGJ$_2$}, **123**, and 9-deoxy-$\Delta^{9,12}$-13,14-dihydro-[^{3}H]PGJ$_2$, **124**.

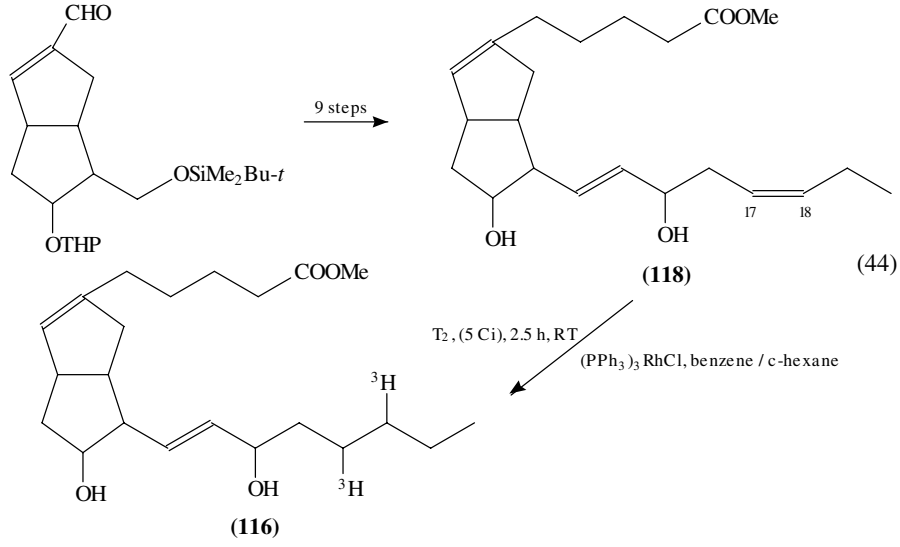
L-Selectride, LiB[CH(Me)Et]$_3$H, was found to be a more effective reducing agent than $NaBH_4$ in the synthesis of compound **122**. Specific activities of starting **120** and **121** were 120 Ci mmol^{-1}, and that of arachidonic acid was 180 Ci mmol^{-1}.


OTHP
OTBDMS
THPO
OPh
OH
$^3H_2$ - Lindlar
EtOAc
^3H ^3H
OPh
OH
+
(114)
1 : 1
(115)
preparative HPLC
114
1. p-MeC6H4SCl[94]
2. (MeO)3P, Et2O / Et3N
THF / TsOH
O
CrO3 / Py
CH2Cl2
n-Bu4N+ F−
THPO
OTHP
CHO
HC≡CMgCl
THF
MeC(OEt)3
HOAc
COOEt
LiAlH4
Et2O
CH2Cl2 / –40 °C
1. MsCl / Et3N
OMs
KCN
DMSO, 75 °C
CN
1. KOH / H2O
MeOCH2CH2OH / 130 °C
2. (MeO)2SO2
OR1
COOR2
R1O

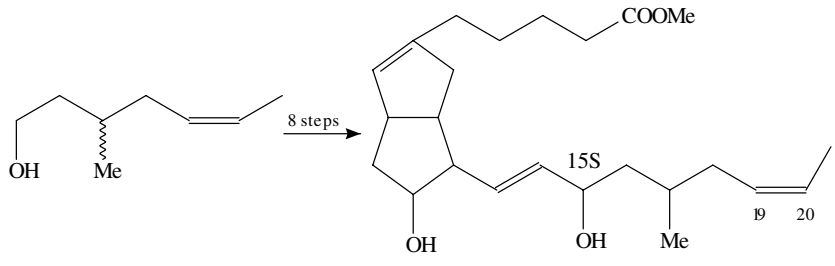
(43)



(43 *continued*)

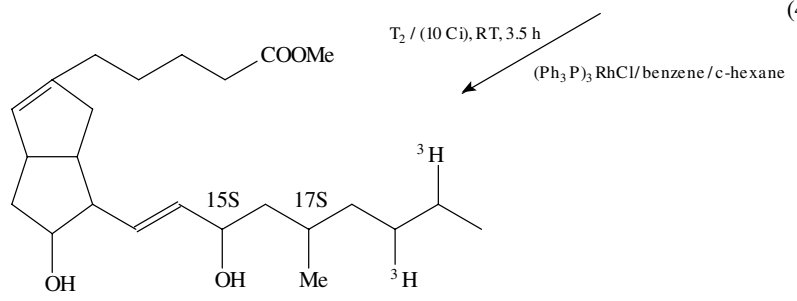


(44)

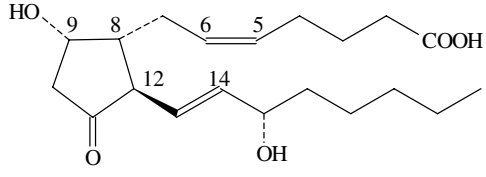


(119)

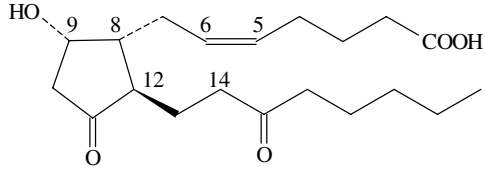
(45)



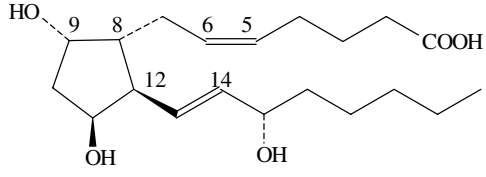
(117) specific activity 50 Ci mmol^{-1}



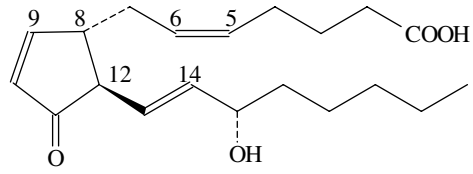
(120)



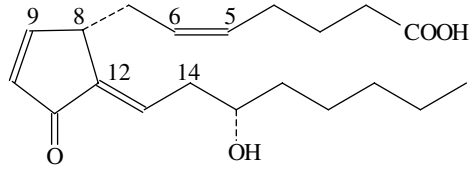
(121)



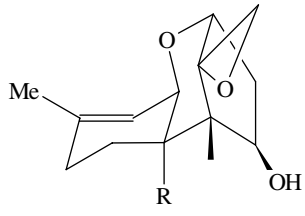
(122)

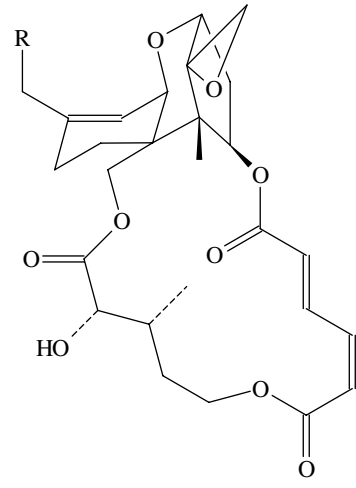


(123)



(124)





(125) R = CHTOH. 32% yield, specific activity 266 mCi mmol^{-1}

(126) R = T, specific activity 130 mCi mmol^{-1}, 4% yield

(127) R = CH_2OH

(128) R = CHO

(129) R = OH

(130) R = OSO_2Me

*4. Synthesis of tritium-labelled [15-^{3}H]-verrucarol, **125**, and [16-^{3}H]-verrucarin A, **126***

The naturally occurring mycotoxins, **125** and **126**, produced mainly by fungi[99] and implicated in the variety of toxicoses in man and animals[99,100], have been tritium labelled[101] (equations 46 and 47) for use in toxicology metabolism and pharmacokinetic studies. Position 15 in verrucarol and position 16 in verrucarin A have been tritium-labelled, because they should not suffer from the loss of labelling protons during the

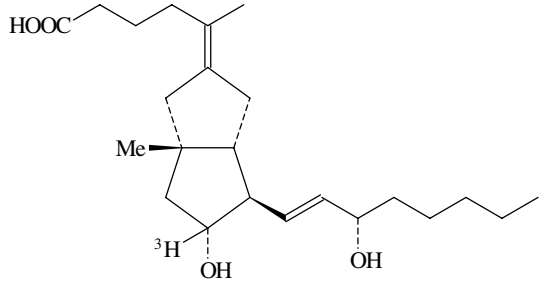
metabolic studies in animals.

$$\mathbf{127} \xrightarrow{RuCl_2(Ph_3P)_3} \mathbf{128} \xrightarrow[\text{overnight}]{[^3H]NaBH_4,\ THF,\ RT} \mathbf{125} \quad (46)$$

$$\mathbf{129} \xrightarrow[Et_3N\ /\ CH_2Cl_2,\ 0\ ^\circ C]{MeSO_2Cl} \mathbf{130} \xrightarrow[CH_2Cl_2,\ C_{16}H_{33}\overset{+}{P}(C_4H_9)_3Br^-]{[^3H]NaBH_4,\ 200\ mCi,\ \text{specific activity } 11.4\ Ci\ mmol^{-1}} \mathbf{126} \quad (47)$$

5. Synthesis of tritium-labelled ciprostene

The tritium-labelled title compound, (U-3H)-61,431, **131**, has been synthesized[102] by treating the free acid with methyl iodide and diisopropylethylamine, reaction of the U-61,431 methyl ester with *t*-butyldimethylsilyl chloride, separation of the 11-*O*-silyl and 15-*O*-silyl derivatives by column chromatography, oxidation of the 15-*t*-butyldimethylsilyl ether, methyl ester to 11-keto derivative with chromium trioxide and stereoselective reduction of the 11-keto group with sodium borotritide, to give the 11-α-hydroxy epimer. Deprotection of the (U-3H)-15-silyl methyl ester with Bu_4NF, followed by washing out the labile tritium by aqueous KOH/MeOH, gave (11-3H)-U-61, 431, which after semi-preparative HPLC has been injected subcutaneously into rats. During the first 24 h about 40% of dose radioactivity was found in the urine, and about 50% of dose in faeces 72 h after dosing. Less than 1% of tritiated water were excreted in urine, faeces and expired air.



(131)

6. Synthesis of tritium-labelled fluorescent derivatives of prostaglandins

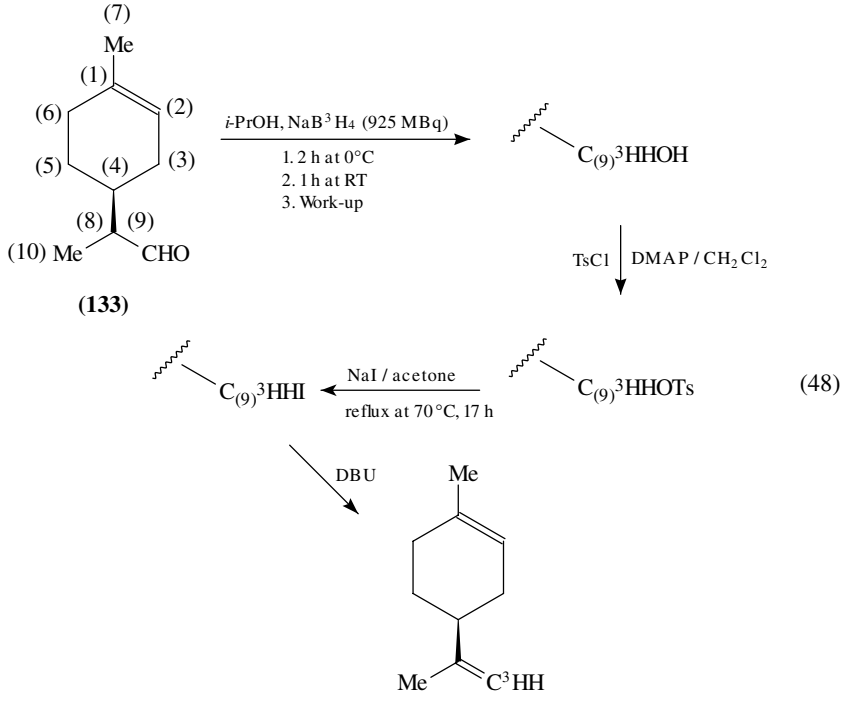
Tritium-labelled PGE_1 (50 Ci mmol^{-1}), $PGF_{2\alpha}$ (150 Ci mmol^{-1}) and PGE_2 (180 Ci mmol^{-1}) have been converted[103] into 1,5-DNS derivative, 1,5-DNS-1-(dimethylamino)-5-naphthalenesulphonic acid hydrate, $Me_2NC_{10}H_5SO_3H{\bullet}xH_2O$, a highly sensitive fluorescent probe for proteins[104–106]. The doubly labelled [^{3}H]-DNS-PGs could therefore be used as a radioactive fluorescent probe for liquid receptor interactions in biological membranes and also for determination of the molar radioactivity isotopically labelled PGs, when the amount of the labelled compound is very small.

D. Synthesis of Limonene

1. Synthesis of (4S)-(−)-[9-^{3}H]-limonene

The title compound, **132**, (4*S*)-[9-^{3}H]-1-methyl-4-(1′-methylethenyl)cyclohexene, has been synthesized[107] from (1′*S*,2*R*,*S*)-2-(4′-methylcyclohex-3′-enyl)propanal [(4*S*,8*R*,*S*)-(−)-1-*p*-menthen-9-al, **133**], via a route shown in equation 48 in 55% overall yield

and improved enantiomeric purity (72% ee, compared with the literature method[108] of 38% ee). The radioactive (4*S*)-(−)-limonene, **132**, was needed as substrate in the course of studies of the biosynthesis[107] of carvone in *Mentha spicata* (spearmint).



(133)

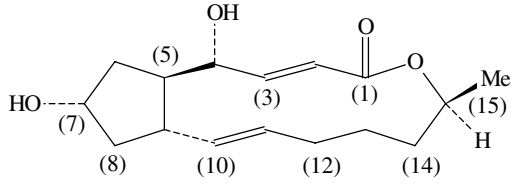
[9-^{3}H]-(**132**)
specific activity 629 MBq mmol^{-1}

(48)

E. Synthesis of Dienes by Catalytic and Radiochemical Methods

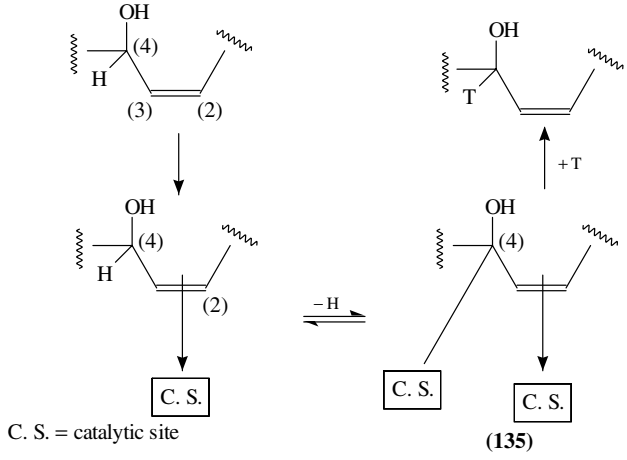
1. Synthesis of tritium-labelled brefeldin-A by catalytic isotope exchange with tritium gas

The title compound BFA, **134**, has a profound effect on the Golgi apparatus and can alter the membrane traffic. Tritium-labelled **134** should help to understand its biological action. **134** has been labelled with tritium[109] at positions α/β to both double bonds (whereas the

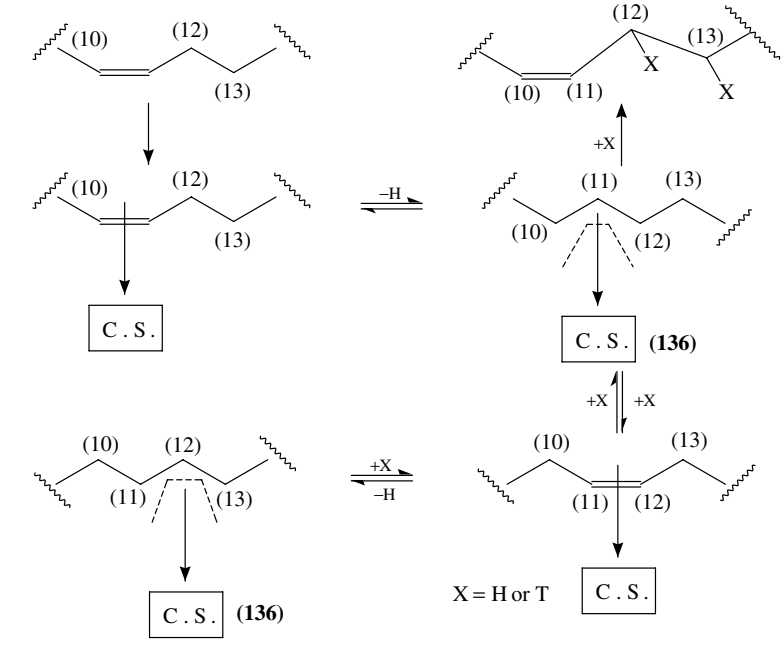


(134) Brefeldin A

labelling on the double bond was of minor importance) by hydrogen isotope exchange of **134** with tritium gas (T_2) in 1,4-dioxane over a commercial palladium catalyst supported on diatomaceous earth (5% metallic weight). The addition of air in the gas phase increased the catalytic activity. The exchange has been considerably enhanced when the air/T_2 ratio was about four. The specific activities of **134** were up to 2.8 Ci mmol^{-1}. Two mechanisms for tritium incorporation into **134**, involving two different adsorbed species, '$\sigma-\pi$', **135**, and 'π–allylic', **136**, on the catalyst surface have been proposed[110] (equations 49 and 50, respectively) and discussed[109]. The investigation of all factors governing the exchange reaction should result in obtaining higher tritium specific activities of **134**.



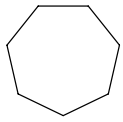
(49)



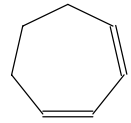
(50)

2. Synthesis of simple seven-membered ring compounds labelled with tritium

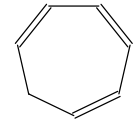
The following 14 seven-membered ring compounds, increasing in complexity from cycloheptane to complicated benzodiazepine systems, have been labelled with tritium[111] using 'activated tritium' (AcT method) employing a microwave power generator[112], 'adsorbed tritium' at RT (AdT method[113]) and high-temperature tritium ion ('HTI' method[111]): cycloheptane, **137**, 1,3-cycloheptadiene, **138**, 1,3,5-cycloheptatriene, **139**, 2-cyclohepten-1-one, **140**, (*t*)-3,3,5-trimethylhexahydroazepine, **141**, 2-oxohexamethyleneimine (caprolactam), **142**, 1-aza-2-methoxy-1-cycloheptene, **143**, 1,4-diazacycloheptane (homopiperazine), **144**, azulene, **145**, 1-benzosuberone, **146**, 1,8-diazabicyclo-[5.4.0]undec-7-ene, **147**, 5*H*-dibenzo[*b*,*f*]azepine (iminostilbene), **148**, *trans*-10,11-dibromodibenzosuberone, **149**, and 8-chloro-11-(4-methyl-1-piperazinyl)5*H*-dibenzo[*b*,*e*]diazepine (clozepine), **150**.



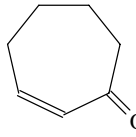
(137) 10.5 mCi yield, specific activity 31.8 mCi mmol^{-1}



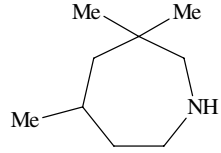
(138) 8.6 mCi yield specific activity 8.9 mCi mmol^{-1}



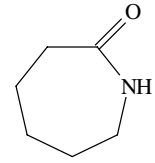
(139) 6.8 mCi yield specific activity 17 mCi mmol^{-1}



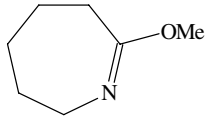
(140) 134 mCi yield specific activity 157 mCi mmol^{-1}



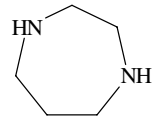
(141) 2.4 mCi yield specific activity 16 mCi mmol^{-1}



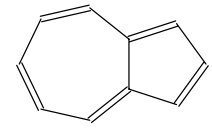
(142) 166 mCi yield specific activity 107 mCi mmol^{-1}



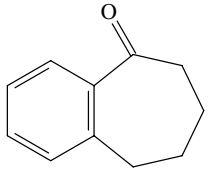
(143) 299 mCi yield specific activity 428 mCi mmol^{-1}



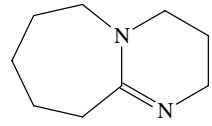
(144) 32 mCi yield specific activity 48 mCi mmol^{-1}



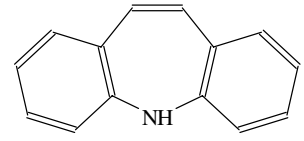
(145) 48 mCi yield specific activity 185 mCi mmol^{-1}



(146) 172 mCi yield specific activity 1833 mCi mmol^{-1}

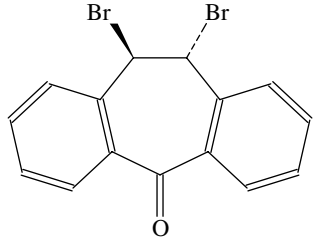


(147) 101 mCi yield specific activity 151 mCi mmol^{-1}

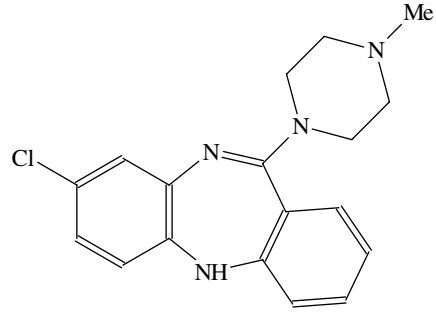


(148) 117 mCi yield specific activity 238 mCi mmol^{-1}

Many biologically active substances and neuroleptic drugs have a seven-membered ring in their structure. Benzodizapines of extremely high specific activity used in receptor binding studies are isotopically labelled by synthesis[114]. The specific activities of compounds **137–150** are sufficiently high for *in vitro* metabolic and radiotracer studies.



(149) 17 mCi yield
specific activity 43 mCi mmol^{-1}



(150) 2 mCi yield
specific activity 562 mCi mmol^{-1}

The distribution of tritium in compounds **137–150** can be determined by tritium NMR spectroscopy without chemical manipulations[115]. The structure retention index relationship (SR IR)[116] has been used for identification of unknown radioactive peaks and to differentiate by-products from radioimpurities from extraneous sources.

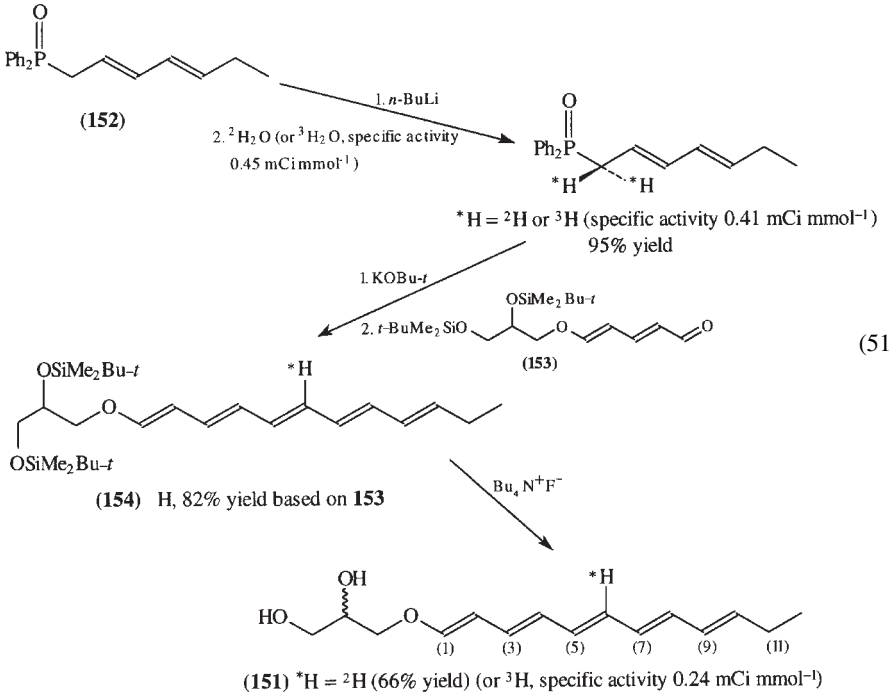
F. Tritium Isotope Effects in Synthesis of Polyenes

1. Synthesis of [6-^{2}H] and [6-^{3}H] fecapentaene

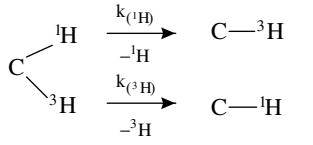
Fecapentaene **151**, a potent mutagen, potential inducer of colon cancer, first isolated from human feces[117,118], has been deuterium and tritium labelled[119] by exchange of the α-protons of (*E*,-*E*)-2,4-heptadienyldiphenylphosphine oxide, **152**, with ^2H_2O or ^3H_2O, followed by Wittig–Horner condensation with aldehyde **153**, and deprotection of the silylated derivative **154** with fluoride (equation 51), **151** is used in the study of its interactions with DNA[119].

The maximum specific activity of tritium[120] ($I_{1/2} = 12.33$ years) equals 9664 Ci g^{-1}.

Tritium specific activity of the product **151** [^{3}H] indicates a slightly higher retention of ^{3}H relative to ^{1}H in the coupling second step. No tritium, deuterium and carbon-14 KIE and exchange systematic study of the mechanism of the Wittig–Horner coupling reaction[119] has been carried out. The determined specific activities of the α-tritiated 2,4-heptadienyldiphenylphosphine oxide **152** (0.41 mCi mmol^{-1}) and of the product **151** (equation 52) (0.24 mCi mmol^{-1}) indicate a rather small intramolecular C$-^1$H/C$-^3$H KIE in the rupture of one of the two α-carbon–hydrogen bonds in the coupling reaction above. This is characteristic for highly asymmetrical transition states if the rupture of the C–H bond takes place in the rate-determining step and the double $C_{(5)}$=$C_{(6)}$ bond formation occurs in the subsequent fast product **154** formation step. We assume also that silylated derivative **154** and product **151** are tritium-labelled in non-labile $C_{(6)}$ position. Silylated derivative **153** tritium-labelled at the terminal keto group has not been investigated. ^{14}C KIE have also not been studied. The interpretation of the small k_H/k_T value of 1.4 should therefore be postponed. We note that no yield of **154** with respect to the tritiated precursor **152**, which is needed for intermolecular ^{3}H KIE estimation, was given.



(51)

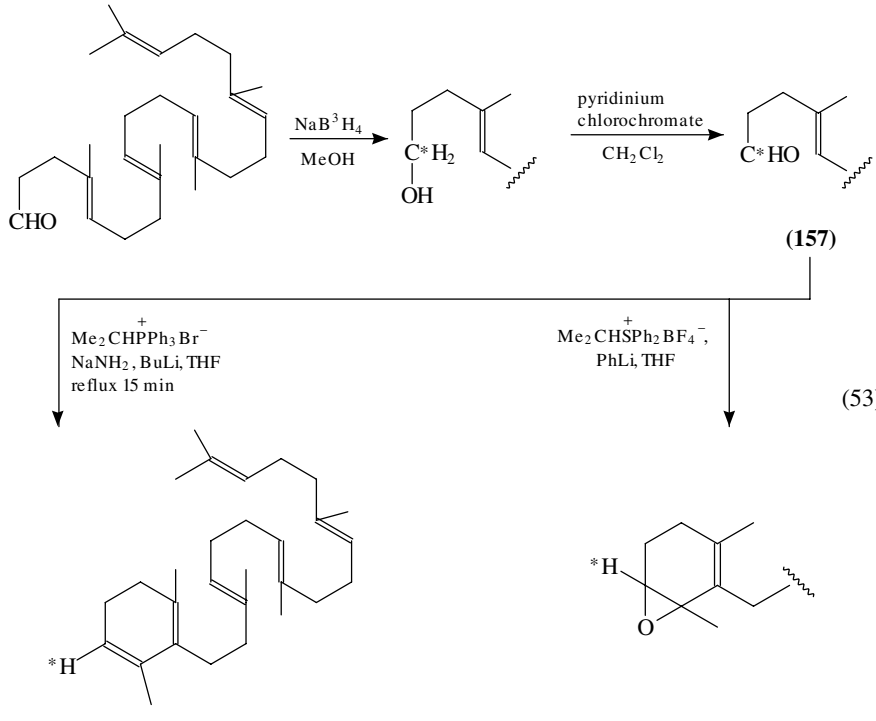


$$k_{(^1H)} \Big/ k_{(^3H)} \cong 1.412 \qquad (52)$$

2. Synthesis of [3-^{3}H] squalene and [3-^{3}H]-2,3-oxidosqualene

[3-^{3}H]Squalene, **155**, and [3-^{3}H]-2,3-oxidosqualene, **156**, the key compounds in studies of the biosynthesis of sterols[121], have been obtained[122] according to the route shown in equation 53, which involves the modified Wittig reaction of [1-^{3}H]trisnorsqualene aldehyde **157** with phosphorus ylide to give **155** or with sulphur ylide to give **156** in high radiochemical yield and high purity.

At room temperature the chemical and radiochemical yields of **155** were different. The chemical yields were in the 30–40% range, while the radiochemical, not very reproducible yields were in the 6–15% range. Cattel and coworkers[122] assigned these differences to tritium isotope effect in the Wittig reaction. No correlation between the specific activity of **155** and the degree of chemical conversion of **157** into **155** has been presented. The temperature dependence of the observed secondary tritium isotope effect has also not been



(53)

(155) [3-^{3}H] squalene, 84% radiochemical yield

*H = ^{3}H

(156) 77% chemical yield

26 mCi, specific activity 1.9 Ci mmol^{-1}

studied. The C—*H bond at the aldehyde carbon is not broken in the course of Wittig reaction but the vibrational motion of the aldehyde hydrogen should be less constrained in the transition state corresponding to formation of **155** from **157**.

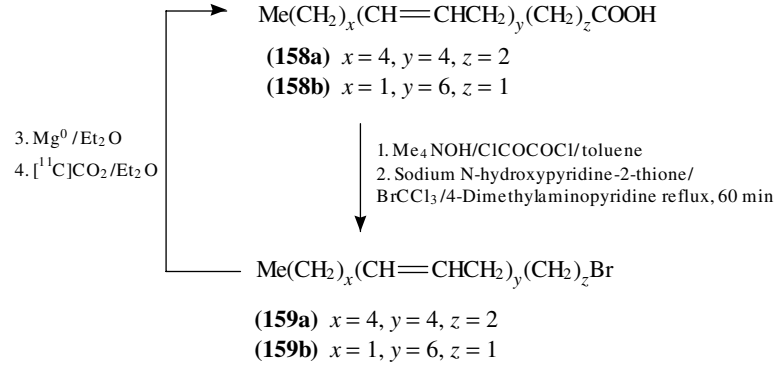
IV. SYNTHESIS AND USES OF DIENES AND POLYENES LABELLED WITH RADIOISOTOPES OF CARBON

A. Synthesis and Uses of Dienes and Polyenes Labelled with Carbon-11

1. Remote radiosynthesis of 1-[^{14}C]polyhomoallylic fatty acids

1-[^{11}C]arachidonic acid, **158a-^{11}C** and 1-[^{11}C]docosahexaenoic acid, **158b-^{11}C**, have been prepared[123] applying a retro-synthesis involving a radical decarboxylation of *N*-hydroxypyridine-2-thione esters[124] of both arachidonic and docosahexaenoic acid, formation of the polyhomoallylic magnesium bromide from the corresponding (all-*Z*)-1-bromononadeca-4,7,10,13-tetraene, **159a**, and (all-*Z*)-1-bromoheneicosa-3,6,9,12,15,18-hexaene, **159b**, and subsequent carbonylation of the Grignard reagents with [^{11}C]CO_2 (equation 54). The final radiochemical purities of **158a-^{11}C** and **158b-^{11}C** were in excess of 95% by radio-HPLC. **158a-^{11}C** and **158b-^{11}C** were used[123,125] for *in vivo* evaluation of regional brain phospholipid metabolism by PET. Both **158a-^{11}C** and **158b-^{11}C** are

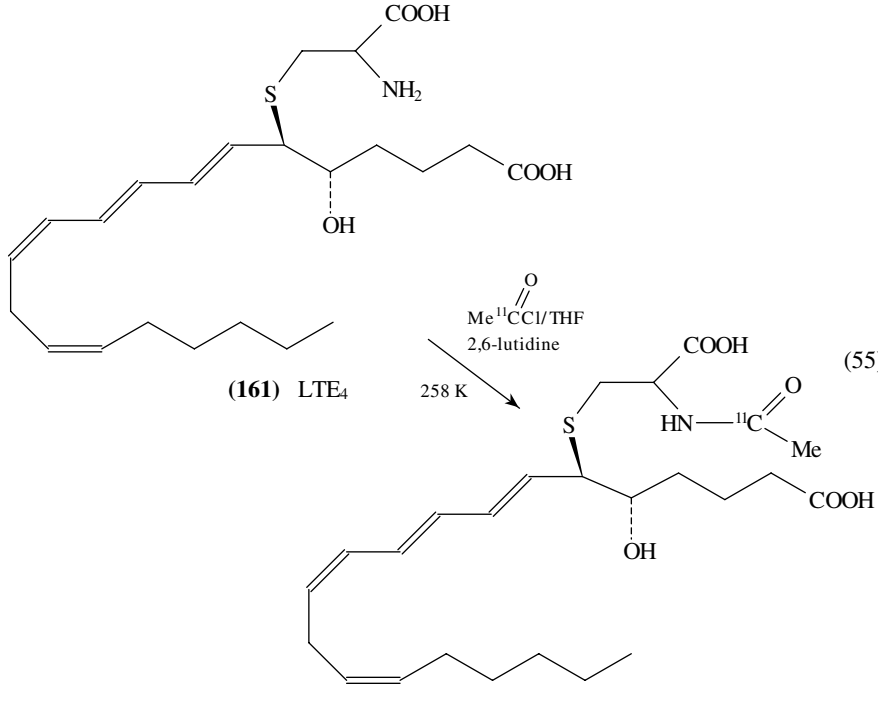
rapidly and selectively incorporated into brain phospholipids[126].



(54)

2. Synthesis of 5(S)-hydroxy-6(R)-(N-[1-^{11}C]acetyl)cysteinyl-7, 9-trans-11, 14-cis-eicosatetraenoic acid

The title compound **160**, a biologically potent metabolite of arachidonic acid metabolism, produced in the 5-lipoxygenase pathway in some mammalian cells[127,128], has been synthesized[129–131] by the reaction of leukotriene E_4, **161**, with [1-^{11}C[acetyl chloride in 1.3% yield based on [1-^{11}C] acetyl chloride[129] (equation 55).

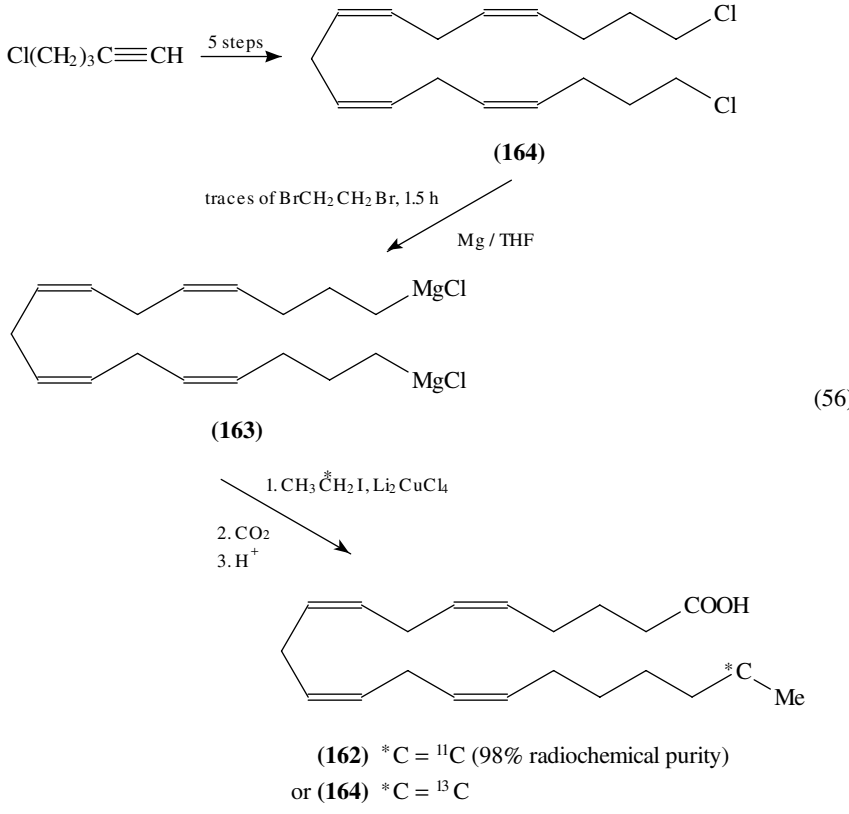


(55)

The complete preparation required 50 min. The PET scans with **160**, performed in normal and mutant rats, showed[129,132] that N-[1-^{11}C]acetyl-LTE$_4$ may be used to study various human diseases with impaired bile flow and reduced liver function.

3. Synthesis of [19-^{11}C]arachidonic acid

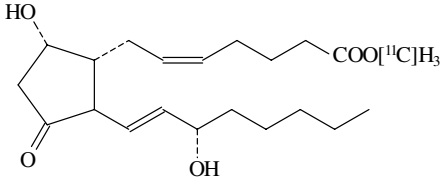
[19-^{11}C]Arachidonic acid **162** has been prepared[123,133,134] in 23% decay corrected radiochemical yield within 52 min in a coupling reaction of *bis*-Grignard reagent **163** of (all-*Z*)-1,17-dichloro-4,7,10,13-heptadecatetraene, **164**, with [1-^{11}C] ethyl iodide followed by carbonation with CO_2 (equation 56). Starting with 20 GBq $^{11}CO_2$, 760 MBq of **162** has been obtained with a specific activity 1.6 GBq μmol^{-1}. [19-^{13}C]Arachidonic acid, **164**, has been synthesized by trapping the mixture of $^{13}CO_2$ and [^{11}C]carbon dioxide in methyl magnesium bromide in THF. The subsequent steps were carried out in an analogous manner to that in equation 56.



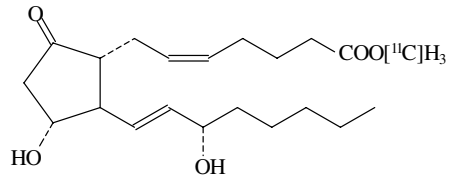
(56)

(162) *C = ^{11}C (98% radiochemical purity)
or **(164)** *C = ^{13}C

The authors have also synthesized[134] fatty acids labelled with deuterium and carbon-11 in order to investigate if kinetic isotope effects related to fatty acid metabolism can be observed *in vivo* by PET[133,135–137]. *In vitro*, the large kinetic deuterium isotope effects are observed in the oxidation of deuteriated aliphatic carboxylic acids with alkaline permanganate and manganate[135–139].



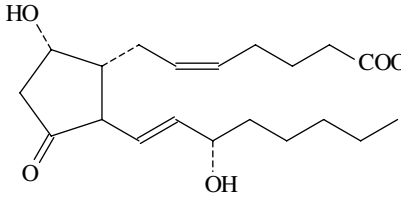
(165) PGD_2[^{11}C]Me



(166) PGE_2[^{11}C]Me

4. Synthesis of [^{11}C]methyl esters of prostaglandins D_2 and E_2

^{11}C-Labelled methyl esters of prostaglandin PGD_2, **165** and prostaglandin PGE_2, **166**, for PET investigations, have been synthesized[140] with the use of [^{11}C]methyl iodide via direct estrification of their carboxylate anion, generated *in situ* by the use of tetramethylpiperidine (TMP), to avoid rapid degradation of the prostaglandin when treated with aqueous NaOH in DMF (equation 57).



PGD_2

1. TMP, DMSO / DMF
2. [^{11}C]H_3I, −78 °C
3. 42 °C, 5 min

165 (57)

specific activity 0.9 GBq μmol^{-1}

Starting with 3 GBq [^{11}C]carbon dioxide produced in a ^{14}N(p,α)^{11}C nuclear reaction, the radiochemical yield of **165** was 0.5 GBq at the end of preparative purification performed in *Sep-Pak C18* columns. The methyl esters of prostaglandins have a high affinity for the specific binding sites[141].

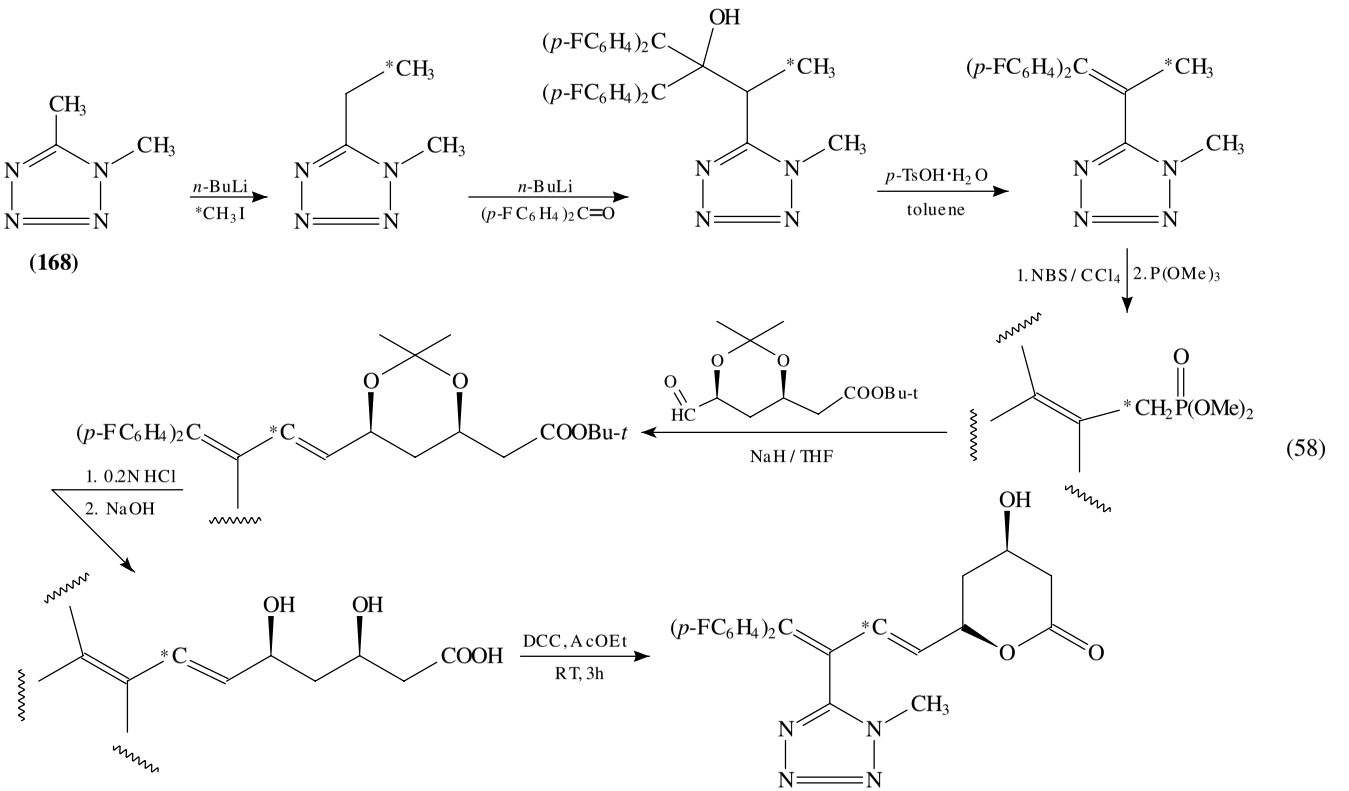
B. Synthesis and Uses of Dienes and Polyenes Labelled with Carbon-14

1. Synthesis of (±)-trans-6-[4,4-bis(4-fluorophenyl)-3-(1-methyl-1H-tetrazol-5-yl)-1(E),3-[2-^{14}C]butadienyl-4-hydroxy-3,4,5,6-tetrahydro-2H-pyran-2-one

The recently discovered[142] title compound BMY-22089, **167**, is more potent than the natural products compactin and mevinolin[143] in lowering the serum cholesterol levels in both animals and man by inhibiting the action of enzyme, 3-hydroxy-3-methylglutaryl coenzyme A (HMG-CoA) which determines the biosynthesis of cholesterol[144]. It has been prepared[143] in 20% overall yield in various steps starting with the tetrazol **168** (equation 58), for pharmacokinetic and drug distribution studies.

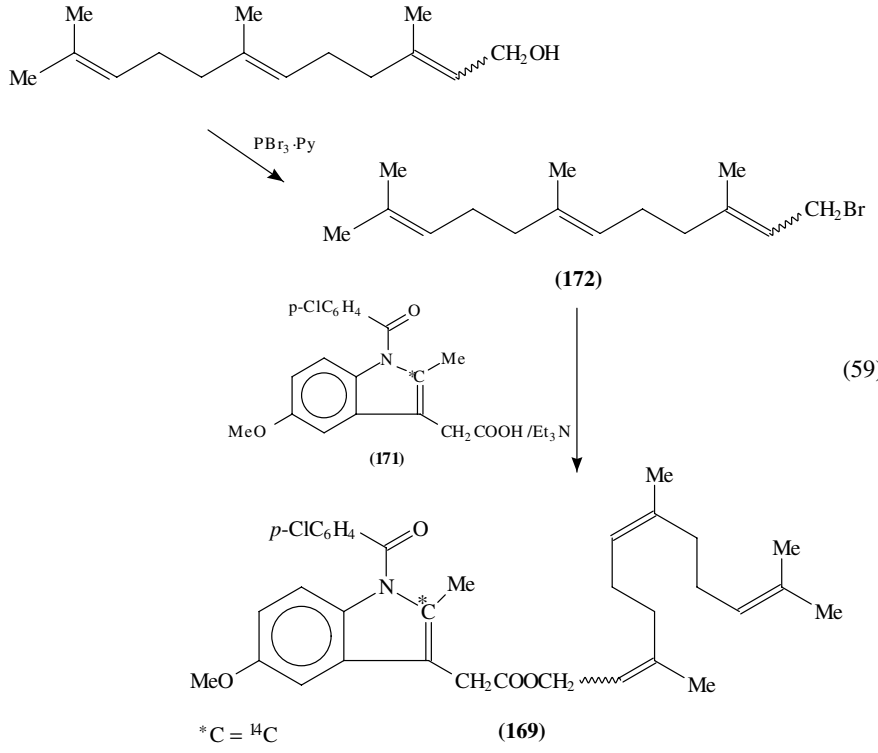
2. Synthesis of ^{14}C-labelled indometacin farnesil

E-0710 (IMF), the farnesil esters of indometacin[145], **169** and **170**, prodrugs showing anti-inflammatory activity with diminished gastro-intensinal irritation, have been synthesized[146] according to two schemes shown in equations 59 and 60. ^{14}C-IMF- **169** has been obtained by esterification of commercially available ^{14}C-IND, **171**, with farnesyl


(168)
n-BuLi
*CH3I
n-BuLi
(p-FC6H4)2C=O
p-TsOH·H2O
toluene
1. NBS / CCl4
2. P(OMe)3
NaH / THF
1. 0.2N HCl
2. NaOH
DCC, AcOEt
RT, 3h
(167) specific activity 31.4 μCi mg–1
DCC = Dicyclohexylcarbodiimide
*C = 14C

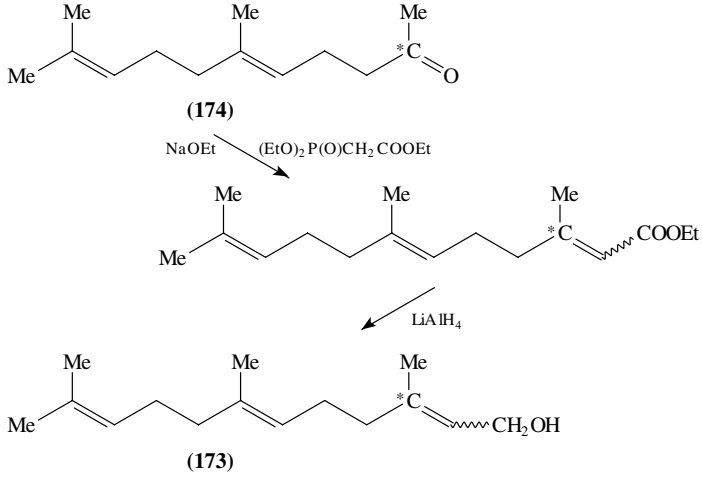
(58)

bromide **172** in the presence of triethylamine (equation 59).

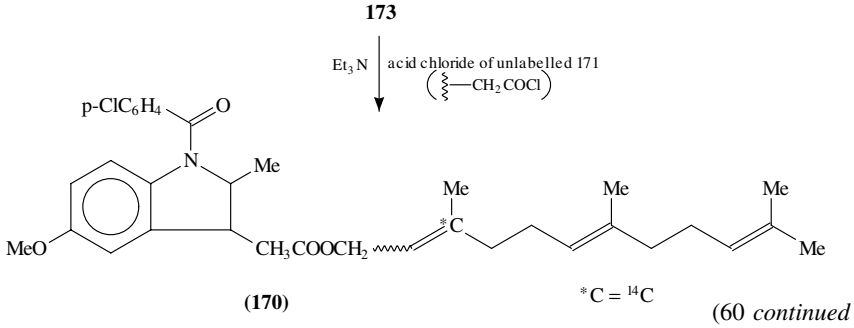


(59)

^{14}C-F-IMF, **170**, containing farnesyl moiety labelled with ^{14}C, has been obtained involving the synthesis of ^{14}C-labelled farnesol [^{14}C-F, **173**] from ketone **174** (equation 60). **169** and **170** have been synthesized in order to clear the pharmacokinetic profile of these drugs *in vivo* and *in vitro*.



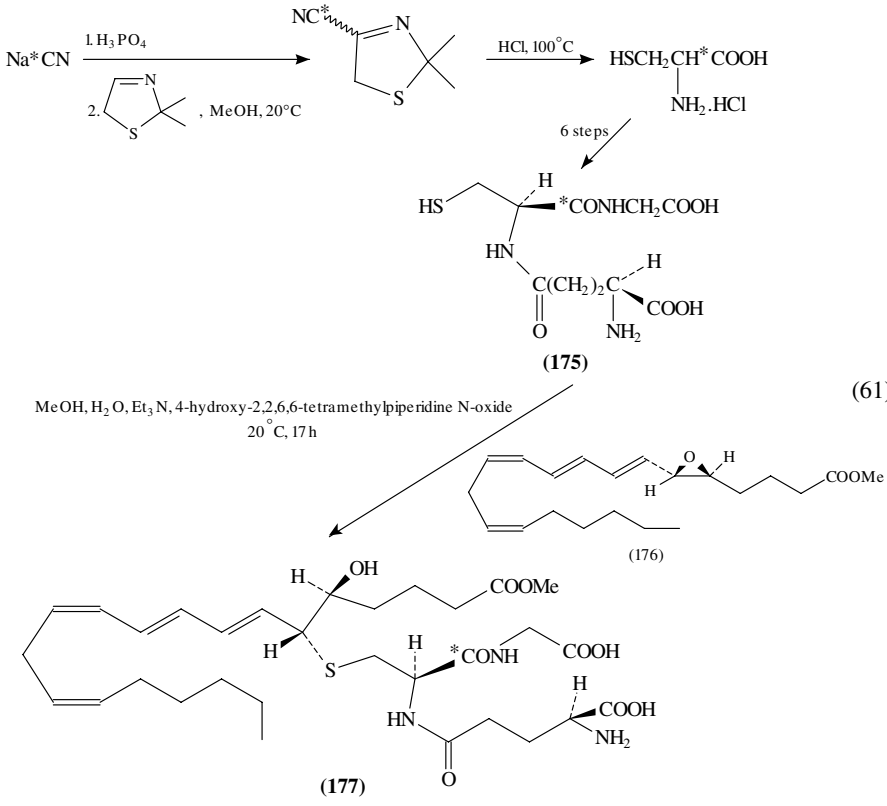
(60)



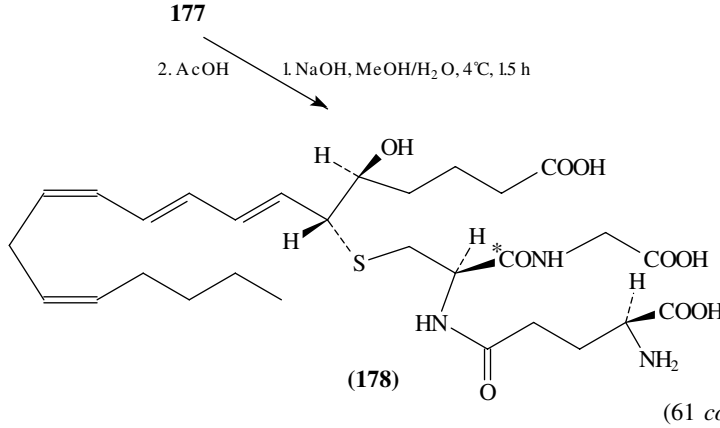
(60 *continued*)

3. Synthesis of [5S,6S]-[Cys-^{14}CO]-LTC$_4$

The labelled tripeptide (L,L)-glutathione-^{14}C, **175**, prepared in an eight-step chemical synthesis[147] starting with Na^{14}CN, has been coupled with (5*S*,6*S*)-LTA$_4$ methyl ester, **176**, yielding (5*S*,6*R*)-[Cys-^{14}CO]-LTC$_4$ methyl ester, **177**, which after hydrolysis (NaOH/MeOH/H_2O) and neutralization by acetic acid provided *N*-{*S*-[1-(4-carboxy-1-hydroxybutyl)pentadeca-(2*E*,4*E*,6*Z*,9*Z*)-tetraenyl]-*N*-λ-L-glutamyl-L-[1-^{14}C]}cysteinyl glycine, **178**, in 74% yield (specific activity 50 mCi mmol^{-1}, 3.88 MBq) (equation 61).



(61)



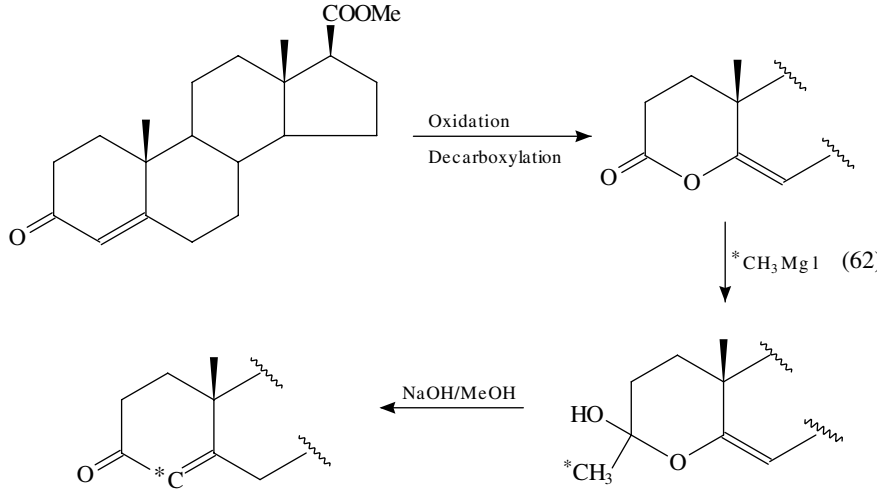
(178)

(61 *continued*)

178 is used in the study of peptidoleukotrienes biosynthesis and metabolism[147] in view of their biological activities, like contraction of smooth muscles or vasodilatation, and in asthma-related diseases[148].

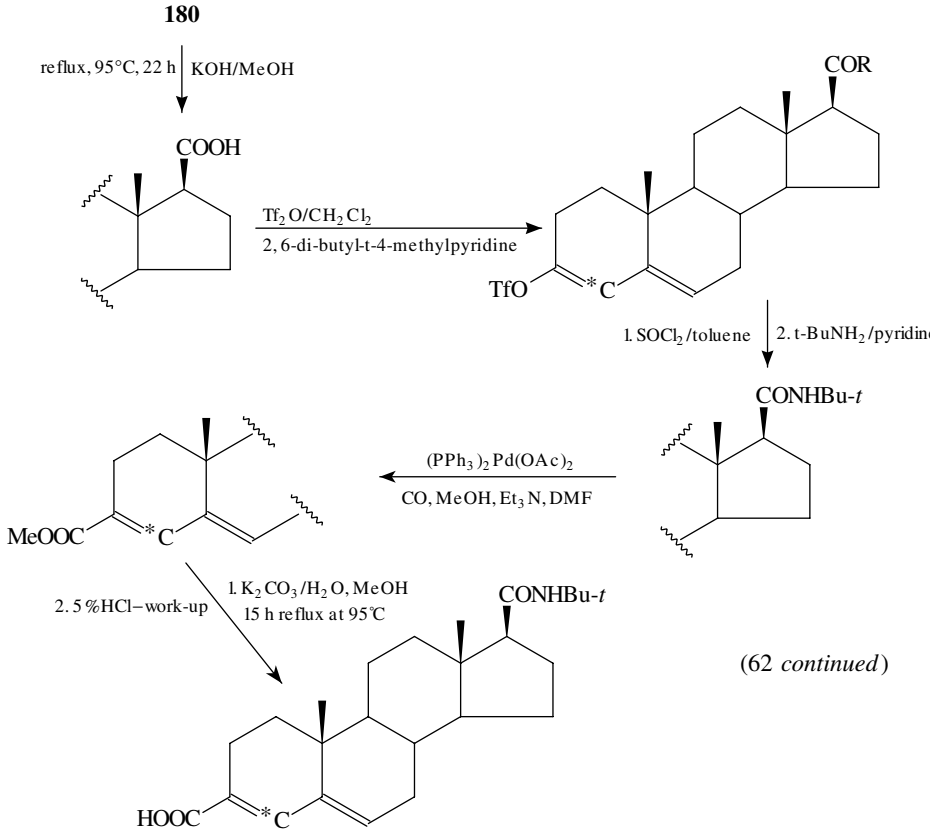
4. Synthesis of [^{14}C]SK and F 105657 and tritiated SK and F 105656, the prostatic steroidal 5α-reductase inhibitors

a, 17β-[*N*-(1,1-Dimethylethyl)carbamoyl]androsta-3,5-diene-4-^{14}C-3-carboxylic acid ([^{14}C]SK and F 105657), **179**, suppressing the human biosynthesis of 5α-dihydrotestosterone, essential for normal prostatic growth to reach puberty, but causing the benign prostatic hyperplasia (BPH) at the later age[149], has been synthesized[150,151] in the sequence shown in equation 62 involving *t*-butyl amidation, triflation and carbomethoxylation.



(62)

(180)



(62 *continued*)

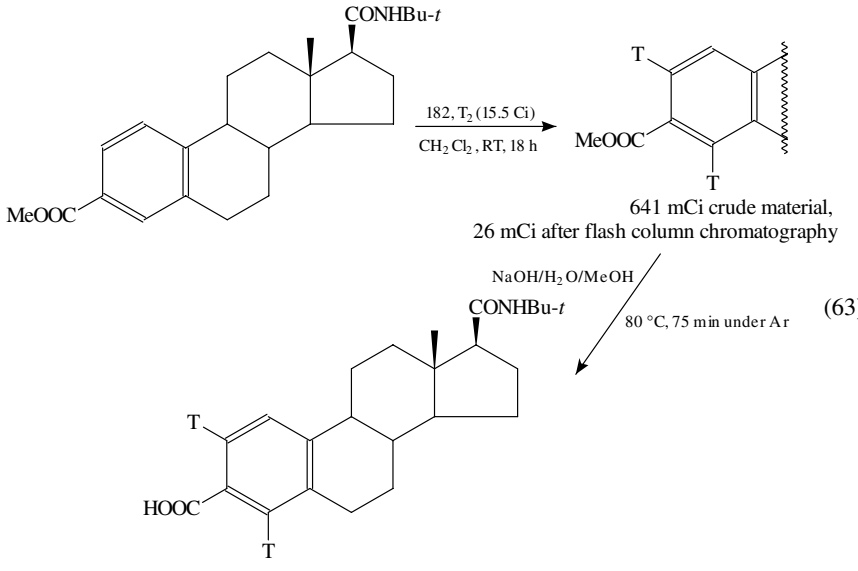
(179) 98% radiochemical purity,
47% yield from **180**

b. Synthesis of 17β-[*N*-(1,1-dimethylethyl)carbamoyl]estra-1,3,5(10)-triene-2,4-$^3H_2$-3-carboxylic acid, **181**. The A-ring aromatic analogue SK and F, 105656, **181**, has been tritium-labelled[150] (equation 63) by iridium-mediated exchange methodology[150,152] using $[IrH_2(Me_2CO)_2(PPh_3)_2]$ BF_4, **182**.

Both **179** and **181**, therapeutic agents for treatment of BPH, have been prepared to profile their pharmacokinetic and binding characteristic in various biomedia[150]. Tritium labels were incorporated exclusively into $C_{(2)}$ and $C_{(4)}$ positions of the A ring as observed by the ^3H NMR spectra[150]. It has been suggested that the isotopically labelled hydrogen is channeled into the *ortho* positions of the A aromatic ring through the catalytic cycle[150,153] shown in equation 64.

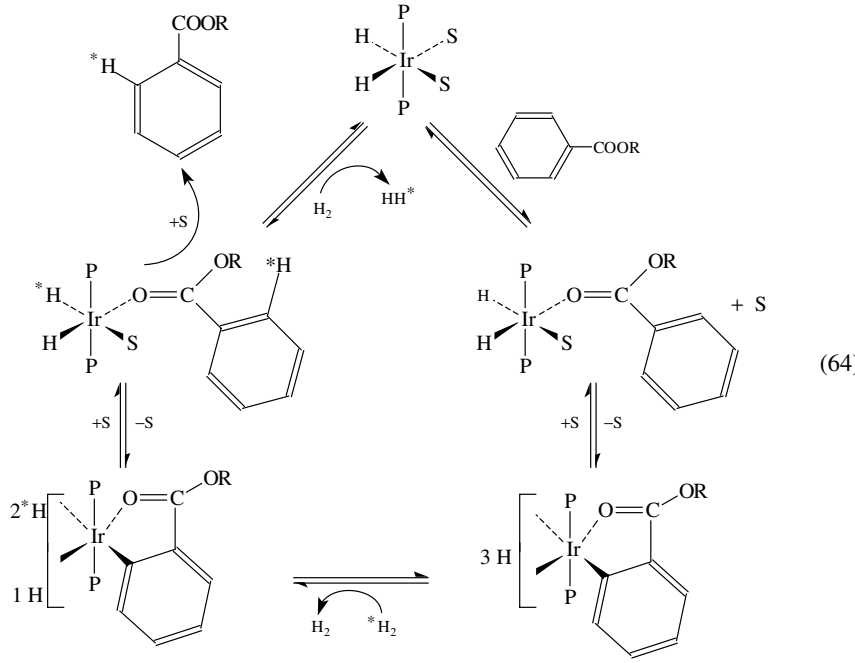
5. Synthesis of sodium 3-[1-^{14}C]-ethyl-7-isopropyl-1-azulenesulphonate

The title compound **183**, a new therapeutic agent[154] for stomatitis, pharyngitis and ophthalmia, has been labelled[155] with ^{14}C in the ethyl group attached to the azulene ring (equation 65) for the study of metabolism in animals.



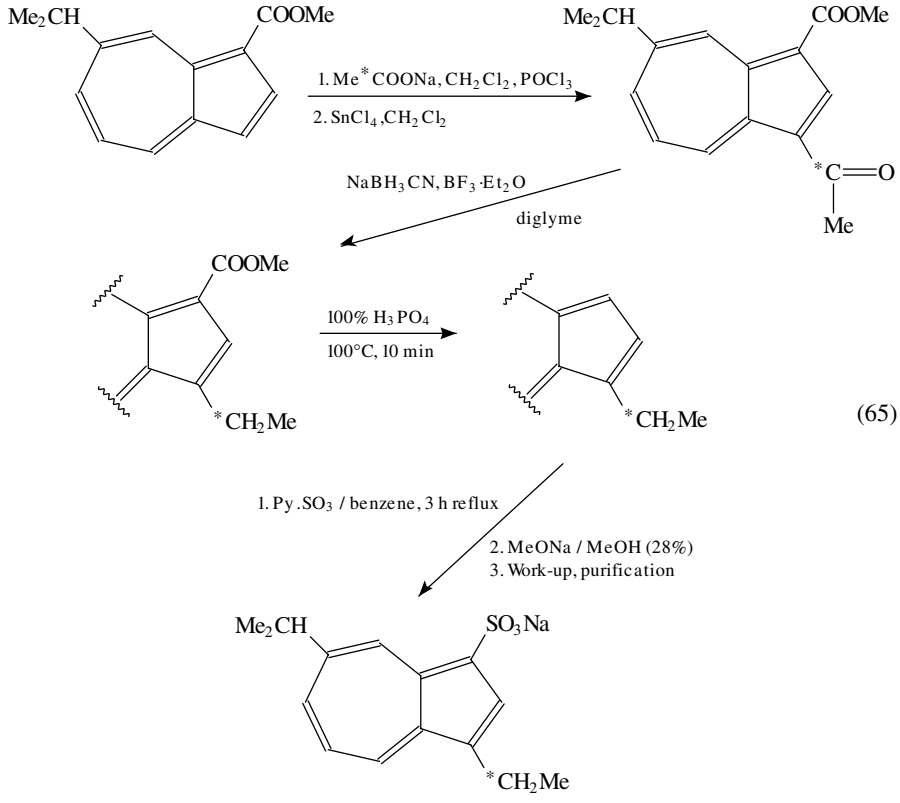
(63)

(181) 17 mCi, radiochemical puity > 99 %
specific activity 774 mCi mmol^{-1}



(64)

P = Triphenylphosphine
S = Acetone
*H = ^{3}H or ^{2}H



(65)

(183) 93.4% step yield, specific activity 1.98 GBq mmol^{-1}

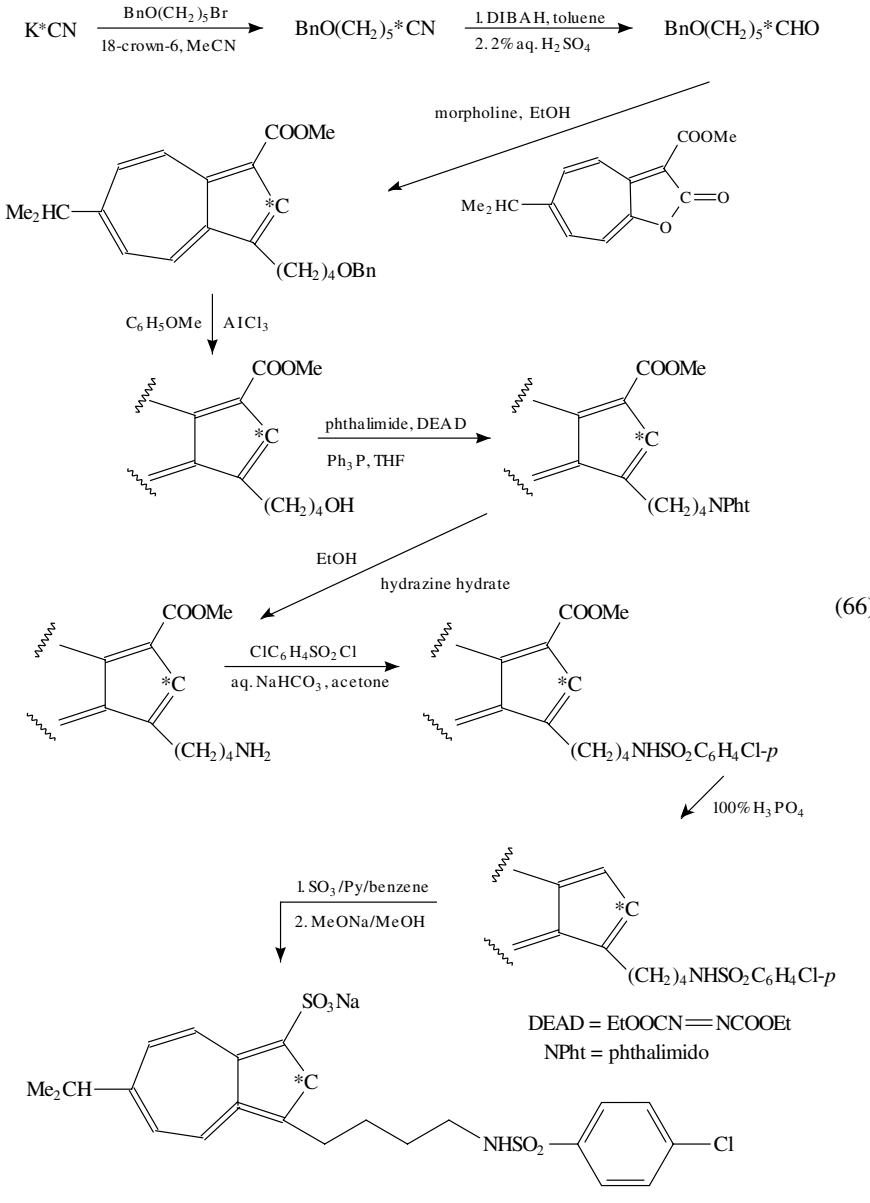
The Friedel-Crafts acylation at the 3-position of the azulene ring was possible due to the effect of the electron-withdrawing 1-methoxycarbonyl group. **183** has been prepared previously in an eight-step synthetic route in an unsatisfactory reaction yield[156].

6. Synthesis of sodium 6-isopropyl-3-[4-(p-chlorobenzenesulphonylamino)butyl]-[2-^{14}C] azulene-1-sulphonate

The title compound, KT2-962, **184**, possessing excellent TXA_2 receptor antagonistic activity[157] (Thromboxane A_2 is the vasoconstricting and platelet-aggregating agent[158]), has been labelled with carbon-14 at the 2-position of the azulene ring[159] in a nine-step procedure using potassium [^{14}C]-cyanide (equation 66) in 64% overall radiochemical yield in NCA (non-carrier added) form for metabolism and disposition studies.

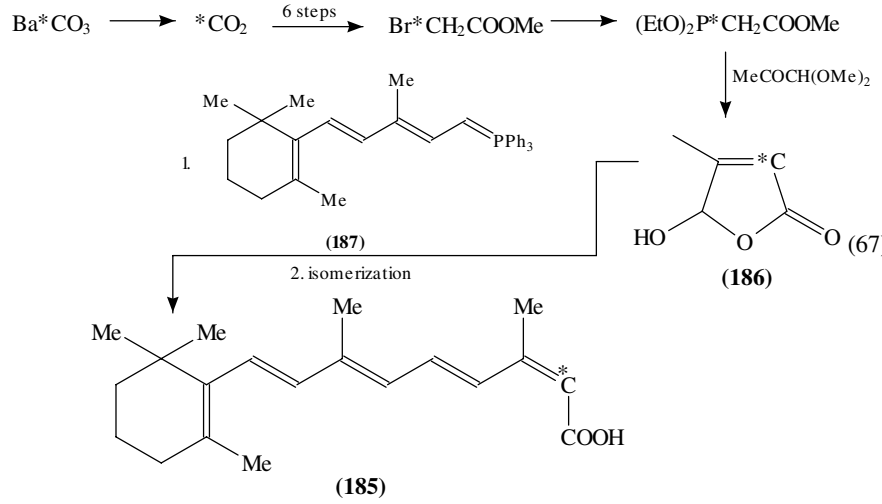
7. Synthesis of 13-cis retinoic [14-^{14}C] acid

13-*Cis* retinoic acid **185**, labelled with carbon-14 at the 14 position, has been obtained[27,100] in the reaction of ^{14}C-labelled butenolide **186** with C-15 Wittig reagent **187** (equation 67).



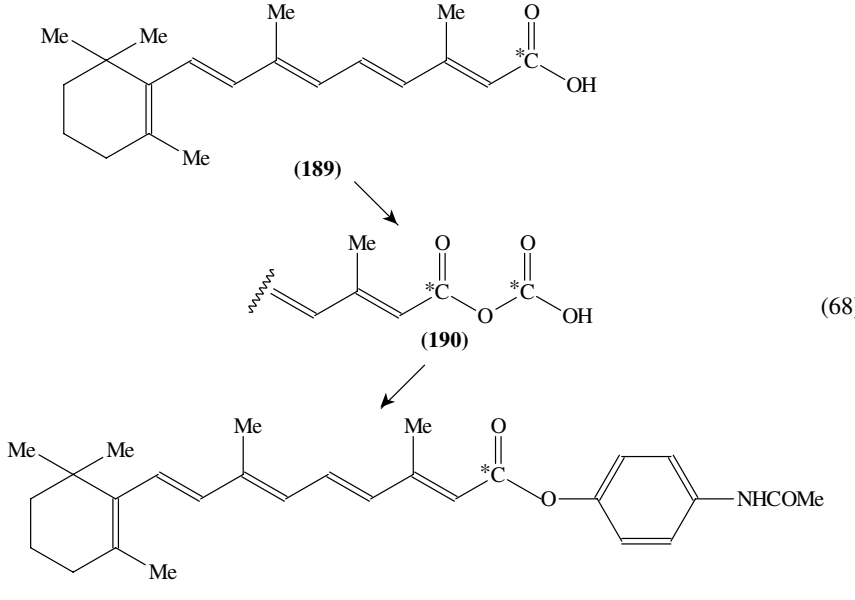
(66)

(184) 1.9 GBq, specific activity 2.36 GBq mmol^{-1}, 85% step yield, 99% HPLC purity



8. Synthesis of 4-(N-acetylamino)phenyl-1-[^{14}C] retinoate

The title compound **188**, currently under development for the treatment of acne, psoriasis and photoaging via a topical application, has been synthesized[161] in two steps by reacting carboxyl-[^{14}C]vitamin A, **189**, with ethyl chloroformate and subsequent treatment of the mixed anhydride **190** with acetamidophenol in the presence of a catalytic amount of 4-dimethylaminopyridine (equation 68), Carbon-14-labelled compound was needed to investigate its metabolism and the extent of systematic adsorption of **188** after dermal application.

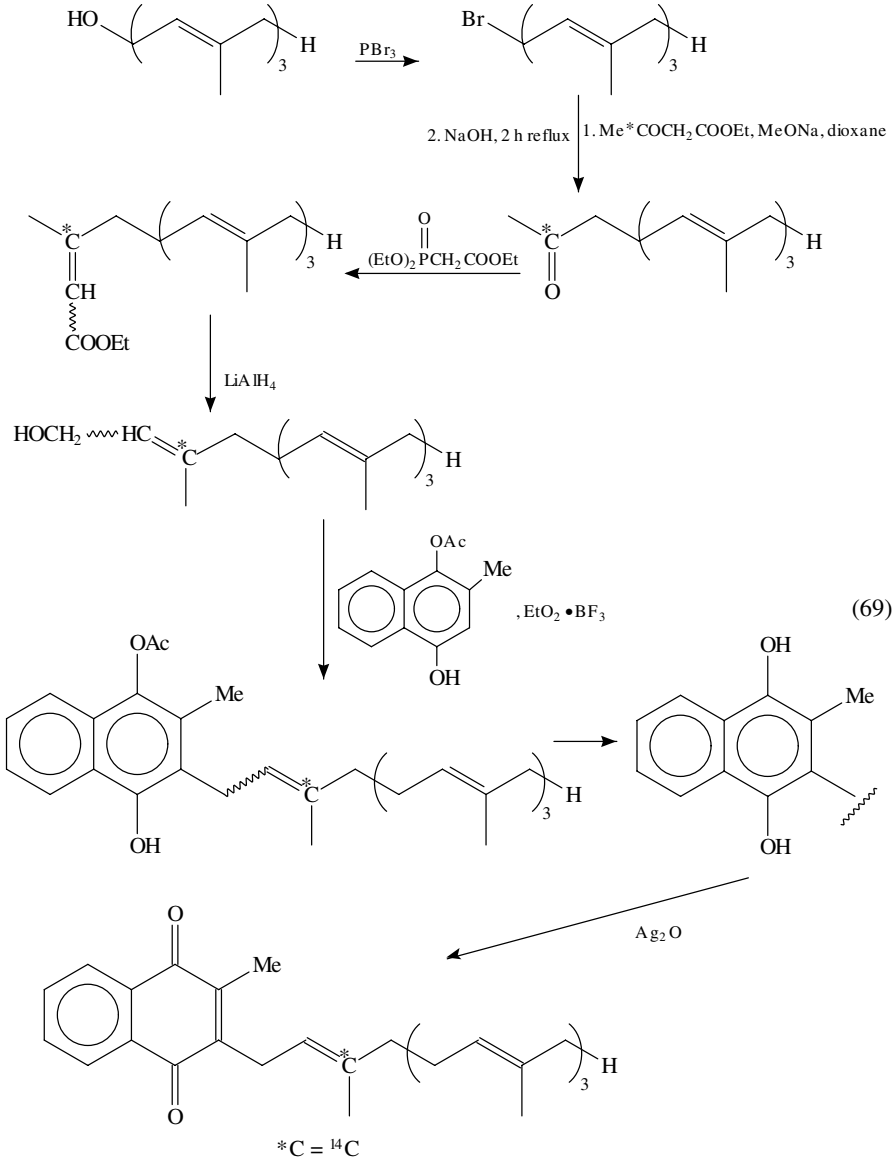


(68)

(188) 42% overall yield, 97.5% radiochemical purity, specific activity 23 μCi mg^{-1}

9. Synthesis of all-trans-[3-^{14}C]menaqinone-4

All-*trans*-menaquinone-4, **191**, potentially useful for therapy of hypoprothrombinemia due to vitamin K deficiency, has been synthesized[162] using ethyl [3-^{14}C]acetoacetate as shown in equation 69, for drug disposition studies in animals.

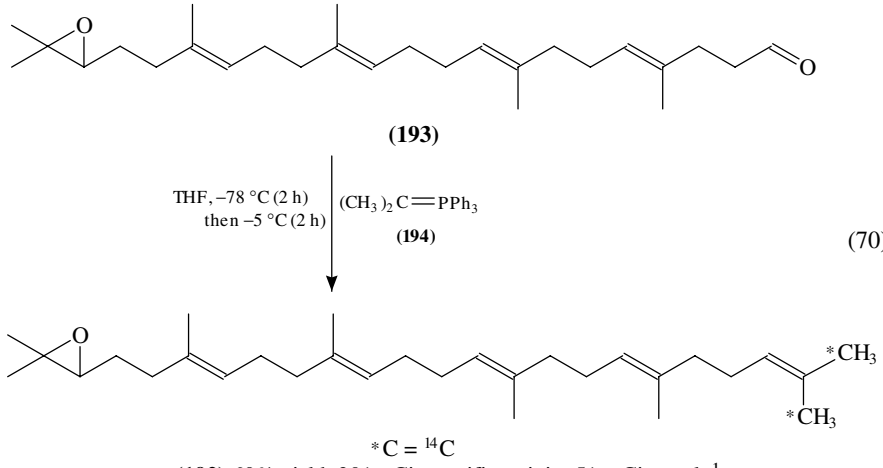


(69)

(191) overall radiochemical yield 12%, specific activity 669 MBq mmol^{-1}, *trans* isomer ≥ 96% after chromatography and recrystallization

10. Synthesis of [24,30-^{14}C]-labelled-2,3-epoxysqualene

[24,30-^{14}C]-(3*S*)-2,3-epoxysqualene and its racemate have been prepared by two routes in a metabolically non-labile position relative to the demethylation of lanosterol to cholesterol (equation 70 and 71). The racemic [24,30-^{14}C]-2,3-epoxysqualene, **192**, has been obtained[163] by condensation of (3*S*, 3*R*)-2,3-epoxytrisnorsqualene aldehyde **193** with freshly prepared ^{14}C-labelled isopropylidenephosphorane, **194** (equation 70).



(70)

(192) 60% yield, 301 μCi, specific activity 51 mCi mmol^{-1}

The optically active (3*S*)-^{14}C-labelled 2,3-epoxysqualene **195** has been prepared[163] by treating (3*S*)-2,3-epoxytrisnorsqualene aldehyde **196** with $(^{14}CH_3)_2C{=}PPh_3$ in THF solution as shown in equation 70. The (20*S*)-(4*E*,8*E*,12*E*,16*E*)-20,21-epoxy-4,8,13,17,21-pentamethyl-4,8,12,16-decosatetraen-1-al, **196**, has been synthesized in six steps as shown in equation 71.

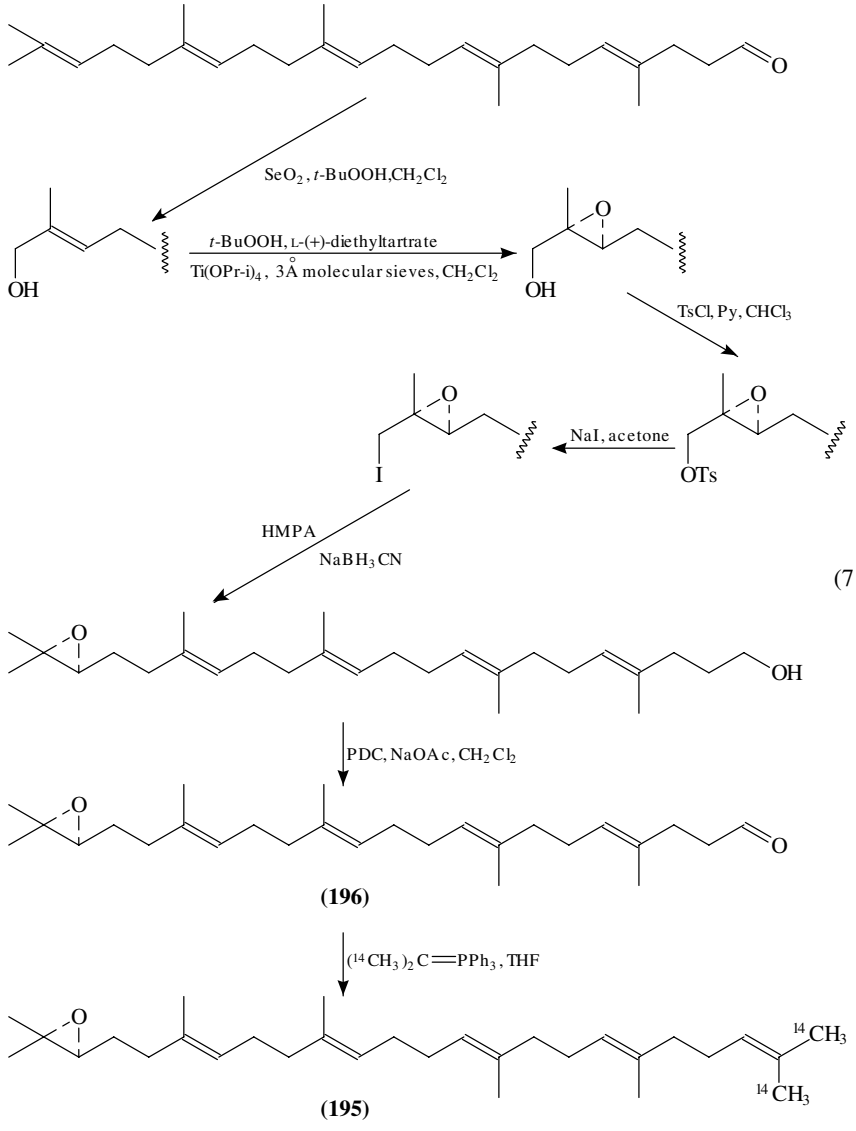
Optically active (3*S*)-form, **195**, is a key intermediate in the biochemical synthesis of triterpenes and sterols in vertebrates, plants and fungi[164].

*11. Synthesis of ^{14}C-chloroacetates of 2-demethylthiocolchicine, **197**, of 3-demethylthiocolchicine, **198**, of N-acetylcolchinol, **199**, and of the ^{14}C-9-isocyanato-9-deoxy-N-acetylcolchinol, **200***

The title compounds **197** and **198**, covalently binding with high specificity to the β-subunit of tubulin[165,166,169], have been obtained[167] by treating 2-demethylthiocolchinine, **201**, and 3-demethylthiocolchinine, **202**, respectively with $ClCH_2{}^{14}COCl$ in CH_2Cl_2 solution containing triethylamine.

The radiolabelled 9-chloroacetoxy-*N*-acetylcolchinol, **199**, has been prepared[167] by reacting *N*-acetylcolchinol **203** dissolved in CH_2Cl_2 and containing Et_3N, with $ClCH_2{}^{14}COCl$ during 24 h at 55 °C.

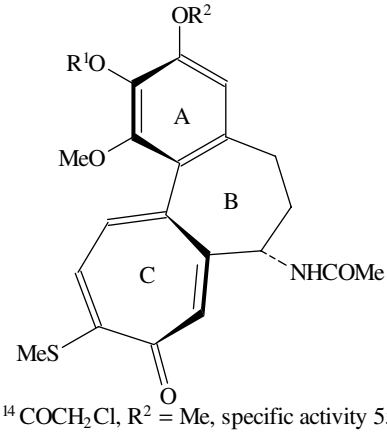
The radiolabelled isothiocyanate **200** has been prepared[167] by an early published procedure[168] using radiolabelled $^{14}CH_3I$ (50 mCi mmol^{-1}, 2 mCi, 0.04 mmol).



(71)

PDC = Pyridinium dichromate

The ^{14}C-chloroacetate of *N*-acetylcolchinol **199** and the ^{14}C-isothiocyanate **200** were also found to react covalently with tubulin, but in a non-specific manner[167], contrary to compounds **197** and **198** which react covalently with the colchicine binding site on tubulin with a β-subunit: α-subunit marking ratio[169] of about 4:1.

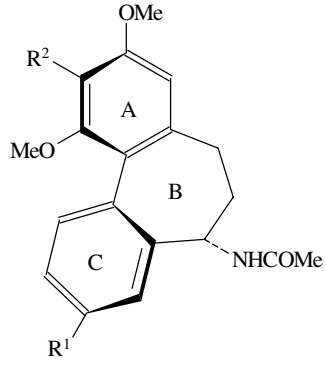


(197) $R^1 = {}^{14}COCH_2Cl$, R^2 = Me, specific activity 55 mCi mmol^{-1}, radiochemical yield 26.1%

(198) R^1 = Me, $R^2 = {}^{14}COCH_2Cl$, specific activity 55 mCi mmol^{-1}, radiochemical yield 5.7%

(201) R^1 = H, R^2 = Me

(202) R^1 = Me, R^2 = H



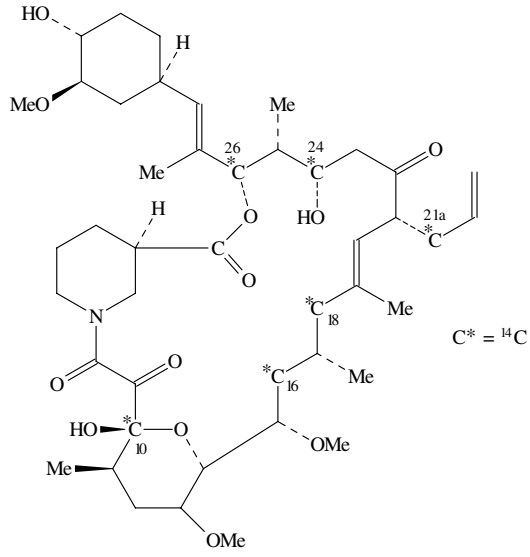
(199) $R^1 = O{}^{14}COCH_2Cl$, R^2 = OMe, specific activity 56 mCi mmol^{-1}, radiochemical yield 7.8%

(200) R^1 = NCS, $R^2 = O{}^{14}CH_3$, specific activity 50.0 mCi mmol^{-1}, radiochemical yield 32%

(203) R^1 = OH, R^2 = MeO

12. Synthesis of ^{14}C-labelled FK-506, ***204***

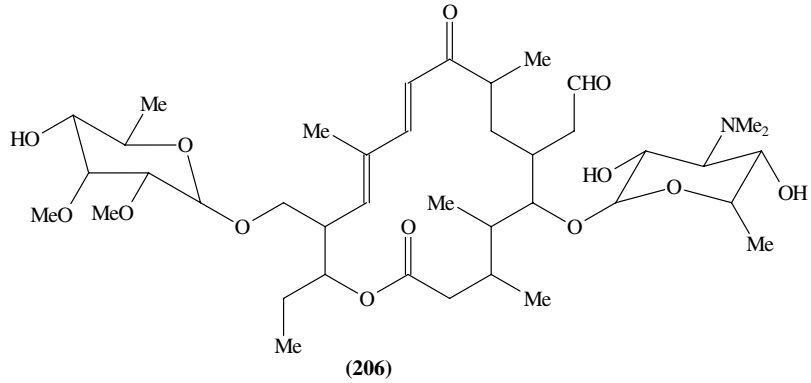
The immunosuppressant compound[170] FK-506, similar in effect to cyclosporin A, the leading drug for use in immune system suppression to prevent rejection of transplanted organs[171], has been labelled at carbon atoms 10, 16, 18, 21*a*, 24 and 26 by fermentative biosynthesis using sodium [1-^{14}C]propionate as a precursor[172]. The same ^{13}C-labelled positions were derived from [1-^{13}C]propionate. FK-506 producing culture *Streptomyces tsukubaenis* no 9993 has been utilized in this biosynthesis (120 h incubation at 29 °C).



(**204**) FK-506, 3.6 mCi after HPLC, 0.6% from 614 mCi of [1-^{14}C]propionate (specific activity 57.7 mCi (mmol^{-1}).

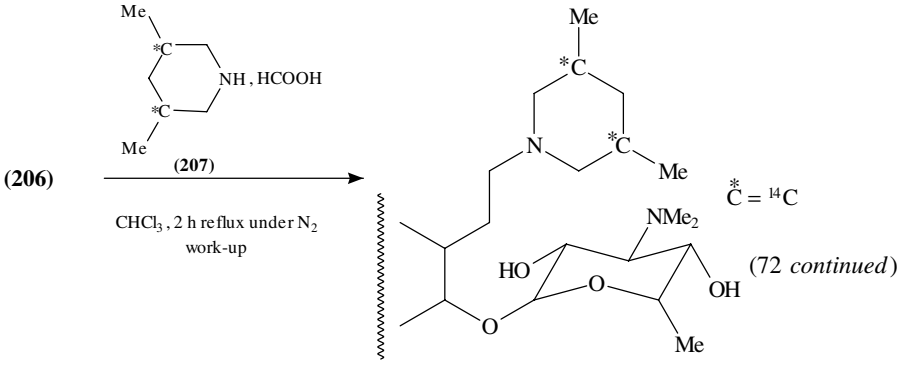
13. Synthesis of ^{14}C-radiolabelled tilmicosin

Tilmicosin **205** has been ^{14}C-labelled on the 3,5-dimethylpiperidinyl side chain[173] by reductive amination of the C-20 aldehyde of desmycosin **206** with 3,5-dimethylpiperidine hydrochloride-3,5-^{14}C, **207**, using 95–97% formic acid in boiling chloroform (equation 72). The required 3,5-lutidine radiolabelled in the piperidine ring, has been prepared in a six-step radiosynthetic route starting with 2-^{14}C-diethyl malonate as shown in equation 73. **205** (EL-870) is an antibacterial[174] used in treating respiratory diseases in cattle and swine. Radiolabelled EL-870 was required for biochemical studies. It is currently under development as a parenterally administered antibacterial agent for treatment of pneumonic pasteurellosis in calves and for use in feed for the control of pasteurella pneunomia in pigs.

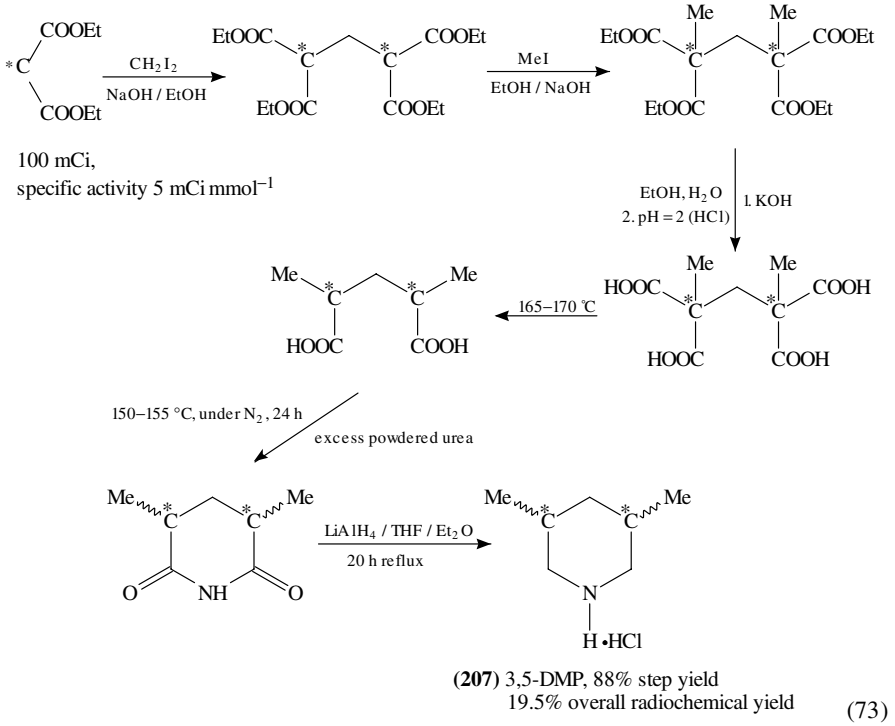


(206)

(72)



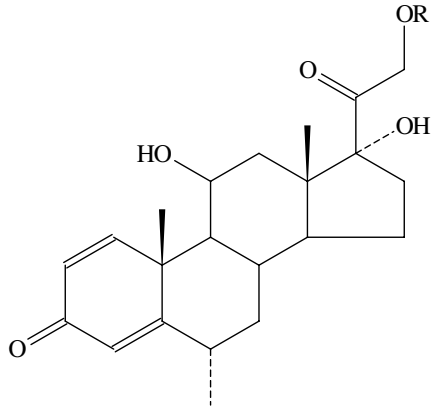
(205) EL 870, 97% yield, total activity 19.5 mCi, specific activity 6.48 mCi mmol^{-1}

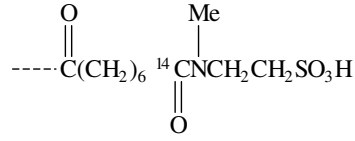


(207) 3,5-DMP, 88% step yield
19.5% overall radiochemical yield (73)

14. Synthesis of ^{14}C-labelled methylprednisolone suleptanate

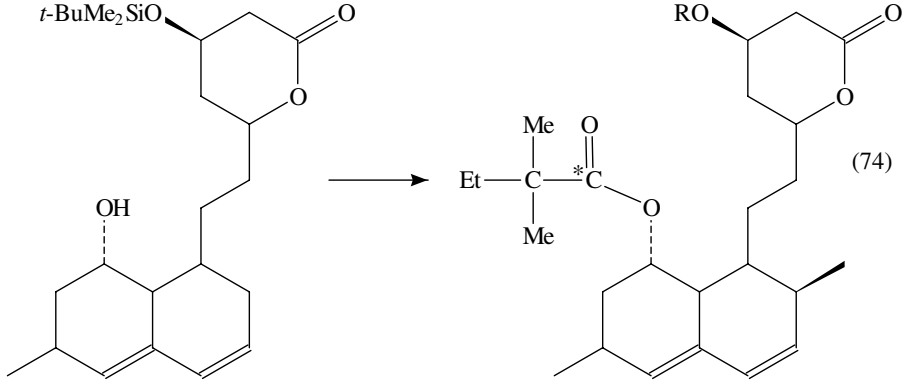
The methylprednisolone suleptanate **208b**, the water-soluble prodrug of the methylprednisolone corticosteroid **208a**, has been labelled with ^{14}C exclusively at the carboxamide carbon[175] which was found to be metabolically stable with no loss of $^{14}CO_2$ after administration to test animals and man.



(208a) R = H, **(208b)** R = 

*15. Synthesis of ^{14}C-labelled simvastatin, **209***

This potent inhibitor of cholesterol biosynthesis has been synthesized[178] by one-pot esterification of the alcohol **210** with the acid chloride of 2,2-dimethylbutanoic[1-^{14}C] acid, obtained by carbonation of the Grignard reagent prepared from 2-chloro-2-methylbutane (equation 74). Desilylation of **211** afforded [^{14}C]simvastatin **209** in 29% radiochemical yield from ^{14}C-labelled CO_2. This ^{14}C-labelled drug was needed for elucidation of its metabolic fate in experimental animals.



(74)

(210)

(209) R = H
(211) R = $SiMe_2Bu$-*t*

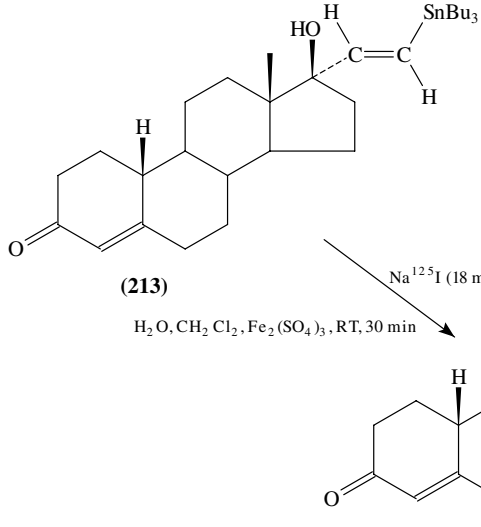
*C = ^{14}C

V. SYNTHESIS AND USES OF DIENES AND POLYENES LABELLED WITH HEAVY RADIOISOTOPES

A. Synthesis of Iodine-125-labelled Compounds

1. Synthesis of NCA 17α{2-(E)-[^{125}I]-iodovinyl}-19-nortestosterone

This ^{125}I-labelled steroid hormone (E-^{125}I VNNT), **212**, needed for human breast cancer therapy, has been synthesized[177] by [^{125}I]-iododestannylation of 17α-[2-(*E*)-tri-*n*-butylstannylvinyl]-19-nortestosterone (E-TBS VNNT), **213**, using [^{125}I]-sodium iodide/ferric sulphate in mixed CH_2Cl_2 water solvent, as the iodinating agent (equation 75). This avoided standard oxidants like $KMnO_4$, KlO_4, K_2CrO_4 or H_2O_2, chloramine-T and *N*-chlorosuccinimide which can oxidize the stannyl steroid substrate.



(75)

(212) 10 mCi,
specific activity 2200 Ci mmol^{-1}

Ferric sulphate is a mild oxidant and is non-reactive with the steroid substrate. It liberates iodine quantitatively (equation 76), and the iodine is extracted into CH_2Cl_2 and consumed as in equation 75.

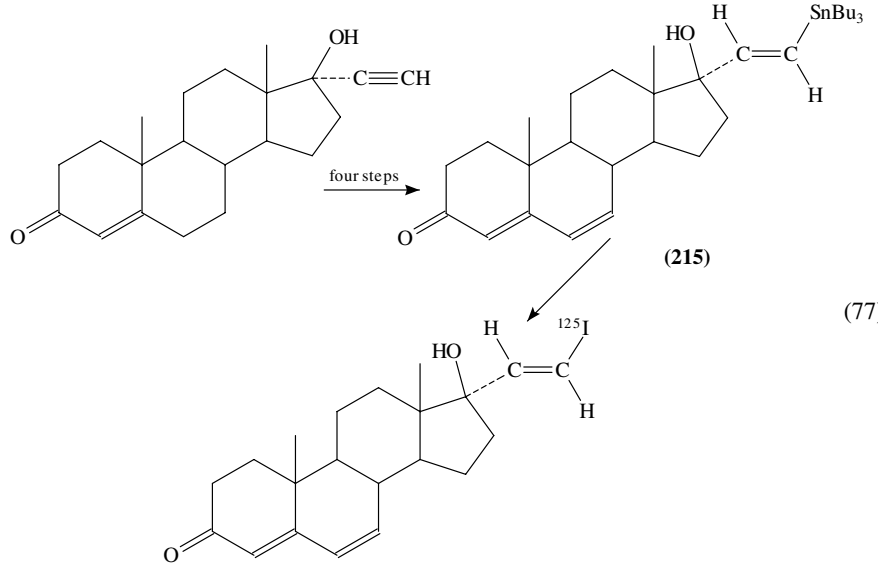
$$Fe_2(SO_4)_3 + 2Na^*I \xrightarrow[\text{or neutral solvent}]{H^+} 2FeSO_4 + Na_2SO_4 + {}^*I_2 \qquad (76)$$

In the non-labelled reaction, **213** reacts with excess of iodine and quantitative yield of E-IVNNT is obtained[177,178]. The formation of E-^{125}IVNNT, **212**, is ascribed to the generation of a four-membered transition state, formed by two polarized bonds, C^--Sn^+ and I^+-I^-, in which the two radioiodine atoms are shared by the two reactive centres, carbon and tin. The reaction leads to the formation of steroid-CH=CH^{125}I and of iodostannyl compound, $^{125}ISnBu_3$, which is lost during the evaporation and/or during chromatography lowering the yield of **212** to about 50% radioactive yield. The 30–90% radiochemical yield observed in ^{125}I-iododestannylation[179], using CAT or H_2O_2, are caused by formation of an HO–I species and the product 'C–I' and by-product 'HO–Sn' formation (little or no iodine is captured by tin).

The cultures of T47D human breast ductal carcinoma (2×10^5 cells) have been used to determine the uptake of E-^{125}IVNNT and specific progesterone receptor binding *in vitro*[177]. Cell binding assays demonstrated that **212** binding to T47D breast carcinoma was specific and saturable with an affinity for the progesterone receptor 10-fold greater than that of commercially available PgR ligand ^{3}H-R5020. E-^{125}IVNNT should be useful for determining PgR + tumors and for measuring the number of progesterone receptors in these tumors[177].

2. Synthesis of 17α-{(E)-2-[^{125}I]iodoethenyl} androsta-4,6-dien-17β-ol-3-one

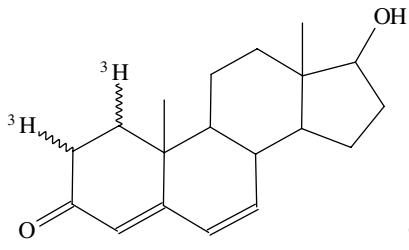
The synthesis of the title compound, **214**, the active-site-directed photoaffinity radiolabel for androgen-binding proteins ('ABP'), has been accomplished[180,181] by treatment of excess 17α-[(*E*)-2-tributyltin(IV)ethenyl]androsta-4,6-dien-17β-ol-3-one, **215**, with sodium iodide-125 of specific activity 27 Ci mmol^{-1} in a sodium acetate–AcOH buffered solution and a solution of 30% H_2O_2 in glacial AcOH (equation 77).



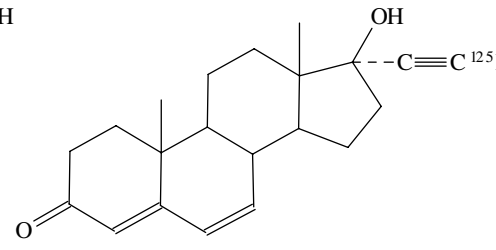
(77)

([^{125}I] **214**) 52% radiochemical yield after HPLC, specific activity 27 Ci mmol^{-1}, 100% radiochemical purity

The ability of [^{125}I] **214** as well as of the previously prepared[182] [^{3}H]Δ^6-testosterone, **216**, and 17α-[^{125}I]iodoethynylandrosta-4,6-dien-17β-ol-3-one[183], [^{125}I] **217**, to serve as photoaffinity labelled reagents, resides in the excitation of the conjugated dienone system to an excited singlet state, which then undergoes intersystem crossing to a triplet state in which the excited steroids abstract hydrogen from the protein. The recombination of the resultant steroid-protein radical pair leads to formation of the covalent bond[184]. The extended conjugation of Δ^6-testosterone results in the shift of the carbonyl absorption band from 305 nm to 345 nm. The last absorption band is beyond the absorption band of cytosol and consequently a photoactivation of the unsaturated carbonyl group and subsequent covalent bond formation with the protein is possible. The decomposition of [^{125}I] **217** and its protein complex in the presence of β-mercaptoethanol makes the utility of [^{125}I] **217** very limited.



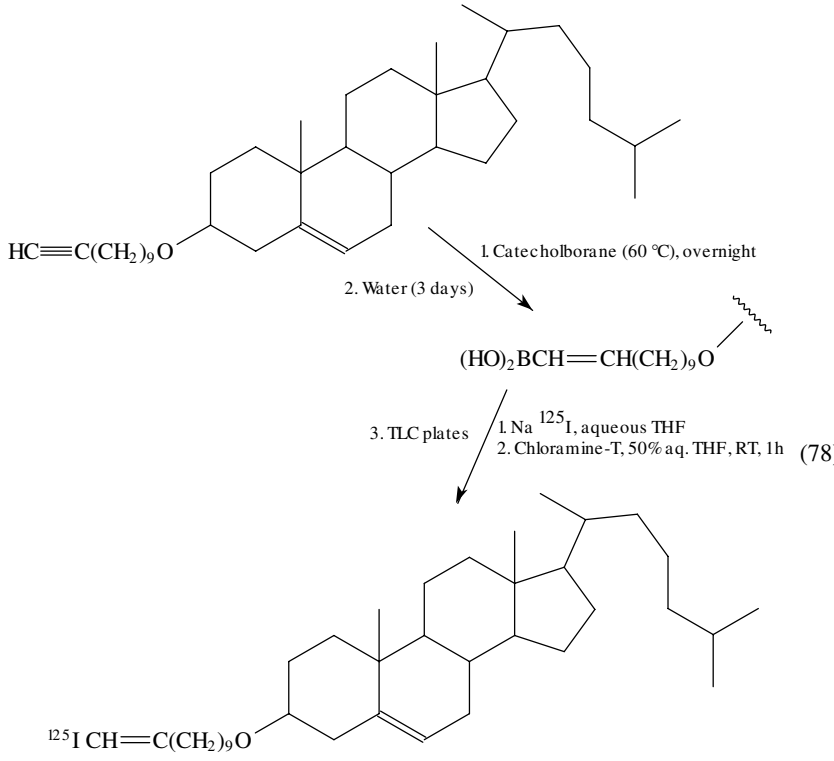
([^{3}H] **216**)



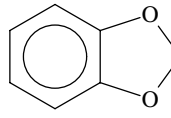
([^{125}I] **217**)

3. Synthesis of iodine-125-labelled ω-iodoundecenyl cholesteryl ether

Radioiodinated vinyl iodides[185] possessing superior *in vivo* stability relative to the alkyl iodides[186] have been used for myocardial imaging[185]. The title vinyl iodide **218** has been synthesized[187,188] therefore for use as a liposomar marker via the hydroboration–iodination sequence shown in equation 78.



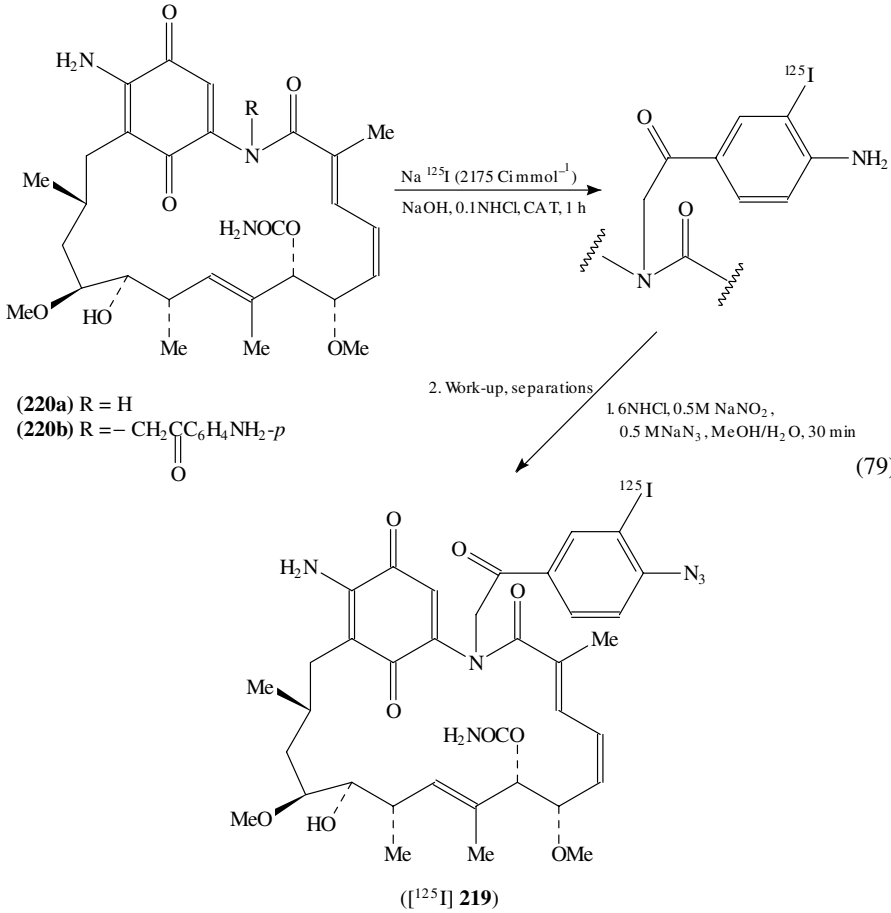
(218) 17% radiochemical yield



= catecholborane

4. Synthesis of 17-amino-22-(4′-azido-3′-^{125}I-iodophenacyl)-17-demethoxygeldanamycin, ***219***

The title compound, **219**, suitable for mechanistic studies with oncogen transformed tumor cells has been synthesized[189] in a one-pot two-step process from 17-amino-22-(4′-aminophenacyl)-17-demethoxygeldanamycin, **220b** (equation 79). (**220a**, 17-amino-17-demethoxygeldanamycin as such, inhibits cell growth of SV40 transformed cells[190]). **220b** has been prepared[189] by treating **220a** with *t*-BuOK in DMSO, then with 4′-aminophenacyl chloride at RT for 3 hours. The use of the 4-azido-3-[^{125}I]iodophenyl moiety as a photolabile radiolabelling tool had been reported by Patel and coworkers[191].



(220a) R = H
(220b) R = $-CH_2C(=O)C_6H_4NH_2$-*p*

(79)

([^{125}I] **219**)

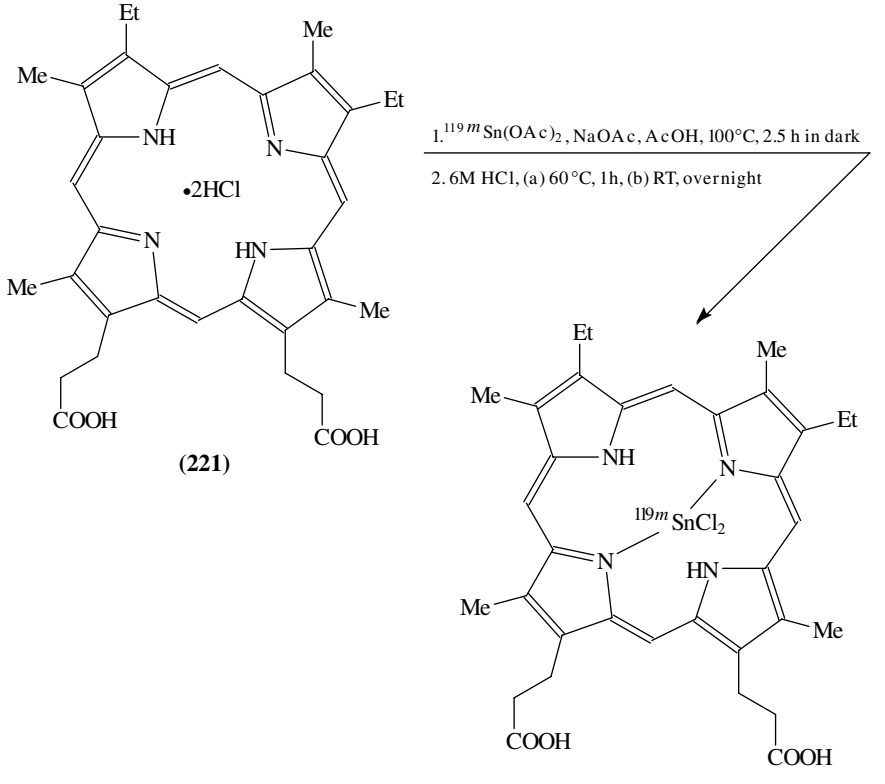
1-2% overall radiochemical yield

B. Synthesis of Compounds Labelled with Tin

1. Synthesis of [^{119m}Sn]-mesoporphyrin IX dichloride

This compound, Sn-MPCl_2, decreases effectively plasma billirubin levels in both adult and neonatal animals[192] and is under current evaluation as an alternative to phototherapy

in the treatment of neonatal hyperbilirubinemia[193]. [^{19m}Sn]-$MPCl_2$, **222**, has been prepared[194] in 60% radiochemical yield by metalation of the porphyrin nucleus of **221** with tin(II)-119*m* acetate (equation 80). A 1% radiochemical impurity presumably arose from traces of unreacted tin-119*m* reagent. The amount of unmetalated mesoporphyrin starting material found in labelled product **222** was <3% by HPLC analysis.



(221)

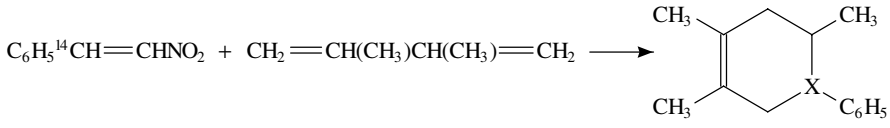
(222) 633 μCi, specific activity 43.4 mCi $mmol^{-1}$ (58 μCi mg^{-1}), 99% radiochemical purity (80)

VI. ISOTOPE EFFECT STUDIES WITH DIENES AND POLYENES

A. Carbon-14 and Deuterium Isotope Effect Studies of the Diels-Alder Reaction

1. Experimental ^{14}C KIE study of the Diels-Alder addition of β-nitrostyrene to 2,3-dimethylbutadiene

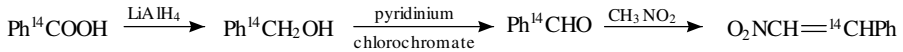
The title Diels-Alder (DA) addition reaction shown in equation 81[195] has been reinvestigated recently[196] by labelling **223** with ^{14}C successively at $C_{(1)}$ and at $C_{(2)}$. The [2-^{14}C]-1-nitro-2-phenylethene has been obtained in the reaction of [7-^{14}C]benzaldehyde with nitromethane (equation 82).



(223) **(224)** **(225)**

X = ^{14}C

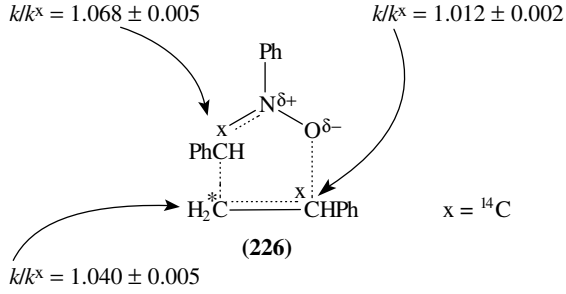
(81)



(82)

The [^{14}C]nitromethane needed for preparation of [1-^{14}C]**223** has been made by reaction of [^{14}C]MeI with silver nitrite[197]. The low-conversion and high-conversion isotopic experiments have been carried out using 1.20 mmol of **224** and 5.00 mmol of [2-^{14}C]**223** in dry toluene or 3.35 mmol of **224** and 1.68 mmol of [2-^{14}C]**223** in 3 ml of toluene, respectively. The reactants, sealed in a snap-neck ampoule, were placed in an oven at 115 °C for 3 days to achieve the 100% conversion. The [1-^{14}C]**223** KIE and [2-^{14}C]**223** KIE were found to be 1.0438 ± 0.0012 and 1.0474 ± 0.0015, respectively. The earlier workers[195], counting data on KIE at $^{14}C_{(1)}$, erred probably because they achieved 60% rather than 100% conversion in their experimental work. No exchange at 130 °C during 24 h between **223** and unlabelled adduct **225** at melt has been found. Thus the possibility that the KIE in the DA reaction studied is masked by the exchange between the adduct and unreacted dienophile has been eliminated. The DA reaction (equation 81) is suggested to be concerted[196].

The primary ^{14}C KIEs in the 1,3-dipolar addition of *N*-α-diphenylnitrone, PhCH=N(O)Ph, and styrene to yield 2,3,5-triphenylisoxazoline **226**[198] are also consistent with Huisgen's[199] concerted, cyclic mechanism and inconsistent with the diradical mechanism[200] (structures **227** and **228**).



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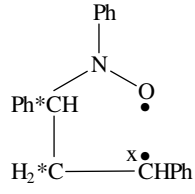

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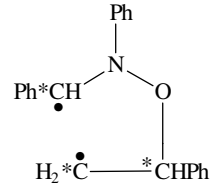
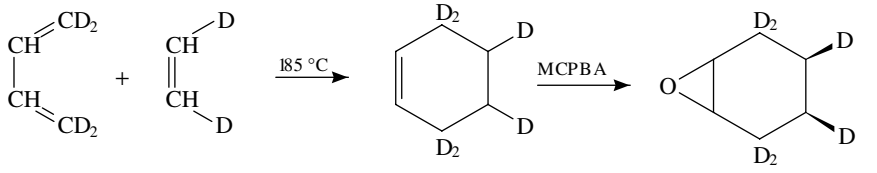


(228)

The prototype concerted addition of ethene to butadiene is discussed in the next section.

2. Experimental studies of the DA reaction with the use of deuterium

a. Evidence for the concerted mechanism of the DA reaction of butadiene with ethylene has been provided by Houk and coworkers[201], who established the stereospecificity of this addition by carrying out the reaction of 1,1,4,4-tetradeuterio-1,3-butadiene with *cis*- or *trans*-1,2-dideuterioethylene at 185 °C for 36 h at a pressure of 1800 psi in a stainless steel bomb (equations 83 and 84). The dideuterioethylenes do not isomerize under these conditions. The cyclohexene products, separated from butadiene dimers by GLC, were then epoxidized with *m*-chloroperbenzoic acid (MCPBA) and their NMR spectra determined.



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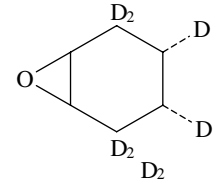
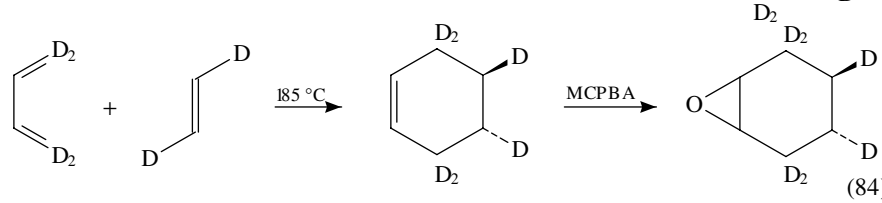
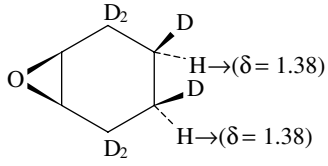




(84)

The proton NMR spectra corresponding to the cyclohexene oxides **229** and **230**, obtained in the reaction with *cis*-dideuterioethylene, and to cyclohexene **231**, obtained in the



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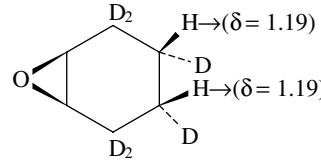

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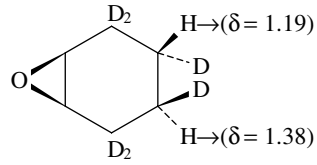
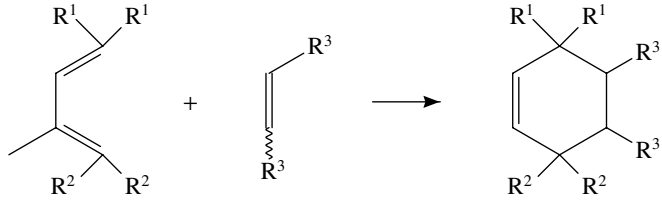


(231)

reaction with *trans*-dideuterioethylene, have been recorded and analysed[201]. Calculations of the transition state frequencies[201] are consistent with a synchronous concerted mechanism for the reaction of butadiene with ethylene.

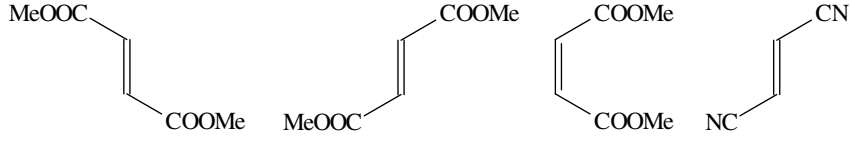
b. Secondary kinetic deuterium isotope effects have been determined[202–206] in the various Diels-Alder additions of symmetrical addends[202–204] expressed by equation 85, in Diels-Alder reactions of unsymmetrical addends[205] (equation 86) and in the Diels-Alder reaction of anthracene, butadiene and cyclopentadiene with maleic anhydride[206].



$R^1 = R^2 = D$
$R^1 = D, R^2 = H$
$R^3 = CN, COOMe$

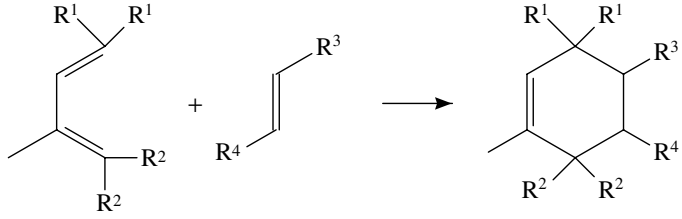
	Expt. KIE at 373 K
$R^1 = D, R^2 = H, R^3 = CN$[d]	0.95
$R^1 = H, R^2 = D, R^3 = CN$	0.95
$R^1 = D, R^2 = D, R^3 = CN$	0.90
$R^1 = H, R^2 = D, R^3 = COOMe$[a]	0.92
$R^1 = D, R^2 = D, R^3 = COOMe$[b]	0.85
$R^1 = H, R^2 = D, R^3 = COOMe$[c]	0.92
$R^1 = D, R^2 = H, R^3 = COOMe$[b]	0.93
$R^1 = D, R^2 = D, R^3 = COOMe$[c]	0.87

(85)



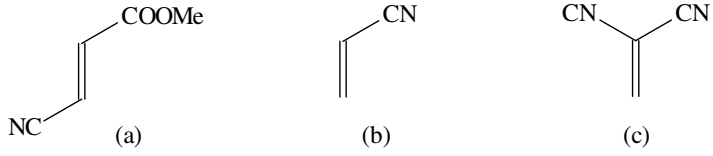
(a) (b) (c) (d)

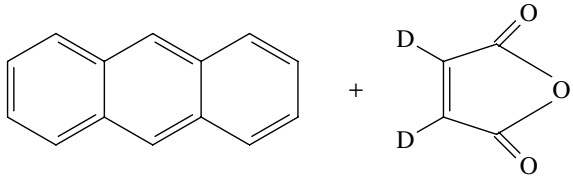
In the reaction of cyclopentadiene with maleic-D_2 anhydride[206] an inverse experimental KIE of 8% (KIE = 0.92) was found at 298 K. The reaction between butadiene-D_4, $D_2C{=}CHCH{=}CD_2$ and maleic anhydride gave a large inverse D_4-KIE of 0.76. The two reactions between anthracene and maleic anhydride presented below also favour the concerted rather than the stepwise mechanism which requires 3–6% KIE in the normal direction (i.e. >1).



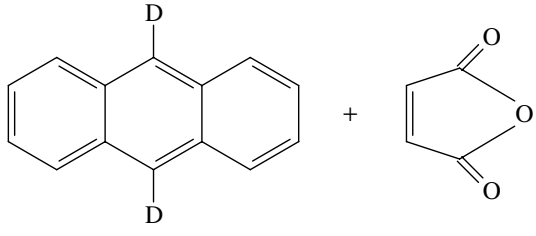
		Expt. KIE		
R^1 = D, R^2 = H, R^3 = COOMe,	R^4 = CN[a]	0.88	at	298 K
R^1 = H, R^2 = D, R^3 = COOMe,	R^4 = CN	0.92		298
R^1 = D, R^2 = D, R^3 = COOMe,	R^4 = CN	0.81		298
R^1 = D, R^2 = H, R^3 = CN,	R^4 = H[b]	0.91		373
R^1 = H, R^2 = D, R^3 = CN,	R^4 = H	0.98		373
R^1 = D, R^2 = D, R^3 = CN,	R^4 = H	0.89		373
R^1 = D, R^2 = H, R^3 = $(CN)_2$,	R^4 = H[c]	0.79		298
R^1 = H, R^2 = D, R^3 = $(CN)_2$,	R^4 = H	0.98		298
R^1 = D, R^2 = D, R^3 = $(CN)_2$,	R^4 = H	0.78		298

(86)



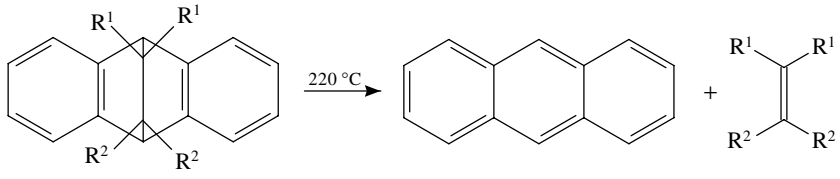


KIE = 0.93 at 373 K



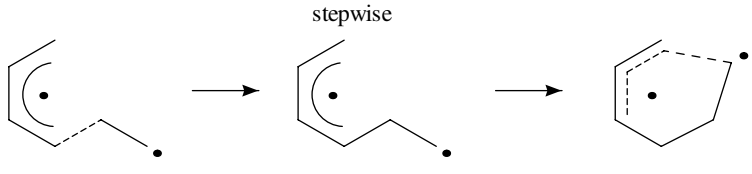
KIE = 0.91 at 373 K

The secondary deuterium KIEs for the retro-Diels-Alder reaction of ethanoanthracene has been investigated also[207] (equation 87)[206].

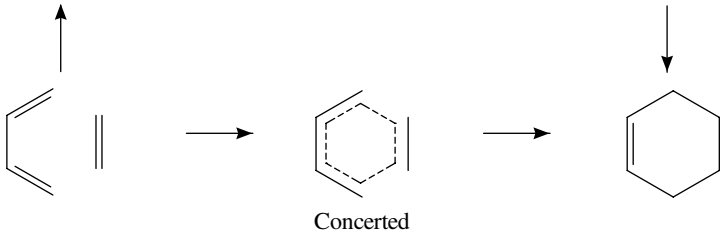


$R^1 = D, R^2 = H; R^1 = R^2 = D, k_H/k_{D_2} = 1.08$ and $k_H/k_{D_4} = 1.17$ at 220 °C (87)

These experimental secondary deuterium KIEs observed in Diels-Alder reactions have been compared with the respective theoretical KIEs for the stepwise mechanism involving a diradical intermediate (equation 88a) and for concerted synchronous and asynchronous mechanisms (equation 88b) for the Diels-Alder reaction of butadiene with ethylene[207].



(88a)



(88b)

Vibrational analysis has been carried out for each isotopomer transition state and the k_H/k_D values were calculated[207] with the transition state theory approximation (equation 89)[208,209]:

$$k_H/k_D = (\nu_H^{\neq}/\nu_D^{\neq}) \frac{\prod^{3N-6}\left(\frac{u_H}{u_D}\right)\prod^{3N-6}\frac{[1-\exp(-u_H)]}{[1-\exp(-u_D)]}\exp\left(\sum^{3N-6}\frac{(u_H-u_D)}{2}\right)}{\prod^{3N^{\neq}-7}\left(\frac{u_H^{\neq}}{u_D^{\neq}}\right)\prod^{3N^{\neq}-7}\frac{[1-\exp(-u_H^{\neq})]}{[1-\exp(-u_D^{\neq})]}\exp\left(\sum^{3n^{\neq}-7}\frac{(u_H^{\neq}-u_D^{\neq})}{2}\right)} \quad (89)$$

where $u = h\nu/kT$.

The activation energy of the concerted mechanism is only 3–7 kcal mol^{-1} lower than that for the first step of the stepwise mechanism. However, the geometries of the two transition states are dissimilar, one bond being formed in the stepwise structure while two bonds are formed in the concerted case, and this leads to different KIEs. The secondary KIEs calculated for concerted TS (terminal hydrogens) are always inverse (and vary from 0.93 to 0.99, depending on the position and the level of theory), in agreement with expectations for sp^2 to sp^3 hybridization changes. The most reliable values are 3% and

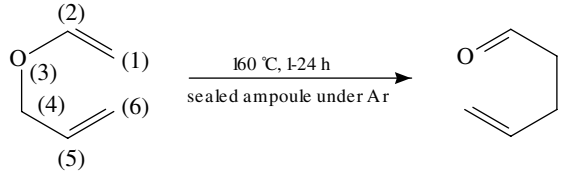
6% for D_2 and D_4 substrates, respectively. The D_2- and D_4-KIEs for TS-1 are normal with values of 1% and 4% for D_2 and D_4, respectively. The KIEs in TS-2 are also normal and opposite in direction to those of the concerted mechanism. The detailed comparison of the theoretical and experimental secondary KIEs for Diels-Alder reactions showed that the concerted mechanism gives a good account of the experimental isotope effects[207,210].

^{14}C Primary kinetic isotope effects for the concerted reaction of butadiene with ethylene, for the stepwise reaction of butadiene with ethylene and for the concerted reaction of butadiene with acrolein, have also been calculated[207]. The experimental values of 1.0438 and 1.0474 found recently[196] in the reaction of 2,3-dimethylbutadiene with [1-^{14}C]- and [2-^{14}C]-1-nitro-2-phenylethylene, respectively, similar at both reacting termini, are in accord with the calculated value of 1.046 for k_{12_C}/k_{14_C} (373.15 K) in a synchronous concerted reaction of butadiene with ethylene. The ^{14}C KIE values predicted for the asynchronous acrolein reaction are 1.015 and 1.045 for the '1' and '2' isotopomer, respectively[207].

B. Kinetic Isotope Effects in the Thermal Rearrangement of 3-Oxa-1,5-hexadienes

1. Heavy atom KIE studies with allyl vinyl ethers

a. The mechanism of the thermal aliphatic Claisen rearrangement[211] has been studied recently by heavy-atom KIE methodology[212]. Carbon-14 KIE in the rearrangement of allyl vinyl ethers, **232**, labelled with ^{14}C at the 2-, 4- and 6-positions, and with ^{18}O at the 3-position, to the corresponding 4-pentenals, **233** (equation 90), have been determined at 160 °C. The isotopomers [4-^{14}C]-**232**, [6-^{14}C]-**232** and [^{18}O]-**232** have been prepared by the reactions of *n*-octyl vinyl ether[213] with [1-^{14}C]-, [3-^{14}C]- and [1-^{18}O] allyl alcohol in the presence of mercuric acetate[214]. [2-^{14}C]-**232** has been prepared from allyl alcohol and *n*-octyl [2-^{14}C] vinyl ether which was synthesized as shown in equation 91.



(90)

(232) **(233)**

(91)

Cp_2TiMe_2 = dimethyltitanocene $C_8H_{17}O^{14}CH{=}CH_2$

The ^{14}C labelled 4-pentenals, **233**, have been converted to their dimedone derivatives for radio assay. The ^{18}O-**233** has been reduced to 4-pentenol for MS isotopic assay. The average ^{18}O and ^{14}C KIEs in the rearrangement of **232** were found to be:

$$1.0506 \pm 0.0007/\text{for}^{18}\text{O isotope},$$

$$1.0271 \pm 0.0006/\text{for } 2 -^{14} \text{C},$$

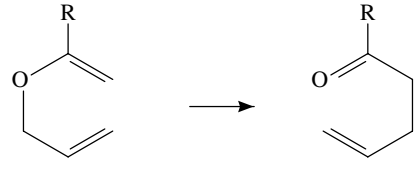
$$1.0720 \pm 0.0008/\text{for } 4-{}^{14}\text{C},$$

$$1.0178 \pm 0.0005/\text{for } 6-{}^{14}\text{C}.$$

The large 3-^{18}O and 4-^{14}C KIEs indicate that the cleavage of the carbon–oxygen bond contributes strongly to the reaction coordinate motion. All the above data collectively show that the six skeletal atoms of **232** are coupled in motion in the transition state. The ^{14}C KIE for $C_{(1)}$ has not been determined. The degrees of bonding changes at $C_{(1)}$ and at $C_{(6)}$ in the transition state of reaction 90 cannot be intercompared. The hybridization at $C_{(1)}$ and at $C_{(6)}$ changes from sp^2 to sp^3. The model calculations with the use of the BEBOVIB IV program[217–219] led the authors[212] to the conclusion that the $C_{(4)}$–O bond is 50–70% broken ('central to product-like') and the $C_{(1)}$–$C_{(6)}$ bond is 10–30% formed ('reactant-like') in the transition state.

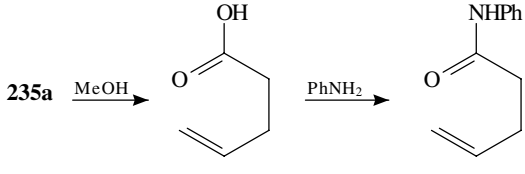
The density functional theory calculations of primary ^{14}C KIE and secondary deuterium kinetic isotope effects (SKIE)[220] did not reproduce satisfactorily all the experimentally determined ^{14}C KIE and deuterium (4,4-$^2H_2$)- and 6,6-$^2H_2$-SKIE, though the non-local DFT methods provide transition state energies on a par with correlated molecular orbital theory[221].

b. Carbon-14 KIE in the rearrangement of 2-(trimethylsiloxy)[222,223] and 2-(methoxycarbonyl)-3-oxa-1,5-hexadiene[203], both labelled with ^{14}C at $C_{(1)}$, $C_{(2)}$, $C_{(4)}$ and $C_{(6)}$ positions, have been measured at 22 °C and 80 °C, respectively[224] (equation 92), and the ^{14}C KIE have been compared with deuterium SKIE in the rearrangement of [4,4-$^2H_2$]**234a** and [6,6-$^2H_2$]**234a**[225,226]. The products **235a** and **235b** have been converted into the solid colourless anilide **236** (equation 93) and semicarbazone **237** (equation 94) for purifications required by precise ^{14}C scintillation counting with 2σ at the 0.5% level.



(92)

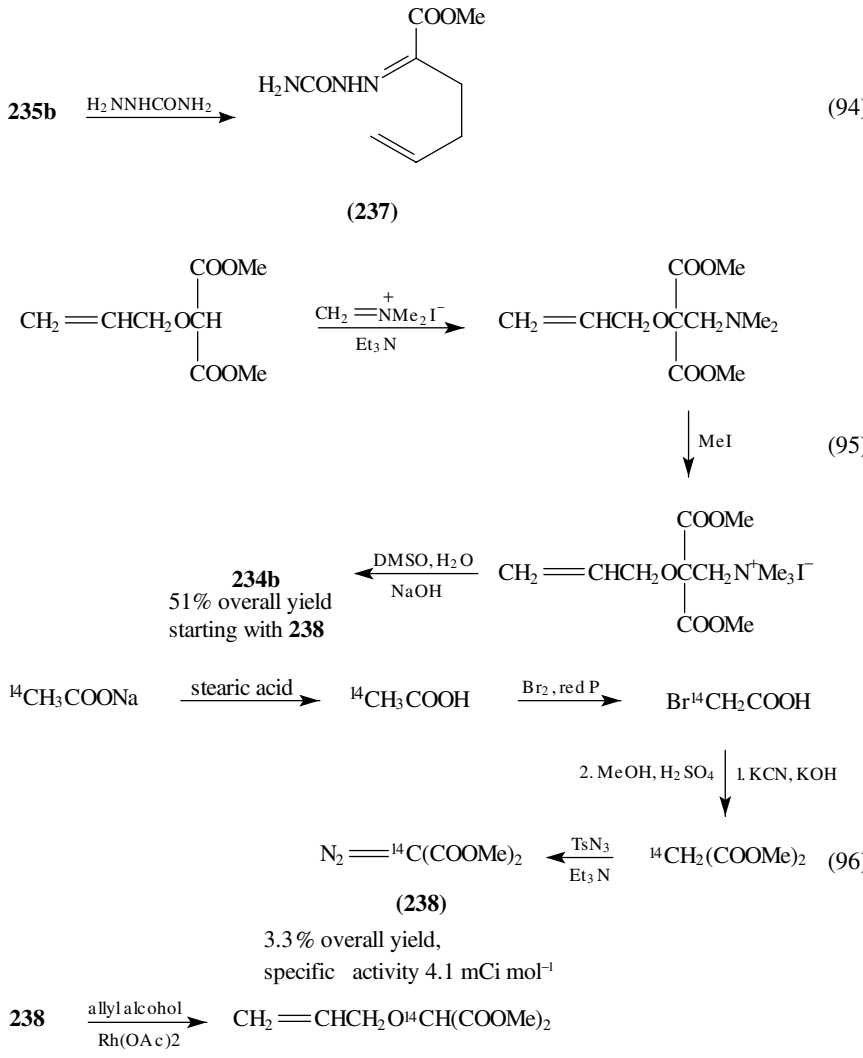
(234a) R = $OSiMe_3$ **(235a)**
(234b) R = COOMe **(235b)**



(93)

(236)

The [1-^{14}C] **234b**, [2-^{14}C] **234b**, [4-^{14}C] **234b** and [6-^{14}C] **234b** (with specific activities in the range 4–8 mCi mmol^{-1}) have been prepared[224] in the reaction sequence shown in equation 95 using [^{14}C] Eschenmoser's salt labelled in the methylene group[227], dimethyl [2-^{14}C]diazomalonate (equation 96), [1-^{14}C] allyl alcohol[213] and [3-^{14}C] allyl alcohol[213].



The average ^{14}C KIEs for the rearrangement of **234a** to 1-(trimethylsiloxy)-4-pentenal **235a** in THF at 22 °C are:

$$1.0164 \pm 0.0013 \text{ for } [1-{}^{14}C]\mathbf{234a},$$

$$1.0240 \pm 0.0021 \text{ for } [2-{}^{14}C]\mathbf{234a},$$

$$1.1048 \pm 0.0022 \text{ for } [4-{}^{14}C]\mathbf{234a},$$

$$1.0174 \pm 0.0010 \text{ for } [6-{}^{14}C]\mathbf{234a}.$$

(The values 1.1122 ± 0.0045 and 1.0919 ± 0.0031 are the maximum and minimum values of ^{14}C KIE in the series of independent runs aimed at the determination of [4-^{14}C] KIE.)

The deuterium SKIE in the rearrangement of [4,4-D_2]- and [6,6-D_2] **234a**, determined previously[225,226], are 1.48 and 0.917, respectively.

The ^{14}C KIE for the rearrangement of **234b** to methyl 2-oxo-5-hexenoate, **235b**, in CCl_4 at 80 °C, deduced from the scintillation counting data on the semicarbazone **237**, are:

$$\text{Av. } 1.0280 \pm 0.0011 \text{ for } [1-{}^{14}\text{C}]\mathbf{234b},$$

$$1.0087 \pm 0.0009 \text{ for } [2-{}^{14}\text{C}]\mathbf{234b},$$

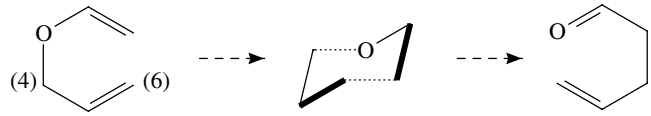
$$1.0330 \pm 0.0015 \text{ for } [4-{}^{14}\text{C}]\mathbf{234b},$$

$$1.0118 \pm 0.0008 \text{ for } [6-{}^{14}\text{C}]\mathbf{234b}.$$

The degrees of partial conversions of **234b** to **235b** were in the range 0.23–0.29. The secondary deuterium KIE in the rearrangement of [4,4-D_2]**234b** and [6,6-D_2]**234b** are 1.12 and 0.91, respectively.

All the ^{14}C primary KIE data above and the $C_{(4)}$ and $C_{(6)}$ secondary deuterium KIEs have been fitted to BEBOVIB modeling calculations and it has been deduced that, in the transition state of the reaction of **234a**, 70–80% bond breaking and 20% bond making occurs, while for **234b** both bond breaking and bond formation amount to 30–40%.

c. Secondary deuterium KIEs at the $C_{(4)}$ and $C_{(6)}$ of the allyl vinyl ether Claisen rearrangement, proceeding via a chair-like transition state[228] (equation 97), have been determined recently[229] in the relatively non-polar *m*-xylene, and in 75% and 25% CD_3OD in D_2O at 100 °C. The $k_{(H)}/k_{(D_2)}$ values were found to be:



(97)

(239)

1.119(0.019 S.D.) for (4 − D_2)**239** in *m*-xylene
0.953(0.015) for (6 − D_2)**239**

1.059(0.007) for (4 − D_2)**239** in 75% CD_3OD:25%D_2O
0.981(0.018) for (6 − D_2)**239**

1.145(0.04) for (4 − D_2)**239** in 25% CD_3OD:75%D_2O
0.958(0.04) for (6 − D_2)**239**

In the gas phase[230] the (k_H/k_{D_2}) SKIE are 1.092(0.005) for (4-D_2) **239** and 0.98(0.005) for (6-D_2) **239** at 160.3 °C.

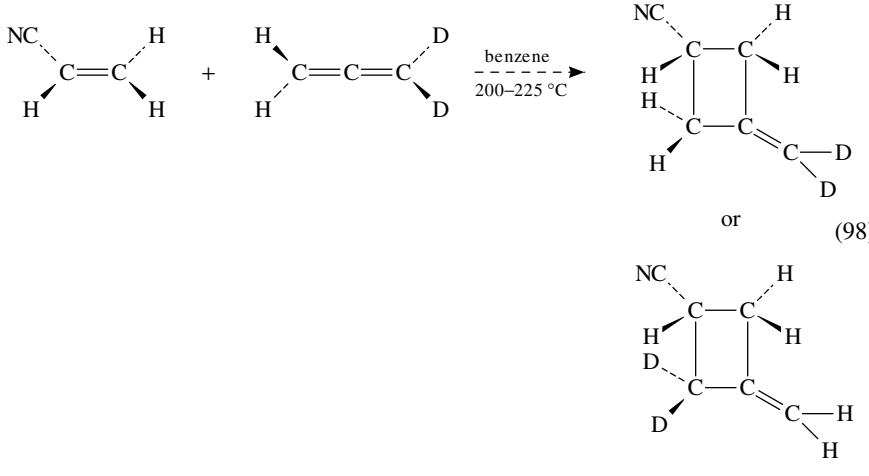
The above SKIE data were taken as evidence against an ionic transition state. Allylic cation-like species would result in much larger normal SKIE at $C_{(4)}$ in a polar medium than in non-polar media by approaching the maximum possible value for conversion of an sp^3 $C_{(4)}$ of the ether to an sp^2 carbon of an allyl cation.

Final remarks. The ^{14}C-KIE and ^{2}H-SKIE data presented in this Section (VI.B) clearly indicate the usefulness of isotope effect methodology in studies of mechanistic details of thermally induced Claisen rearrangement, which provides a synthetic route to γ,δ-unsaturated carbonyl compounds. The primary and secondary ^{14}C KIE supplement strongly the deuterium SKIE. Especially easy for interpretation are ^{14}C and ^{2}H isotope

effects at $C_{(4)}$ and at $C_{(6)}$ (as well as at $C_{(1)}$). They show directly the degrees of $C_{(4)}-O$ bond clearge and $C_{(6)}-C_{(1)}$ bond formation in the 'TS'. Unfortunately, the investigation of the effect of substituents at $C_{(2)}$ is obscured by the lack of the temperature dependencies of the determined ^{14}C and ^{2}H isotope effects. The different isotopic studies are carried out at different single temperatures (at 22 °C, at 80 °C and at 160 °C, respectively) depending on the nature of the substituent at $C_{(2)}$. The value of 1.0720 obtained at 160 °C in the rearrangement of unsubstituted [4-^{14}C]**232** is smaller than the primary ^{14}C KIE of 1.1048 at 22 °C in the rearrangement of [4-^{14}C]-2-(trimethylsiloxy)-3-oxa-1,5-hexadiene, **234a**, chiefly because of the higher reaction temperature in the former case. The ^{14}C KIE in the last case is very close to the ^{14}C KIE expected for the complete rupture of the $^{12}C-^{16}O/^{14}C-^{16}O$ bond pair. The values of the $^{14}C_{(6)}$ KIE equal 1.0178 ± 0.0005 and 1.0174 ± 0.0010 in the rearrangements of **232** and **234a**, both labelled at $C_{(6)}$, respectively. Substituent and 'temperature independent' effects within the experimental error, indicate that the $C_{(6)}-C_{(1)}$ bond is not completely formed in the 'TS' corresponding to the transformation of sp^2 hybridization to sp^3 hybridization at $C_{(6)}$ and at $C_{(1)}$. A negligible $^{14}C_{(6)}$ KIE is expected in the complete transformation of one C=C bond into two C−C single bonds (neglecting the effects of $^{14}C-^{1}H$ changes during the hybridization changes). The ^{14}C KIEs in the Claisen rearrangement were investigated much more computationally than experimentally. Particularly, the dependence of the $^{14}C_{(4)}$ KIE values on the degrees of conversion of **234b** at different reaction temperatures has not been studied.

C. Brief Outline of Isotopic Studies with Unsaturated Compounds

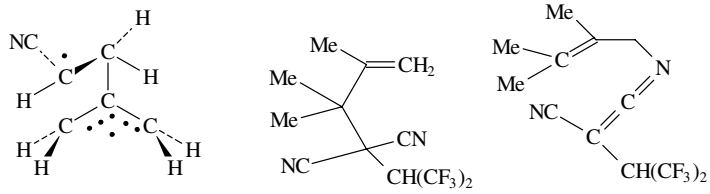
The intramolecular and intermolecular deuterium isotope effects in the cycloaddition of acrylonitrile to allene (equation 98) have been studied by Dolbier and Dai[231,232]. The intramolecular KIEs in the allene–acrylonitrile system were found to be 1.21 ± 0.02 at 206 °C and 1.14 ± 0.02 at 225 °C. A negligible intermolecular SKIE was found in the reaction of the mixture of tetradeuteriated and undeuteriated allene using a limited amount of acrylonitrile; $(k_H/k_D) = 1.04 \pm 0.05$ at 190–210 °C for D_0/D_4 allene. An 'equilibrium deuterium IE' of 0.92 ± 0.01 was found at 280–287± 5 °C (15–45 h reaction time).



(98)

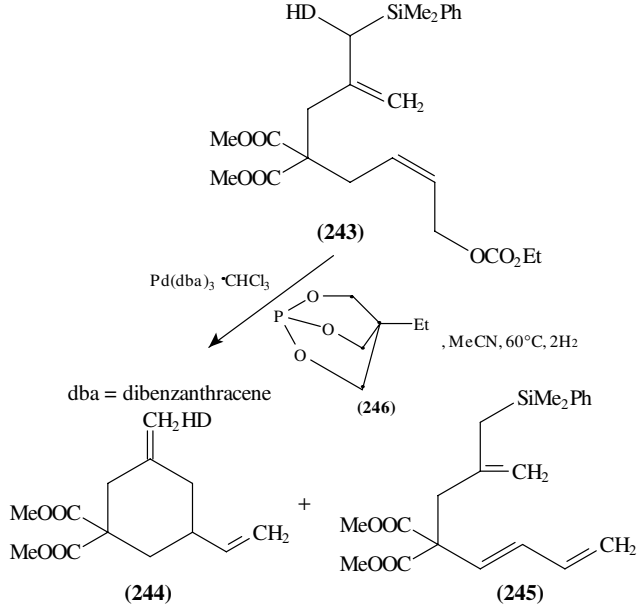
It has been suggested that the reaction in equation 98 proceeds through the biradical intermediate **240**. The 15–20% preference for incorporation of deuterium in the exocyclic

methylene group of vinylcyclobutane has been reproduced theoretically by Halevi and Wolfsberg[233]. The value $k_{exo}/k_{endo} = 1.166$ has been computed using the AM1 Hamiltonian with limited CI. The normal SKIE, $(k_H/k_D) > 1$, was ascribed[232] to slower rotation of the deuteriated methylene group before ring closure from the planar configuration toward the orthogonal geometry which is necessary for σ bond formation. No ^{14}C KIEs have been studied in reaction 98. In the reaction of 1,1-dideuterioallene with hexachlorocyclopentadiene, the intramolecular k_H/k_D values are 0.89 ± 0.01 at 150 °C and 0.92 ± 0.01 at 135 ± 1 °C. The intermolecular KIE is 0.88–0.93±0.04 at 135 °C[231].



'TS' (**240**) (**241**) (**242**)

The deuterium labelling established[234] that the γ,δ-unsaturated, nitrile **241** equilibrates at room temperature with the *N*-allylketene imine **242** through an intramolecular rearrangement mechanism. Deuterium has been applied in the study of the novel palladium(0)-catalysed cyclization of 2,7-octadienyl carbonate containing an allylsilane moiety, **243**, to product **244** (in 89%) and some **245** in the presence of phosphite **246** (equation 99)[235]. Intramolecular KIEs ($k_H/k_D = 3.0$ and 3.5) have been observed in a bicyclic olefin formation (monoterpinene biosynthesis from [1-^{3}H,4-^{2}H$_2$]- and [10-^{2}H$_2$]-geranyl pyrophosphates) catalysed by pinene synthases from sage (*Salvia officinalis*)[236].



(**243**)

(**246**)

dba = dibenzanthracene

(**244**) (**245**)

(99)

70% combined (10:1) yield of (**244**)-D, 28% recovery of **243-D**, D atom resided completely on methylene carbon of (**244**)-**D**.

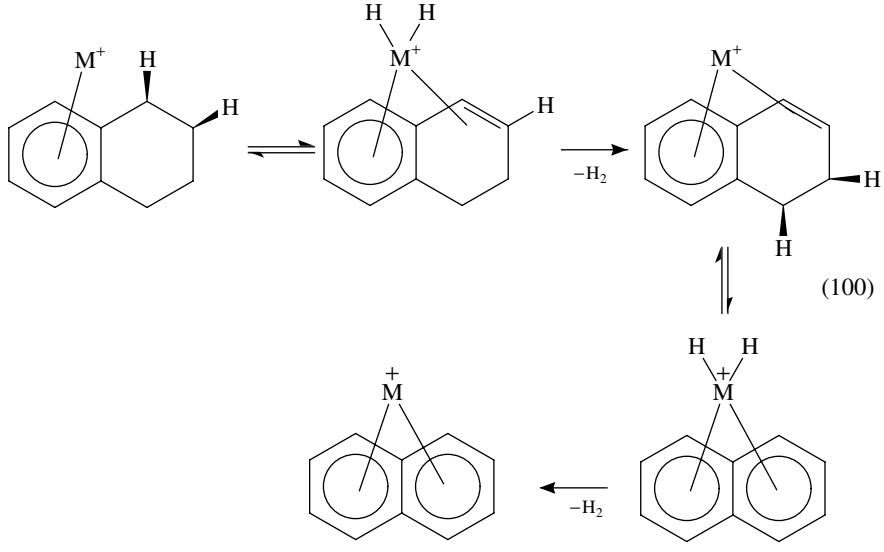
β-Deuterium secondary isotope effects in an olefinic cationic polycyclization have been reviewed by Borcic and coworkers[237].

A tritium isotope effect in high-performance liquid chromatography of 11 eicosanoids has been observed. Multi-tritium-labelled eicosanoids were eluted earlier than the corresponding unlabelled eicosanoid. Variations in retention time are 3–7%, depending on the separation conditions as well as on the number and position of the tritium substituents[238].

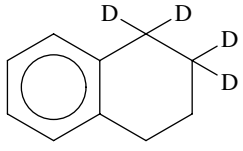
A deuterium kinetic isotope effect of 2 has been found in the hydrogenation of 1,3-pentadiene[239] using a Ziegler–Natta catalyst, cobalt(II,III) μ^3-oxostearate-$AlEt_3$, $Co_2^{III} \cdot Co^{II}O(C_{17}H_{35}CO_2)_6(H_2O)_3 \cdot 5H_2O$–$AlCl_3$. The reaction was found to be of a kinetic order of 0.3 in the diene, and first order in the hydrogen and the catalyst. The kinetics and the selectivity of the reaction has been studied at 253–293 K.

A very large deuterium isotope effect has been observed[240] by ESR at 77 K on hydrogen–deuterium elimination reaction from 2,3-dimethylbutane (H-DMB)-SF_6 and 2,3-dimethylbutane-2,3-D_2 (D-DMB)-SF_6 (0.6 mol% mixtures), γ-irradiated at 70 K and then stored at 77 K. The significant isotope effect, $k_{H_2}/k_{D_2} = 1.69 \times 10^4$ at 77 K, has been explained by tunnelling elimination of hydrogen (H_2) molecules from a DMB^+ ion[240].

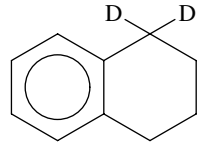
Labelling experiments provided the evidence that the Fe^I- and Co^I-mediated losses of H_2 and $2H_2$ from tetralin are extremely specific. Both reactions follow a clear *syn*-1,2-elimination involving $C_{(1)}/C_{(2)}$ and $C_{(3)}/C_{(4)}$, respectively. In the course of the multistep reaction the metal ions do not move from one side of the π-surface to the other. The kinetic isotope effect associated with the loss of the first H_2 molecule, $k(H_2)/k(D_2) = 3.4 \pm 0.2$, is larger than the KIE, $k(H_2)/k(HD) = 1.5 \pm 0.2$, for the elimination of the second H_2 molecule. A mechanism of interaction of the metal ion with the hydrocarbon π-surface, ending with arene-M^+ complex **246** formation in the final step of the reaction, outlined in equation 100, has been proposed[241] to rationalize the tandem MS studies of the unimolecular single and double dehydrogenation by Fe^+ and Co^+ complexes of tetraline and its isotopomers **247–251**.



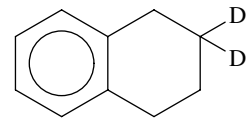
(246)



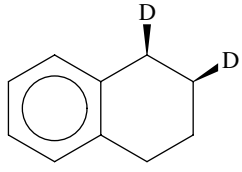
(247)



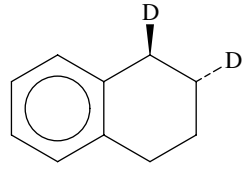
(248)



(249)



(250)



(251)

VII. ACKNOWLEDGEMENTS

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CHAPTER **19**

Allenyl and polyenyl cations

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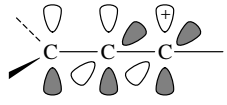
I. INTRODUCTION

Allenyl cations **1** are a stabilized form of vinyl cations[1−3] in which the β-carbon atom of the vinylic structure is part of the substituent which effects the stabilization of the ion via its electron-donating ability. This leads to a resonance hybrid having formally the alkynyl cation structure **2**. Allenyl cations should be distinguished from the allenyl substituted carbenium ions **3** formulated as the mesomeric structures of the vinyl cations **4** (dienyl cations) stabilized by an α-vinyl group (equation 1).

(1) **(2)**

(3) **(4)** (1)

Similar to the allyl cation[4] the stabilization in the allenyl cation **1** occurs by overlap of the incipient vacant p orbital with the allenyl π-system as shown in **5**. The allylic π-orbitals are geometrically constrained to the most favored geometry for overlap with the p orbital due to the orthogonality of the two double bonds and the conjugation is not accompanied by any loss of ground state conjugation.



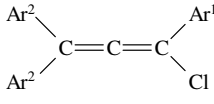
(5)

Allenyl cations have been generated by solvolysis of allenic derivatives, by photolysis of allenyl halides and by reaction of metal salts with allenyl and propargyl halides. This review will delineate these reactions. The related butatrienyl cations are not many and they will be only briefly described.

II. ALLENYL CATIONS

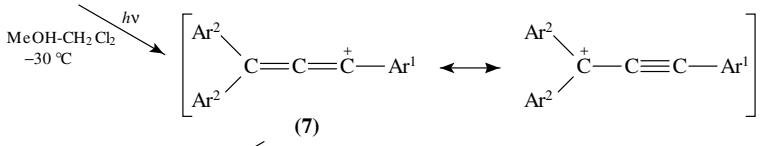
A. Generation by Photolysis

Photolysis of the carbon–halogen bond to give carbenium ions[5,6] has been extended to the formation of vinyl cations by Taniguchi, Kobayashi and coworkers[7]. In this context several chlorotriarylallenes **6** were photolyzed in a mixed solvent system of methanol and dichloromethane[8]. The photolysis was carried out at $-30\,^{\circ}C$ to prevent a thermal solvolysis of the substrate. The major product of the reaction is the 1,3,3-triaryl-3-methoxypropyne **8** with a small amount of the reduced compounds **9** and/or **9′** as the side product. Photolysis of **6** ($Ar^1 = Ar^2 = Ph$) in ethanol and 2-propanol gave the corresponding 3-alkoxy-1,3,3-triphenylpropynes (**8a**-OEt and **8a**-OPr-*i*) in 33 and 37% yields, respectively, together with a small amount of the reduced product **9′** ($Ar^2 = Ar^1 = Ph$)[8].



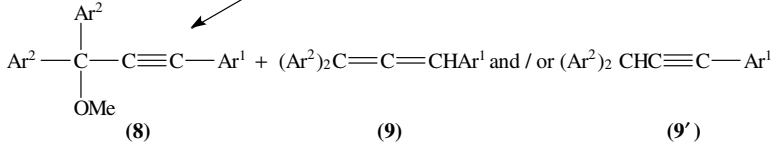
(6)

(a) $Ar^1 = Ar^2 = Ph$
(b) $Ar^1 = Ph$, $Ar^2 = 4\text{-}MeC_6H_4$
(c) $Ar^1 = 4\text{-}MeOC_6H_4$, $Ar^2 = Ph$



(7)

(2)



(8) **(9)** **(9′)**

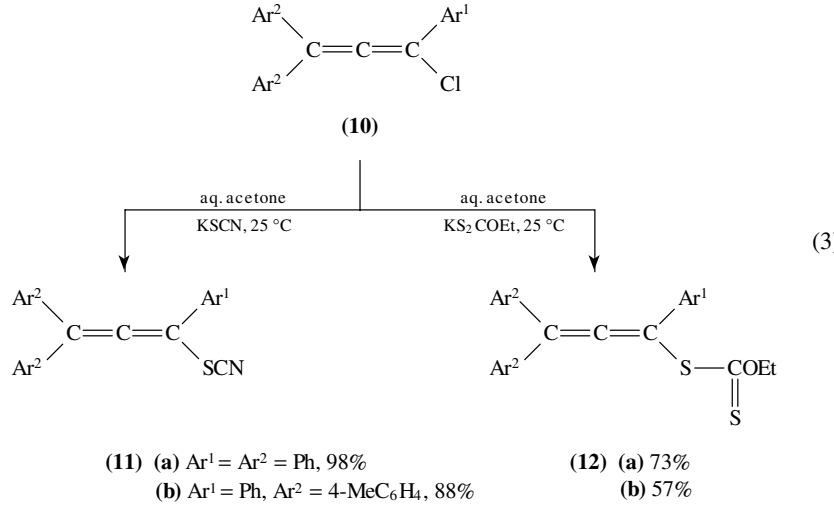
(a) 47% **(a)** 7%
(b) 51% **(b)** trace
(c) 76% **(c)** trace

The formation of solvent-incorporated products **8** suggested that triarylallenyl cations **7** are formed by photolysis of the corresponding chloroallenes **6** (equation 2). However, the products **8** obtained by photolysis were attributed to attack by nucleophiles at γ-positions of the allenyl cation. Although allenyl cations are ambident cations and can produce allenyl or propargyl derivatives by attack at the α- or γ-position, respectively, only γ-attack was observed in this photolysis of triarylchloroallenes. This result is parallel to that observed by Schiavelli and coworkers[9] in the solvolysis of these systems (*vide infra*) which therefore supports the formation of allenyl cations in the photolysis.

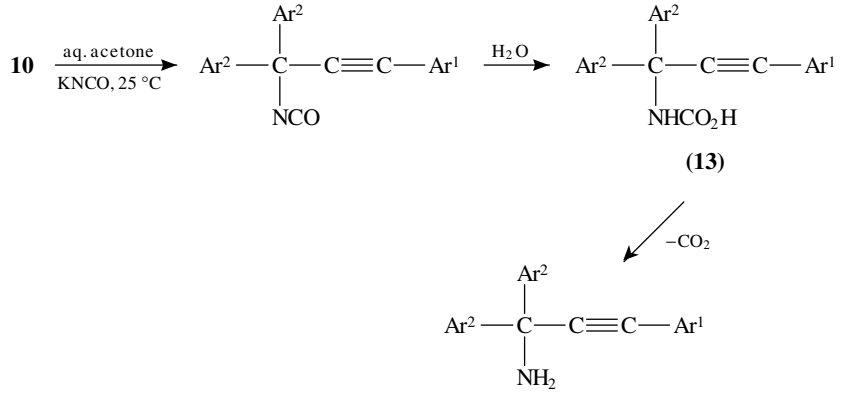
B. Generation by Solvolysis

The intermediacy of allenyl cations in the solvolysis of allenic derivatives was first shown by Jacobs and Fenton[10]. However, the main work on the mechanism of the reaction is that of Schiavelli and coworkers[11–17], who showed with the aid of kinetics and substituent, solvent, salt and isotope effects that the reactions proceed via an initial cleavage of the bond to the leaving group with the formation of the allenyl cations **1**. Chlorotriarylallenes have been shown to solvolyze with convenient rates and even a primary allenyl cation was generated solvolytically. Extensive coverage of earlier work on the solvolytic behavior of allenyl systems are given elsewhere[1b–d]. One of the most interesting features is the ambident character of allenyl cations, which can provide, on reaction with a nucleophile, the allenyl and/or propargyl derivatives. However, most work on solvolysis of allenyl halides indicates that nucleophiles attack at the γ-position of the resulting allenyl cations, unless bulky substituents are present on the γ-position[12].

Recently, the solvolyses of 1-chloro-1,3,3-triarylallenes **10** (and of 1-butyl-3,3-diphenylallenyl chloride) were carried out in the presence of thiocyanate and *o*-ethyl dithiocarbonate anions as nucleophiles and found to give the corresponding allenyl derivatives **11** and **12** in good yield (equation 3)[18]. However, when potassium cyanate was used as a nucleophile, the cyanate ion attacked at the γ-position to give the propargyl amines **14** after decarboxylation of the unstable intermediate **13** (equation 4).



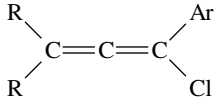
(3)



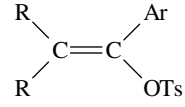
(14) **(a)** $Ar^1 = Ar^2 = Ph$, 45%
(b) $Ar^1 = Ph$, $Ar^2 = 4\text{-}MeC_6H_4$, 68%

These results indicate that the reaction outcome can be controlled by the choice of nucleophile. From the kinetic[12] and theoretical[19] (*vide infra*) studies, it is predicted that nucleophiles react at the propargyl position of the allenyl cation. However, when the γ-position bears a sterically hindered substituent, a nucleophile should attack on the allenyl position[13]. Such a steric factor may be also operative for a bulky nucleophile. Among the nucleophiles used, thiocyanate and *o*-ethyl dithiocarbonate anions are larger than cyanate anion because sulfur atom has a much larger van der Waals radius than that of nitrogen or oxygen atom[20]. The larger nucleophile prefers to attack the less sterically congested allenyl position, while the smaller nucleophile prefers the propargyl position, which is more reactive than the allenyl position[12,19].

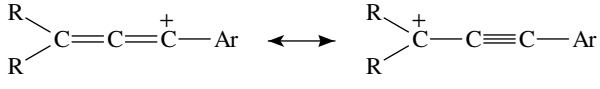
The kinetic studies on the solvolysis of 1-aryl-1-chloro-3-methylbuta-1,2-dienes (**15**, Ar = Ph, *p*-$MeOC_6H_4$) showed that the ρ values ($\rho^+ = -2.8$ in 80% aqueous ethanol and -2.9 in aqueous acetone)[21] are much lower than those of the correspondingly substituted vinyl derivative **16** ($\rho^+ = -4.3$ in aqueous ethanol)[22]. This result indicates that the α-substituent effect in cations **17a** is much smaller than in the vinyl cations, suggesting



(15) **(a)** Ar = Ph
(b) Ar = *p*–$MeOC_6H_4$



(16)

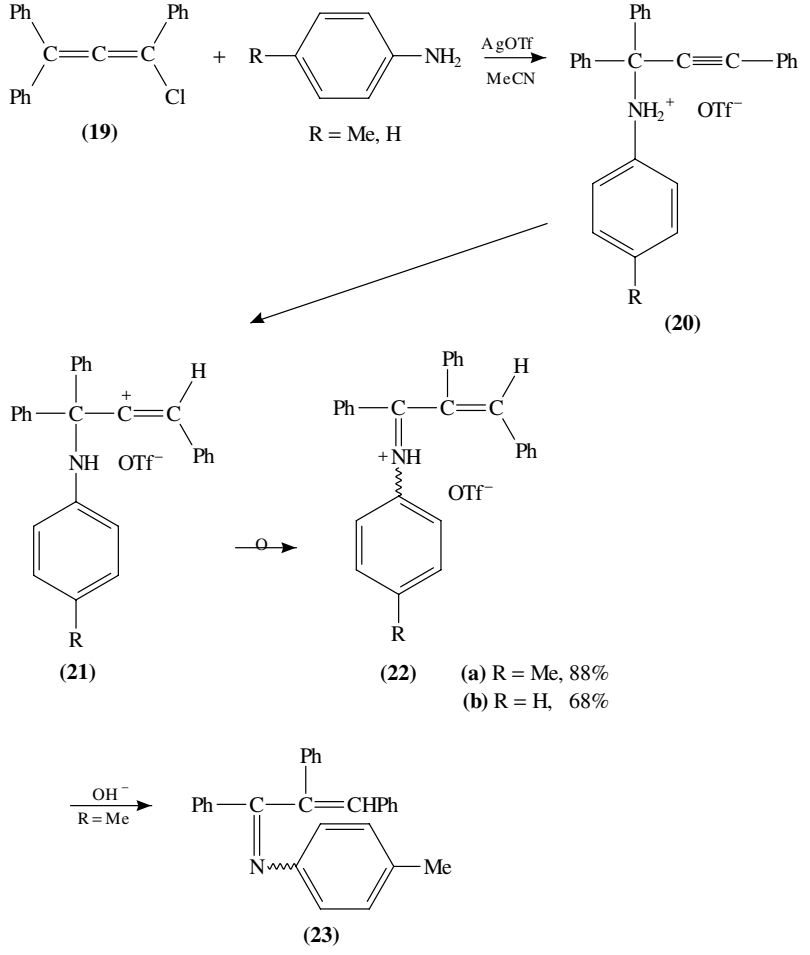


(17)
(a) R = Me
(b) R = Ph

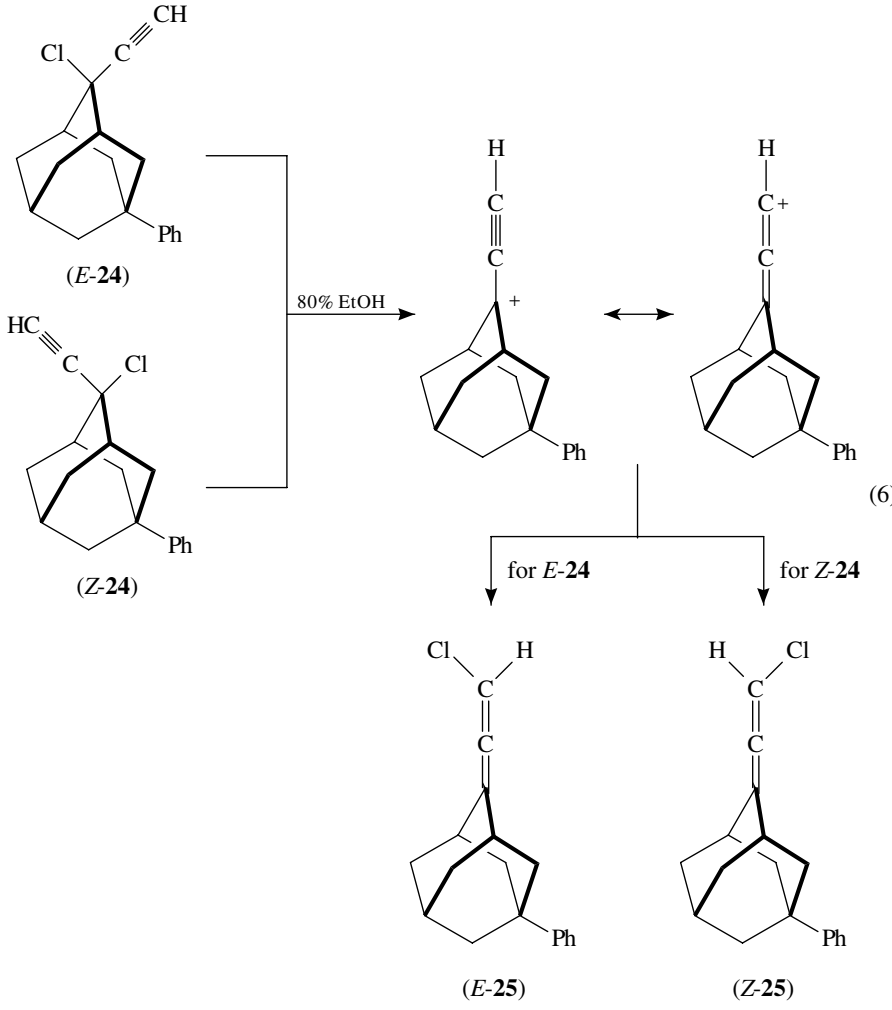
(18)
(a) R = Me
(b) R = Ph

that the contribution of the propargyl structure **18a** in the transition state is important. Furthermore, from these values and comparison of the *m* values (0.88 in aqueous EtOH) for the chloroallene **15a** and the ρ values of the 1-chloro-1,3,3-triarylallenes **10** ($\rho^+ = -2.0$ in aqueous acetone)[10], it was concluded that in the 1-aryl-3,3-dimethyl-substituted allenyl derivative **15** (R = Me) the contribution of the propargyl structure **18a** is greater in the transition state in comparison with the allenyl structure **17a**.

Reaction of 1-chloro-1,3,3-triphenylallene (**19**) with *p*-toluidine in the presence of silver triflate gave 2,3,4-triphenylbuta-1-aza-1,3-diene derivative **22a** via a novel 1,2-phenyl shift not reported earlier in the solvolysis of allenyl chlorides[23]. The reaction takes place via the formation of the allenyl cation, which is captured as its canonical propargyl cation, first affording the protonated amine **20** (R = Me). Proton transfer[24] from the nitrogen to the acetylenic carbon is followed by migration of a phenyl group in the intermediate vinyl cation **21** (R = Me) to afford the iminium triflate **22a**. The latter is hydrolyzed by aqueous sodium hydroxide to the azabutadiene **23** (equation 5). Similar reaction of **19** with aniline and silver triflate afforded the corresponding iminium triflate **22b**[23].



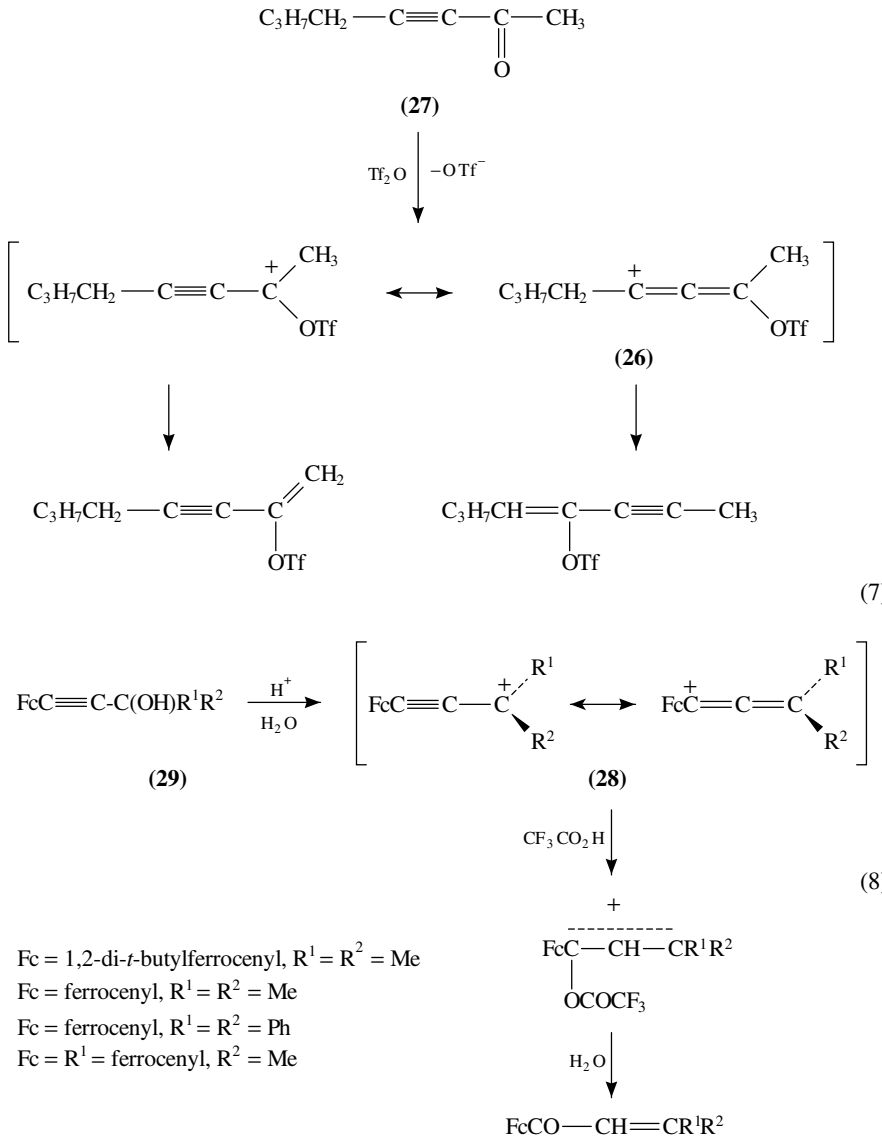
Solvolysis of the propargyl chlorides *E*- and *Z*-**24** (stereochemistry based on Cl and Ph[25]) in 80% aqueous ethanol at 50 °C gave, besides the corresponding solvent captured substituted propargyl products, the allenyl chlorides *E*- and *Z*-**25** formed with complete retention via the allenyl cation intermediate (equation 6)[25].



(6)

Intermediate allenyl cation **26** has been implied in the reaction of oct-3-yn-2-one (**27**) with trifluoromethanesulfonic anhydride, which forms vinyl triflates (equation 7)[26].

Ferrocenyl-substituted allenyl cations **28** were generated when 1,3-diferrocenyl-substituted secondary and ferrocenyl-substituted tertiary alcohols **29** were treated with trifluoroacetic acid[27]. These were rapidly converted into trifluoroacetoxyallylic ions by solvent addition; the ions gave ferrocenyl-substituted enones by reaction with water (equation 8).



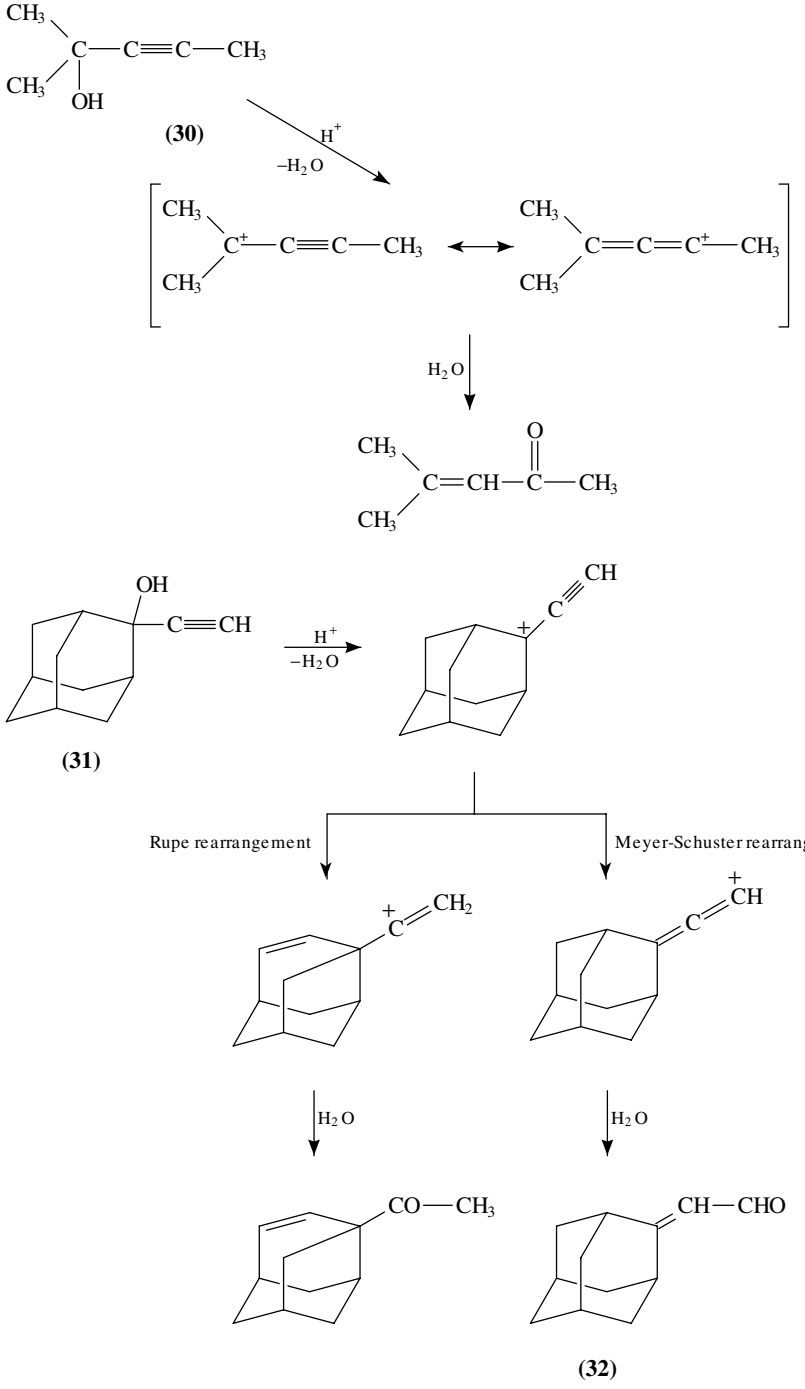
(7)

(8)

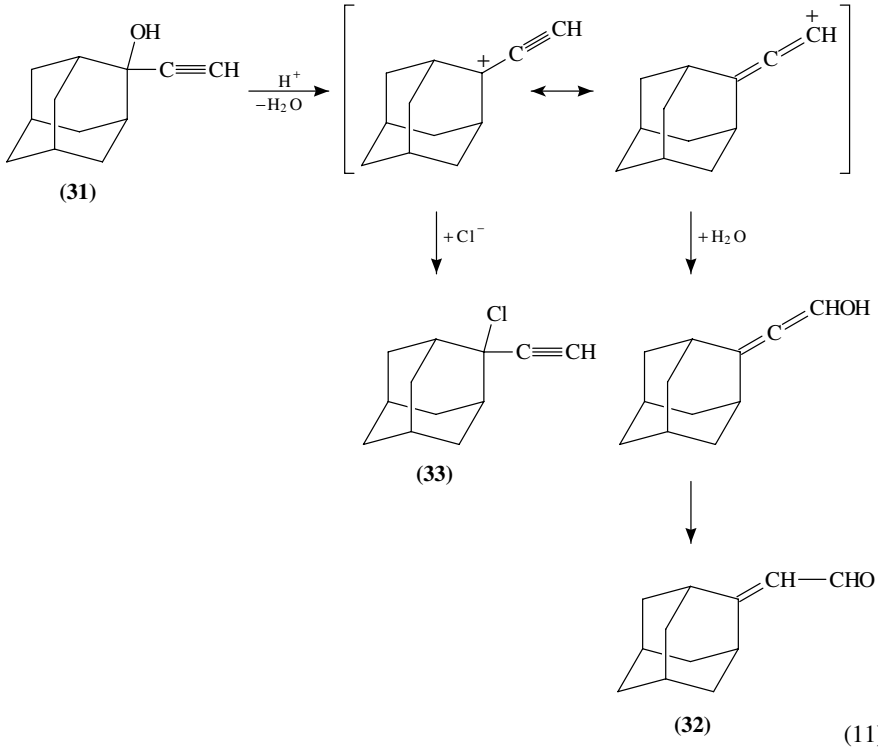
Fc = 1,2-di-*t*-butylferrocenyl, $R^1 = R^2 = Me$
Fc = ferrocenyl, $R^1 = R^2 = Me$
Fc = ferrocenyl, $R^1 = R^2 = Ph$
Fc = R^1 = ferrocenyl, $R^2 = Me$

The products from the acid-catalyzed hydration of α-tertiary alcohols **30** (Meyer–Schuster and Rupe rearrangements) are formed via the mesomeric propargyl-allenyl cation (equation 9) and have been extensively investigated[28].

When 2-ethynyl-2-hydroxyadamantane (**31**) was treated with 95% formic acid or dilute sulfuric acid only a Meyer–Schuster rearrangement took place to give 95% of 2-(formylmethylene)adamantane (**32**) (equation 10). No Rupe rearrangement took place[29].


(30)
H+
–H2O
H2O
(9)
(31)
Rupe rearrangement
Meyer-Schuster rearrangement
H2O
H2O
(10)
(32)

2-Chloro-2-ethynyladamantane (**33**) was the major product when **31** was reacted with concentrated hydrochloric acid. If 1,4-dioxane was used as the solvent, 82% of 2-(formylmethylene)adamantane (**32**) was obtained together with only 3% of the chloro product **33** (equation 11). It is remarkable that no reaction takes place even under reflux conditions with ethereal hydrogen chloride[29].

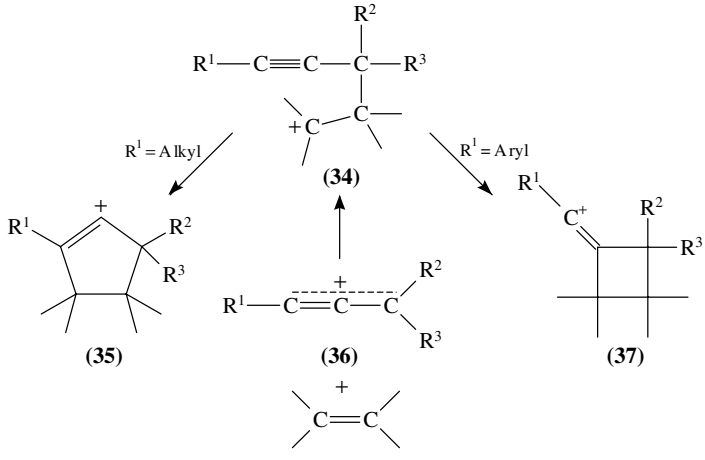


(11)

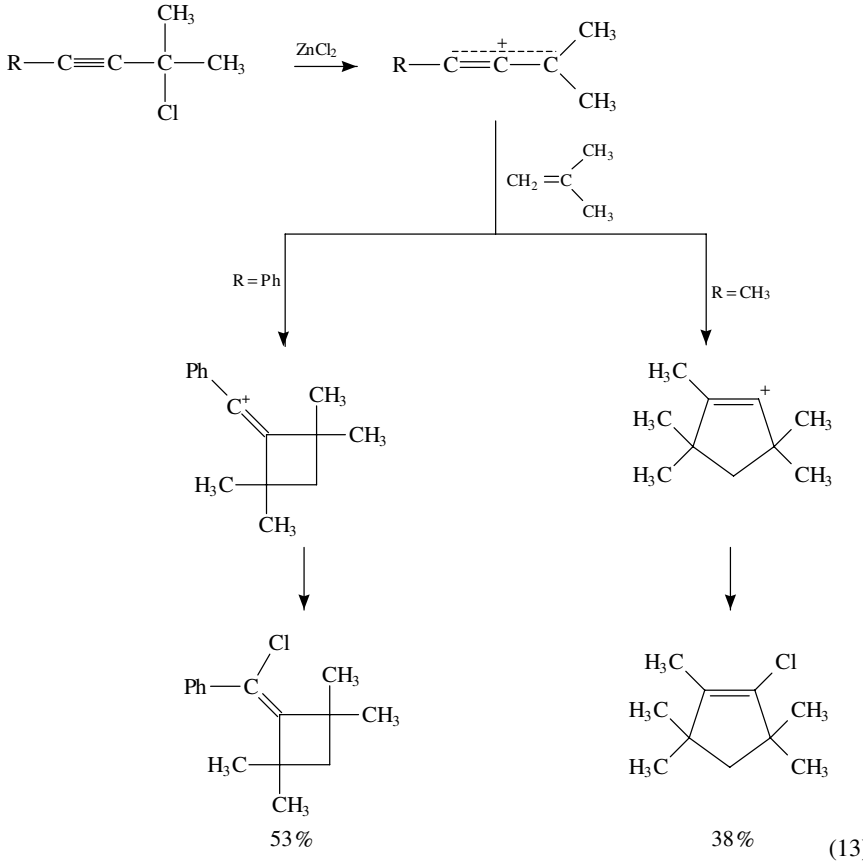
Similar to the cycloaddition of allyl cations[30], allenyl cations have been found to undergo cycloadditions with alkenes to afford bicyclic compounds[31]. The allenyl cations were generated from propargyl chlorides by treatment with Lewis acids. This reaction sequence proceeds via the cyclization **34** ⟶ **35**[32], in spite of the fact that 1-cyclopentenyl cations are highly unstable and are not formed during solvolysis of cyclopent-1-enyl triflates[33]. The reaction takes place by a stepwise cycloaddition of the intermediate allenyl cation **36** to an olefinic C=C bond proceeding via cation **34** to afford vinyl cation **37** (equation 12)[34].

The cycloaddition of allenyl cations with monoolefins lead to [2 + 2]- or [3 + 2]-cycloadducts based on the substituents in the allenyl cations as exemplified in equation 13[32].

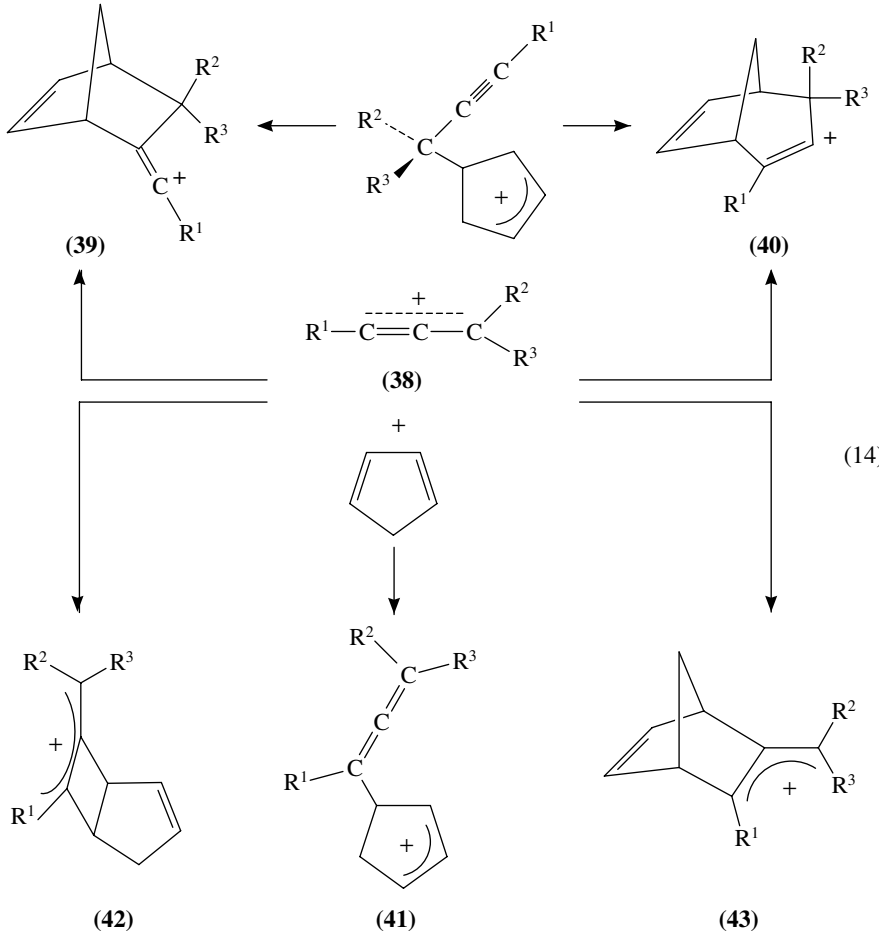
The cycloaddition of allenyl cations with 1,3-dienes results in a number of intermediate cations from which different products result. The allenyl cations **38** are generated first by the reaction of propargyl chlorides with zinc chloride and are then allowed to react with cyclopentadiene or other 1,3-dienes. The products of cycloaddition depend on the substituents on the allenyl cations[32,35]. The products formed with cyclopentadiene are given in equation 14.



(12)



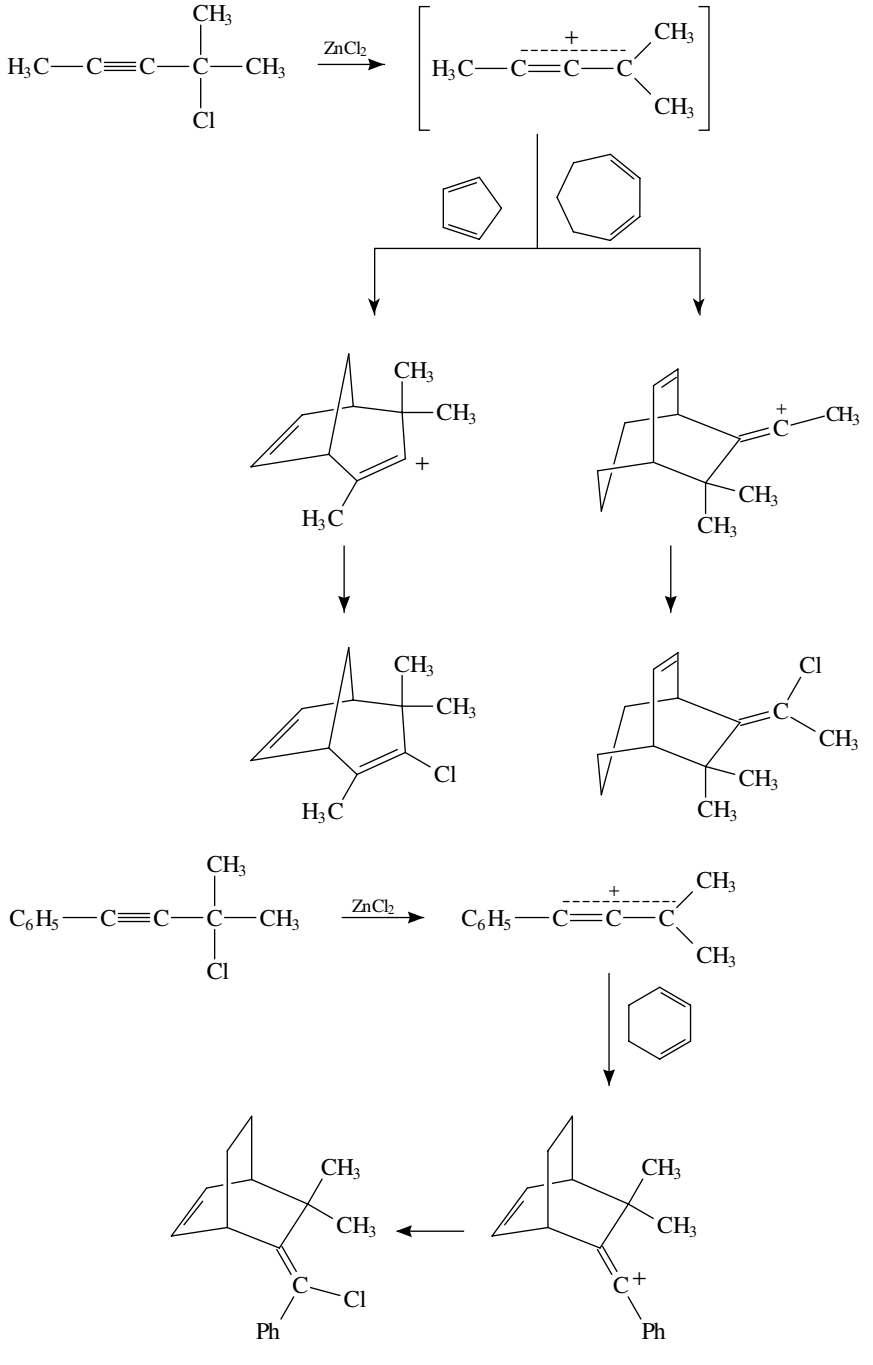
(13)



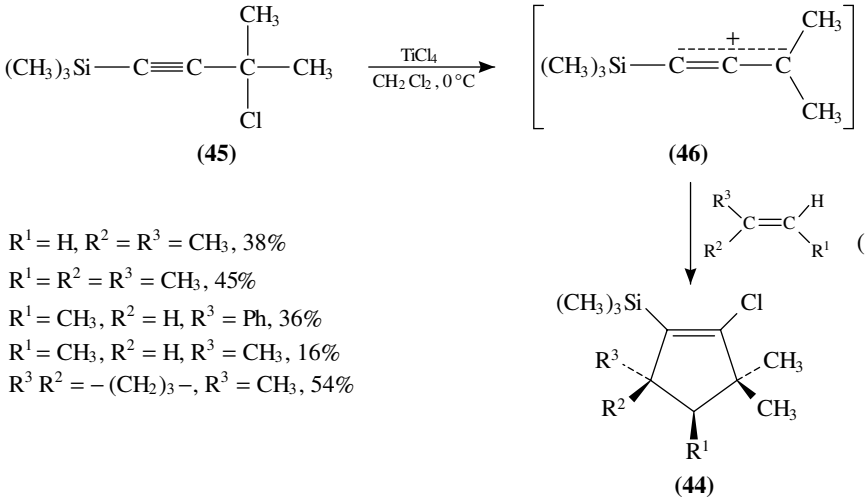
(14)

In general, allenyl cations **38** attack at the sp^2-carbon atom of 1,3-dienes and form vinyl cations **39** and **40** (R′ = H, alkyl) or (R′ = aryl). Although a concerted cycloaddition mechanism is possible, a stepwise mechanism is preferred[34]. If a nucleophilic attack at the sp-carbon atom of the allenyl cation takes place, then cation **41** and the resulting cations **42** and **43** are formed. Some examples of bicyclic products obtained from cyclic 1,3-dienes and propargyl chlorides are given in equation 15[34].

Highly alkylated 1-chloro-2-(trimethylsilyl)cyclopentenes **44**, which are of interest as possible cyclopentyne precursors, were prepared by reacting 3-chloro-3-methyl-1-(trimethylsilyl)but-1-yne (**45**) with 1,1-dialkylated or 1,1,2-trialkylated ethylenes in the presence of titanium tetrachloride[35]. Because of the low S_N1 reactivity of **45**, the yields of the products were moderate. The stepwise [3 + 2]-cycloaddition mechanism discussed above was proven by the isolation of the intermediate acyclic adduct (in 74% yield) when **45** and isobutene were reacted in the presence of BCl_3. Under these conditions, the intermediate **46** could be trapped by Cl^- since BCl_4^- is more nucleophilic than $TiCl_5^-$ (equation 16).



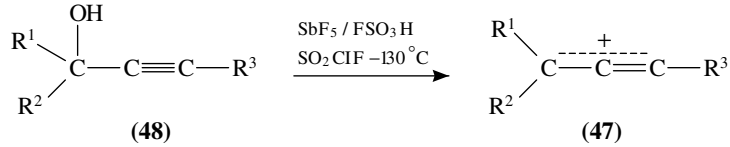
(15)



(16)

C. Spectroscopic Identification of Allenyl Cations

Substituted allenyl cations **47** have been generated from propargyl alcohols **48** under stable carbocation conditions (SbF_5/FSO_3H in SO_2ClF) (equation 17). On the basis of ^{13}C-NMR chemical shifts, the positive charge has been found to be extensively delocalized with the mesomeric allenyl cations contributing highly to the total ion structure[36,37].

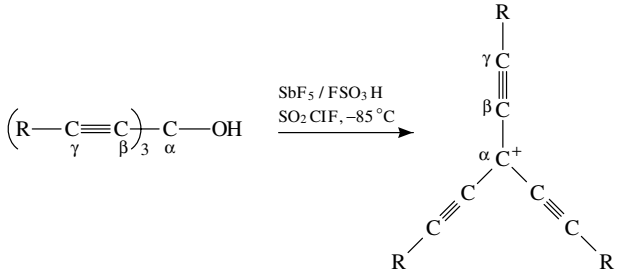


(a) $R^1 = R^2 = R^3 = CH_3$
(b) $R^1 = R^2 = Ph$, $R^3 = CH_3$
(c) $R^1 = R^2 = CH_3$, $R^3 = Ph$
(d) $R^1 = R^3 = Ph$, $R^2 = CH_3$
(e) $R^1 = R^2 = R^3 = Ph$

(17)

^{13}C-NMR spectroscopic studies on α-substituted tris(ethynyl)methyl cations **49** prepared from alcohols **50** (equation 18) provided evidence for the participation of resonance structures with allenyl cationic character[38]. The parent tris(ethenyl)methyl cation (**49**, R = H) cannot be generated under stable carbocation conditions (SbF_5/FSO_3H) presumably due to the highly reactive unsubstituted termini of the three ethynyl groups and the resulting low kinetic stability. The chemical shift data (Table 1) give evidence that in all cases C_α and C_γ are deshielded more than C_β (relative to their precursor alcohols).

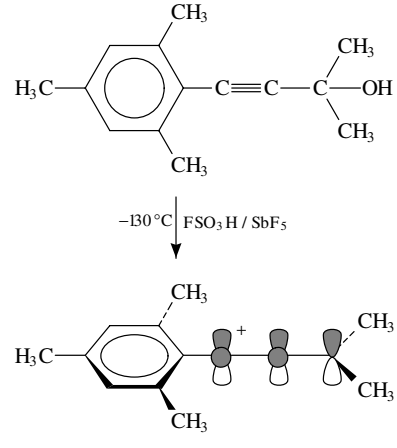
Recently, the ^{13}C-NMR spectrum of 1-mesityl-3,3-dimethylallenyl cation (**51**) generated from the propargyl alcohol was measured (equation 19)[39]. The cation exhibits strong shielding for the C^+-atom (192 ppm).



(18)

(50) **(49)**

(a) R = CH_3
(b) R = *t*-C_4H_9
(c) R = $Si(CH_3)_3$
(d) R = Ph
(e) R = H



(19)

(51)

TABLE 1. ^{13}C-NMR Chemical Shifts of Tris(ethynyl)methyl Cations (**49a–d**) and Their Precursor Alcohols **50a–d**[a]

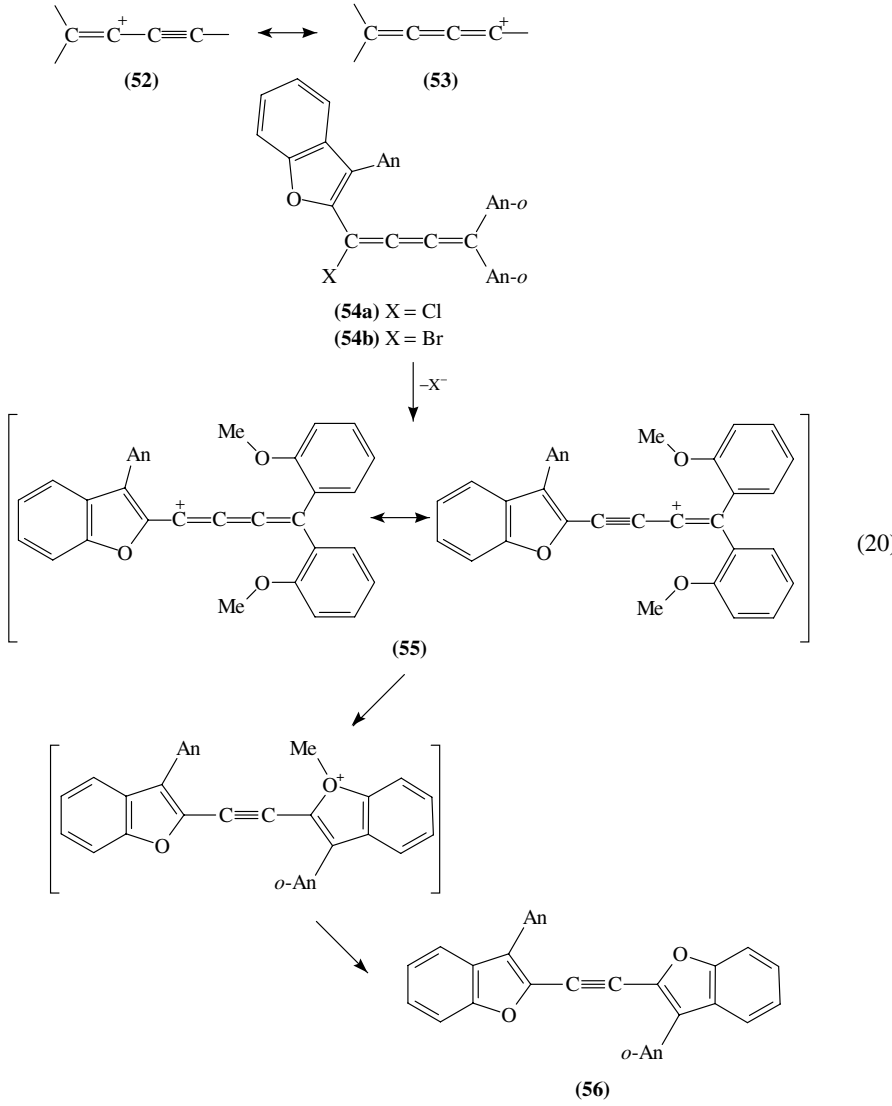
Compound	C_α	C_β	C_γ	Other carbons
49a	164.4	105.6	157.6	9.2
49b	162.6	105.3	164.1	33.1, 27.6
49c	166.3	101.3	144.9	−2.2
49d	140.7	110.5	137.9	118.9, 130.0 137.2, 137.5
50a	54.0	77.9	78.8	3.4
50b	54.5	78.2	90.4	27.2, 30.3
50c	54.7	88.1	101.6	−0.8
50d	55.6	83.1	86.6	121.5, 128.2 129.0, 132.0

[a]In ppm, referenced to TMS. The spectra of cations **49a–d** were measured in SO_2ClF at −60 °C using $(CD_3)_2C{=}O$ (29.8 ppm) in a coaxial capillary tube. The spectra of the precursors were recorded in $CDCl_3$.

III. BUTATRIENYL CATIONS

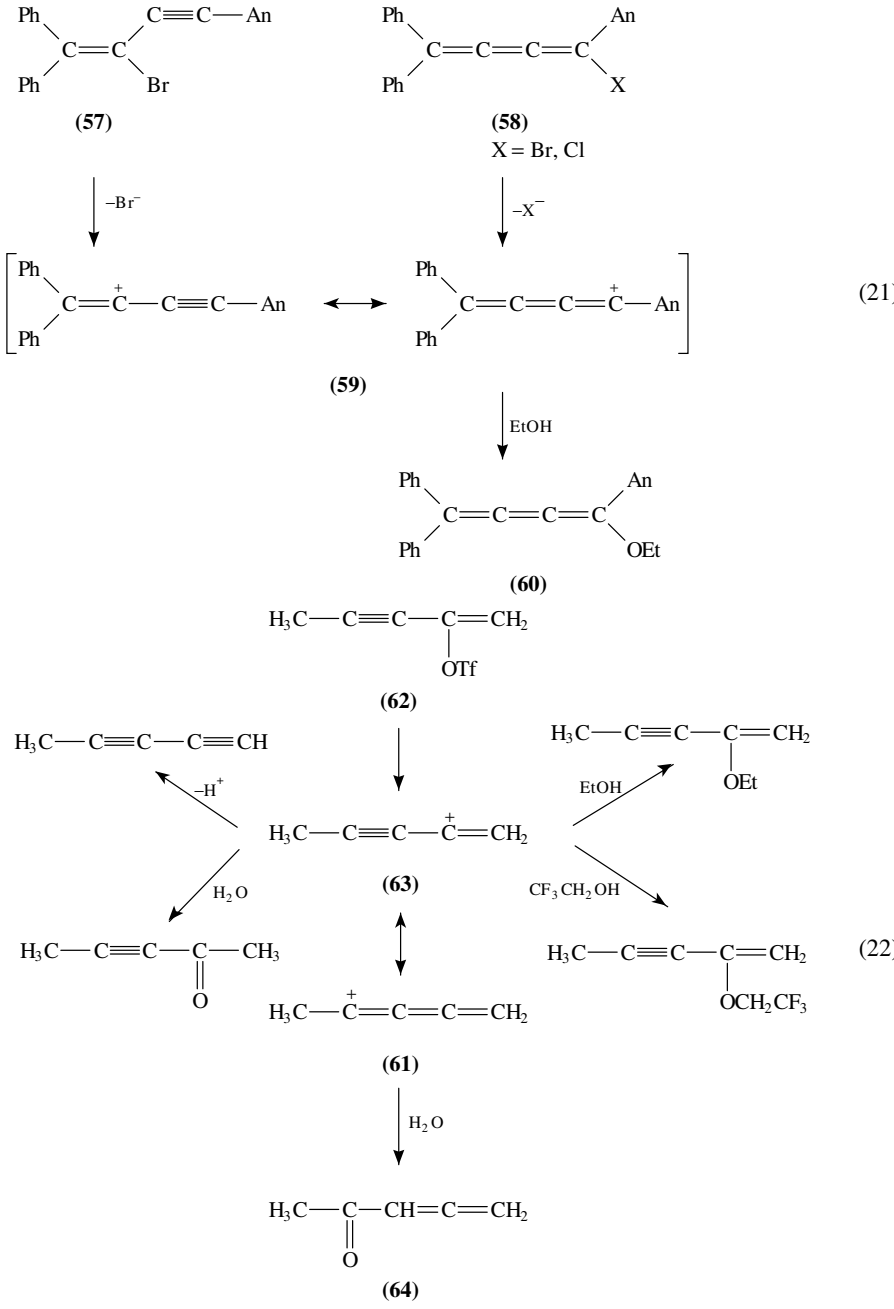
The homologue of allenyl cation, butatrienyl cation **53** is the mesomeric form of α-ethynyl stabilized vinyl cation **52**. Such a species was generated for the first time by Kobayashi, Sonoda and Taniguchi in 1977[40], by the solvolysis of the butatrienyl halides **54a** and **54b** in aqueous ethanol. The first-order kinetics, the leaving-group effect ($k_{Br}/k_{Cl} = 52$) and the Grunwald–Winstein's m value of *ca* 0.5 show that **54a** and **54b** solvolyze by an S_N1 mechanism with the mesomeric butatrienyl cation **55** as the intermediate.

Both the butatrienyl halides **54a** and **54b** gave the alkyne (**56**) as the sole product in 97–100% yield[41]. The kinetics described above fit the mechanistic sequence shown in equation 20 for the formation of the product **56**. The mesomeric butatrienyl vinyl cation **55**



(20)

generated during the solvolysis is intramolecularly attacked by the methoxy group, which is located in a suitable position to form the five-membered ring, followed by elimination of the methyl group.



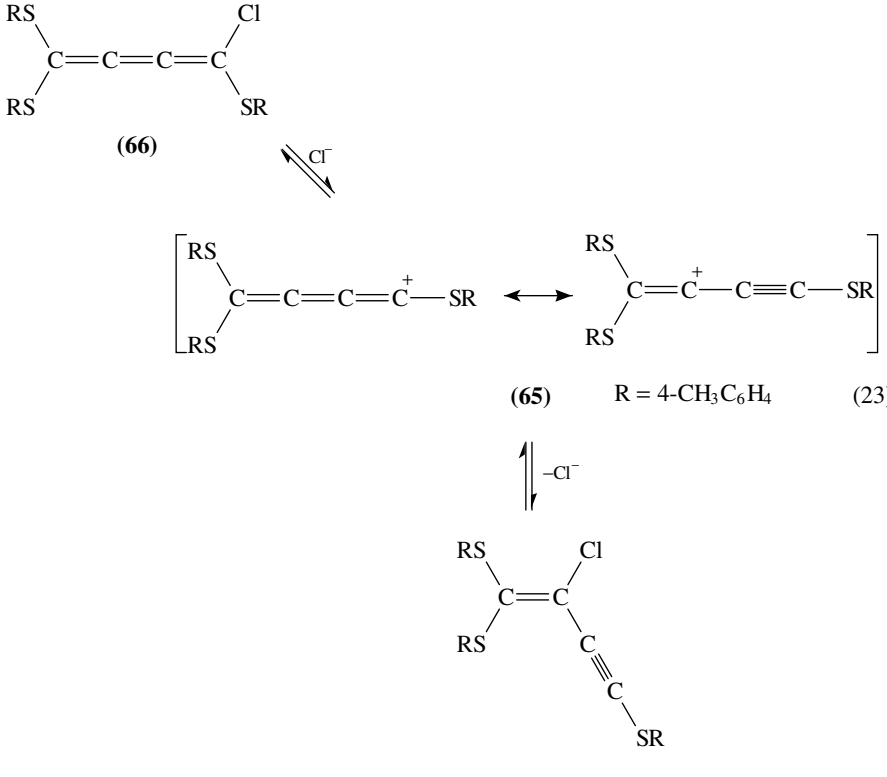
(21)

(22)

If one compares the solvolyses of 2-bromo-1,1-diphenyl-4-(*p*-methoxyphenyl)-but-1-en-3-yne (**57**) and 4,4-diphenyl-1-bromo-1-(*p*-methoxyphenyl)-buta-1,2,3-trienes (**58**, X = Br) in aqueous ethanol (equation 21), the destabilization of the intermediate cation **59** by the large inductive effect of the triple bond as compared to its conjugative effect is evident[42]. Only in the case of **58** could the substitution product butatrienyl enol ether **60** be isolated in 40% yield, while it was only detected by UV and IR spectroscopy in the solvolysis product of **57**. The faster observed reaction rate of **58** as compared to **57** was ascribed to a difference in their ground-state energies[42].

Butatrienyl cations **61** were also implied in the solvolysis of the α-propynyl vinyl triflate **62**[43]. The vinyl triflate solvolyzes 35–70 times faster than the corresponding simple vinyl analogues and gives products resulting mainly from the α-alkynyl vinyl cation **63**. A small amount of the allenic ketone **64** derived from the butatrienyl cation is also detected (equation 22).

An allenyl cation **65** is involved as an intermediate in the room-temperature isomerization of 1-chloro-1,4,4-tris(4-methylphenylthio)butatriene (**66**) to the tris(4-methylphenylthio)butenyne (**67**)[43] (equation 23).



(66) **(65)** (23) **(67)**

Higher homologues than the butatrienyl cations are not known to the best of my knowledge. The summary given here provides strong evidence for the existence of the cumulated vinyl cations, i.e. allenyl and butatrienyl cations. A leap into the preparatory domain, harvesting the potentials of these cations, should definitely be a fruitful venture.

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The Chemistry of Dienes and Polyenes. Volume 1
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CHAPTER **20**

Oxidation of dienes and polyenes

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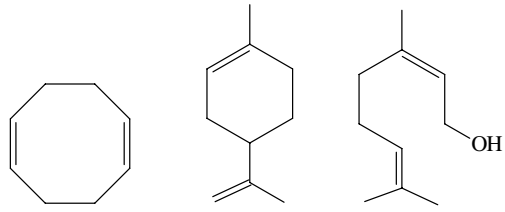
I. INTRODUCTION

The functionalization of a carbon–carbon double bond is a basic procedure in organic chemistry. Oxidation is one of the many different ways in which such a double bond may be transformed. Although the term oxidation is rather a general one, we will mostly concern ourselves in this review with oxygenations, i.e. reactions in which oxygen is added to the substrate with or without cleavage of the carbon–carbon bond. Only some mention will be made of other formally oxidative procedures such as dehydrogenation.

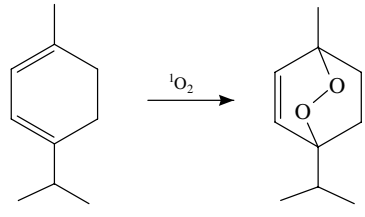
Although oxidation in general and of alkenes in particular is very well documented, it is rather surprising that there has been no systematic description of the oxidation of dienes or polyenes in the literature. In fact, more often than not an early literature example of the oxidation of a diene will be part of or an extension of a report dealing with the oxidation of monoalkenes. Only in recent years has oxidative functionalization of di- and polyenes become an important procedure in itself in fields such as natural product synthesis.

For the purpose of this review, one may view a diene in two ways depending on the structure of the substrate and the specific oxidation reaction to be carried out. The first point of reference is to consider the substrate as a compound having two *independent* monoalkene units. Often but not always this means that the double bonds are non-conjugated. In this case, the relative reactivity of the various carbon–carbon double bonds will usually form the basis of the research described and will deal with the selective formation of a specific product. In the most simple case, such as in substrates with two identical but independently reactive alkene units, for example *cis,cis*-1,5-cyclooctadiene **(1)**, this translates into selectivity based on mono- vs di- or poly-oxidation. In a more complicated substrate, two different double bonds, neither of which are further influenced by additional functional units, may be considered. Such a case is typified by substrates such as limonene **(2)** where the question of regioselectivity and/or stereoselectivity is paramount. The third, more complicated example includes substrates which have additional functional groups such as geraniol **(3)** where one double bond is *cis (Z)* and allylic to a primary alcohol and the other is independent of a functional unit or ligand. In such compounds questions of chemoselectivity as well as regioselectivity and stereoselectivity are the important factors to be considered. For compounds with additional functional groups, we will only discuss in detail examples where one of the double bonds actually react although there are numerous oxidation reactions where dienes are inert in the presence of other reactive centers.



(1) **(2)** **(3)**

In the literature, there are also several examples where the specific oxidation reaction is *dependent* on the presence of a diene. Often the substrates are conjugated dienes where there is simultaneous oxidation of both double bonds. An important prototype of this reaction is the well-known singlet oxygen oxidation of dienes to endoperoxides, for example the oxidation of α-terpinene **(4)** to ascaridole **(5)** (equation 1).



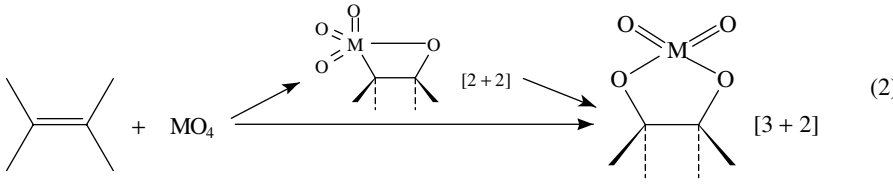
(1)

(4) **(5)**

There are many ways to categorize the oxidation of double bonds as they undergo a myriad of oxidative transformations leading to many product types including epoxides, ketones, diols, endoperoxides, ozonides, allylic alcohols and many others. Rather than review the oxidation of dienes by substrate type or product obtained, we have chosen to classify the oxidation reactions of dienes and polyenes by the oxidation reagent or system used, since each have a common reactivity profile. Thus, similar reactions with each specific oxidant can be carried out on a variety of substrates and can be easily compared.

II. OXIDATION WITH METAL-OXO COMPOUNDS AND INTERMEDIATES

High-valent metal-(M)-oxo compounds have often been used in the oxidation of dienes and polyenes. There are oxidants of alkenes which are exclusively stoichiometric reagents. Especially noteworthy is the use of permanganate but chromium-based reagents such as pyridinium chlorochromate (PCC) have also been used. Others, especially osmium and ruthenium tetraoxide, are known stoichiometric reagents; however, reactions are often carried out catalytically using terminal oxidants such as *N*-methylmorpholine oxide (NMO), ferricyanide, peroxides, periodate and hypochlorite. Finally, there are purely catalytic reactions, where the active intermediate metal-oxo compound is unstable and/or unknown under normal conditions. Most prominent in this last group are the metalloporphyrins and the metal-salen compounds as catalysts, where the metal is most often manganese(III). There are also reports using iron(III). A wide range of terminal oxidants have also been employed. The former reagents, MnO_4^-, OsO_4 and RuO_4, can provide an alkene with two oxygen atoms. Reactions with these oxidants therefore lead to *cis*-diols, α-ketols, diketones and oxidative cleavage. Both [2 + 2] and [3 + 2] cycloadditions, where the alkene adds to either one or both of the metal-oxo bonds, have been cited as the pathway to the key intermediates (equation 2)[1]. On the other hand, manganese-oxo intermediates of salen or porphyrin complexes contribute only one oxygen to the carbon–carbon bond yielding epoxides as initial product (equation 3)[1]. The intermediate and the mechanism in this reaction has been the subject of much research and discussion and is still disputed.



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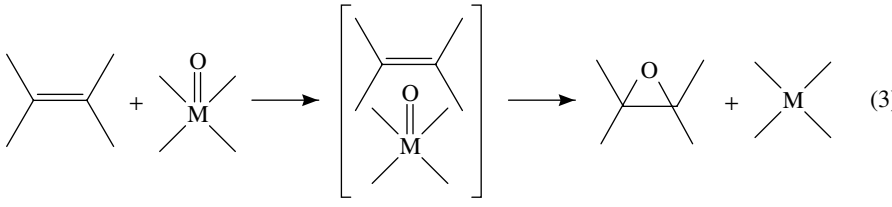
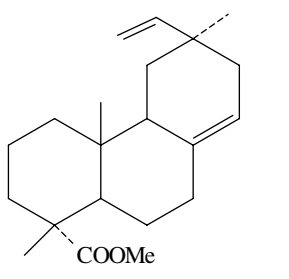


(3)

A. Oxidation with Permanganate

Some of the earliest work in the oxidation of alkenes was performed by oxidation with potassium permanganate. Under acidic and neutral conditions the intermediately formed glycols are oxidized, generally leading to cleavage of the carbon–carbon bond. Thus, such procedures have seldom been synthetically applied to diene oxidation. One notable

exception is the oxidative cleavage of pimaric **(6)** and sandaracopimaric **(7)** esters at the terminal vinylic bond to yield the acids **8** and **9**, respectively[2]. Under basic conditions the oxidizing strength of the permanganate is reduced and it is possible to prepare *cis*-diols and α-ketols. Diol formation is favored by low permanganate and relatively high base concentration and α-ketol formation is favored by high permanganate and low base concentration[3]. Early use of permanganate and base in the oxidation of dienes was first reported in the previous century by Wagner[4] who oxidized limonene **(2)** to the corresponding tetraol. Later on Wallach[5,6] similarly oxidized the 1,4 dienes, γ-terpinene **(10)** and terpinolene **(11)** whereas the 1,3 diene, α-terpinene **(4)**, was ring cleaved. Subsequently, 1,4 cyclohexadiene **(12)** was oxidized in the same manner to both the diol and the *cis, anti,cis* tetraol[7,8]. The *cis,anti,cis* tetraol was preferred over the *cis,syn,cis* tetraol product because of the steric hindrance to the second addition[9].



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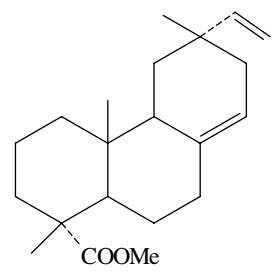

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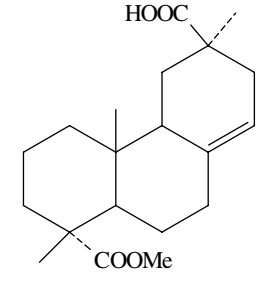

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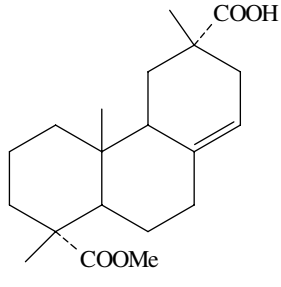

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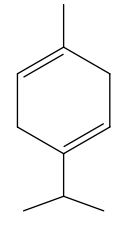

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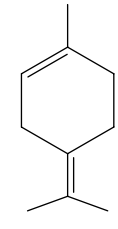

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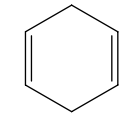
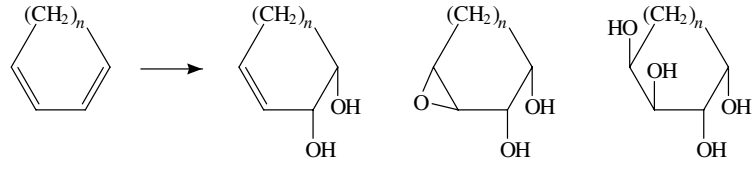


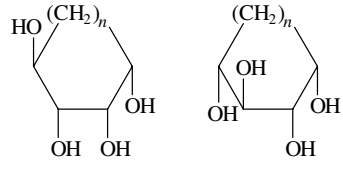
(12)

The basic permanganate oxidation of conjugated 1,3-dienes is different from those reported for the 1,4-dienes above. Therefore, in the oxidation of cyclopentadiene and 1,3-cyclohexadiene **(13)** a mixture of five products **14–18** is obtained (equation 4)[10,11]. In this reaction **14** and **16** are derived from the 'normal' *cis* hydroxylations whereas **17** and **18** were said to be formed from **15** by hydration in what the authors[9] term an epoxidic pathway. Formation of epoxy-diols under similar permanganate oxidations has been found for occidentalol[12] **(19)**, levopimaric acid[13] **(20)** and a 1-chloro- or 1-bromo-1,3-diene[14] **(21)** as an intermediate step in the synthesis of (+)-D-*chiro*-3-inosose and (+)-D-*chiro*-3-inositol (equation 5). The explanation for the epoxide formation in the oxidation of 1,3-dienes (**13**, **19–21**) is not clear but may be connected to the fact that other additions of permanganate to dienes are possible beyond those commonly observed

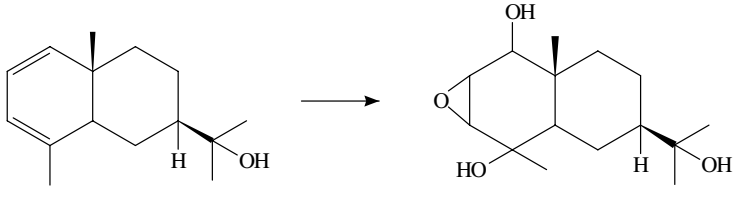
(equation 2). Other unusual additions are clearly observed in the oxidation of 1,5-dienes described below. Other 1,3-dienes, such as ergosterol[15] and abietic acid[16], have also been oxidized with permanganate but yield a complicated mixture of products whose identity is somewhat questionable.



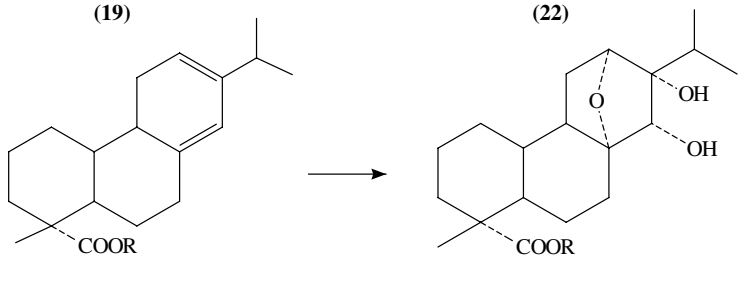
(13) $n = 1, 2$ **(14)** **(15)** **(16)** (4)



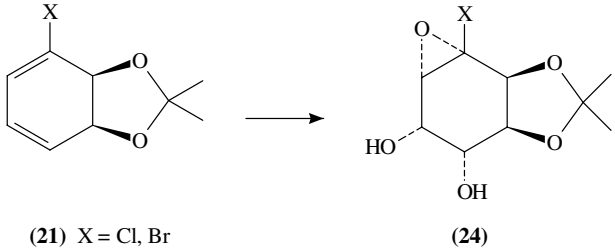
(17) **(18)**



(19) **(22)**

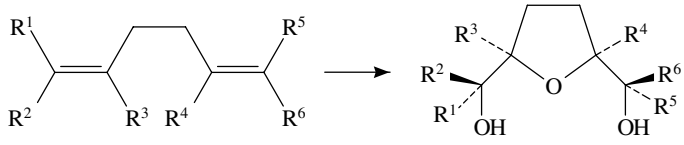


(20) R = H, CH_3 **(23)** (5)



(21) X = Cl, Br **(24)**

A most fascinating and remarkably high-yield permanganate oxidation of 1,5-dienes to stereospecifically form the *cis*-isomers of 2,5-bis(hydroxymethyl)tetrahydrofurans (equation 6) was discovered by Klein and Rojahn thirty years ago[17]. Two groups have suggested mechanisms to explain the stereochemistry of the tetrahydrofuran product. The first introduced a metallaoxetane intermediate, i.e. a [2 + 2] cycloaddition, followed by alkyl migration with retention of configuration, reductive elimination, oxidation and hydrolysis[18]. The second began with a [3 + 2] cycloaddition of one alkene bond with permanganate, and requires oxidation with another permanganate anion followed by intramolecular cycloaddition of the double bond and hydrolysis[19]. Isotopic experiments with ^{18}O-permanganate suggest that neither of these mechanisms is correct, but no further discussion has been presented[20]. In any case the stereochemistry of the cyclization is predictable and controlled by the geometry (*E* or *Z*) of the double bonds. This steroselective transformation has since been used in the synthesis of the tetrahydrofuran unit of ionomycin[21] and the bis-tetrahydrofuran unit of monesin[22]. Also, a high degree of enantioselectivity has been achieved in the neroate diene system functionalized with a chiral auxillary ligand in the total synthesis of ionophores[23]. Finally, this reaction has also been modified using a combination of potassium permanganate and copper sulfate to form butanolides (equation 7)[24].

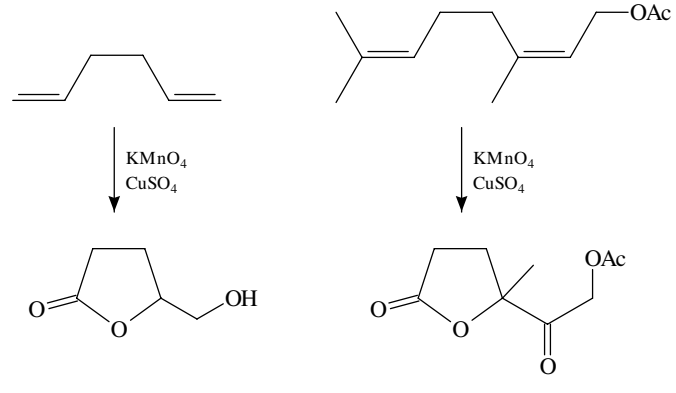


(6)

$R^{1-}R^6 = H$

$R^1 = R^2 = R^4 = R^5 = Me;\ R^3 = R^6 = H$

$R^1 = R^2 = R^4 = Me;\ R^3 = R^6 = H;\ R^5 = CH_2OAc$



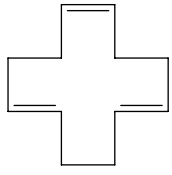
(7)

B. Oxidation with Osmium Tetraoxide

Oxidation of alkenes with osmium tetraoxide is much more moderate than similar oxidations with permanganate. This makes OsO_4 a very reliable reagent for *cis* dihydroxylation.

Both stoichiometric[25,26] and catalytic[27,28] oxidations were developed more or less at the same time. The stoichiometric methods involve reductive cleavage of the intermediate osmium complexes. The most effective reducing agents appear to be bisulfite, hydroxide, hydrogen sulfide and lithium aluminum hydride. Reactions in the presence of a nitrogen ligand, e.g. pyridine (Pyr), often allows the isolation of a $OsO_2(OR)_2Pyr_2$ complex before reductive cleavage. The catalytic methods are now generally considered more applicable due to the high price and toxicity of the osmium tetraoxide reagent. Common terminal oxidants include hydrogen peroxide, *tert*-butylhydroperoxide, *N*-methylmorpholine oxide (NMO), metal chlorates, hypochlorite and, most recently, potassium ferricyanide. Among the substrates in the original work of Milas and Sussman[27] in the hydrogen peroxide catalytic system, limonene **(2)** and 1,5-hexadiene were both oxidized to the corresponding tetraols at moderate yields in reactions carried out at subambient temperatures. Criegee and coworkers[26], on the other hand, prepared *cis*-diols from cyclopentadiene and 1,4-cyclohexadiene using one equivalent of OsO_4 and pyridine. Yields in this case were quantitative. Much later on 1,4-cyclooctadiene was similarly oxidized to the diol; however, in this case the intermediate complex was identified by its ^{1}H NMR, IR and Raman spectra[29]. 1,4-cyclooctadiene **(1)** was also oxidized to the diol in the first reported use of NMO as terminal oxidant[30]. The preference for oxidation at a *trans*-double bond vs a *cis*-double bond was first demonstrated in oxidation of *cis,trans,trans*-1,5,9-cyclododecatriene **(25)** in a non-catalytic system[31]. *Cis*-5-*trans*-9-cyclododecadiene-1,2-diol is formed exclusively. Further reaction of this product in a second step, again selectively, yields the *cis*-9-cyclododecene-1,2,5,6-tetraol.

Osmium tetraoxide has also been used in the oxidation of bicyclic and polycyclic dienes. Thus, oxidation of norbornadiene **(26)** in a stoichiometric reaction was found to yield the *exo-cis* diol exclusively[32]. On the other hand, in the NMO catalytic system a mixture of the *exo-cis* and *endo-cis* products was reported[30]. However, by use of the NMO catalytic procedure for the substituted norbornadiene **27**, the *exo*-diol was formed exclusively at the sterically crowded unsubstituted double bond and this product was utilized in the synthesis of pentalenolactone[33]. Somewhat surprisingly, oxidation of hexamethyl Dewar benzene **(28)** exclusively gave the *endo-cis* diol as sole product[34]. The tricyclic compound **29** gave the usual *cis*-diol oxidation product of one of the double bonds[35].



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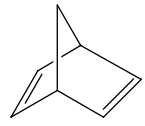

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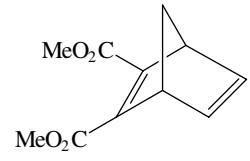

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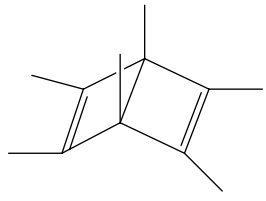

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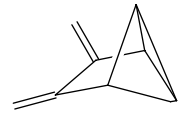
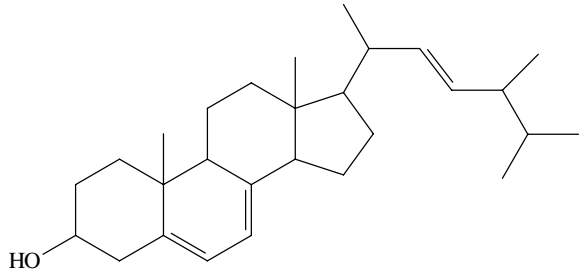


(29)

The use of osmium tetraoxide has also played an important part in the earlier research carried out on the functionalization of steroids. Already in their first reports[26], Criegee and his colleagues oxidized ergosterol **(30)** at the Δ^5 double bond only to form the 5α,6α-dihydroxy compound. At the same time others similarly oxidized 5,17(20)-pregnadiene-3β-ol (**31**, R = H) at the same position. Protection of the hydroxy group by preparation of the acetate (**31**, R = Ac) reverses the regioselectivity and brings about formation of the 17,20-diol[36]. In a further example intermediate **32** was selectively oxidized at the Δ^3 double bond, a useful position for the preparation of steroids methylated at the C-14 position[37]. Interestingly, a series of 4-pregnen-3-ones **33** were all exclusively functionalized at the C-17(20) position[30,38–40]. The enone double bond was much less reactive than the non-functionalized double bond. Finally, the directing effect of C-11 substituents on the addition of OsO_4 to steroidal $\Delta^{1,4}$-3-ketones **(34)** was investigated[41]. Substituents with an α-geometry (11α-hydroxy, 11α-acetoxy and 11α-methyl) brought about addition at the Δ^4 position to form 4β,5β-diols. The same was found for 11-oxo substitution. On the other hand, 11β-hydroxy substitution gave a mixture of diols.



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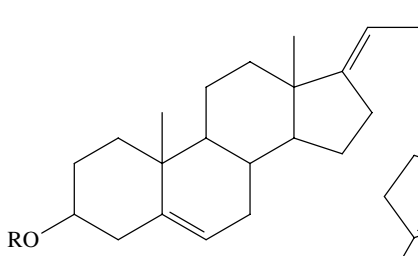

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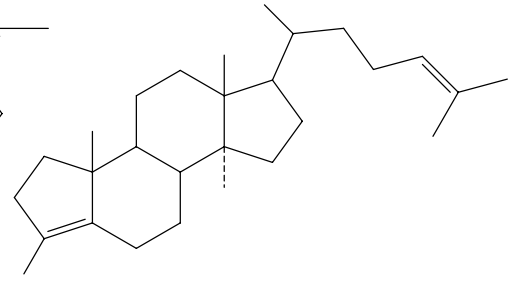
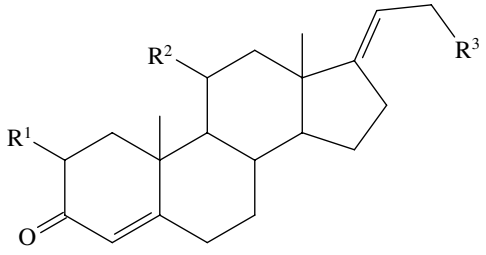
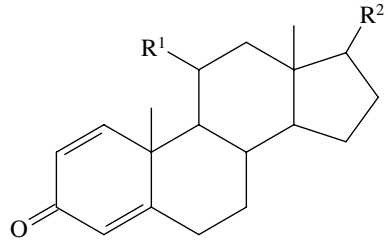


(32)

The effect of an allylic hydroxy group was first observed in divinylglycol (1,5-hexadiene-*cis*-3,4-diol and 1,5-hexadiene-*trans*-3,4-diol). It was shown that the hydroxy substitutions directed the addition of the osmium tetraoxide to *syn* addition, so that the *cis*-diol yielded allitol (all *cis*-hexaol) and the *trans*-diol yielded mannitol[42]. The oxidation of the dienol **35** yielded a lactone ring **36** by *cis*-dihydroxylation and transesterification

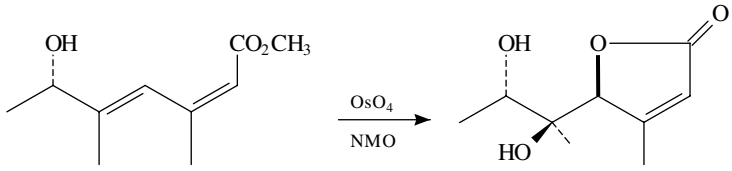


(33) $R^1 = R^2 = H$, $R^3 = OAc$, Br
$R^1 = H$, Me $R^2 = OH$, $R^3 = C$



(34)

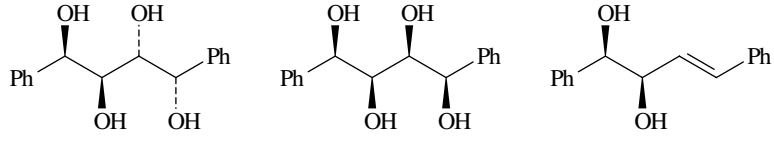
(equation 8), a key intermediate in the synthesis of verrucosidin[43].



(8)

(35) **(36)**

A very important breakthrough in the use of osmium tetraoxide oxidations was made by Sharpless and his group a few years ago. They discovered that by use of chiral cinchonia derivatized alkaloids as nitrogen-containing ligands, the osmylation reaction could be carried out in unprecedented levels of enantiomeric excess[44]. As concerns the use of this technique for the oxidation of dienes, there have been two reports by this group using NMO[45] or potassium ferricyanide[46] as terminal oxidants. In the oxidation of a model compound, *trans,trans*-1,4-diphenyl-1,3-butadiene with NMO, the tetraol was obtained as the major product with only a trace of the diol being obtained. The tetraol was obtained in a diastereomeric ratio of 16:1 (as determined by X-ray diffraction) in favor of the 1,2-*syn*-2,3-*anti*-3,4-*syn* isomer **(37)** vs the all-*syn* isomer **(38)**. Less substituted or *cis*-double bonds gave lower diastereomeric ratios. Use of ferricyanide as terminal oxidation yielded diol **(39)** as the product. Further work in the ferricyanide system showed that for unsymmetrical dienes, osmylation occurred preferentially at the more electron-rich double bond. For example, in 2-methyl-2,7-heptadiene, only the diol at the 2,3 position was formed. Selectivity is less substantial in conjugated dienes. Thus, for 1,3-hexadiene the ratio of products was 3:1 in favor of the more substituted Δ^3-double bond. The preference of

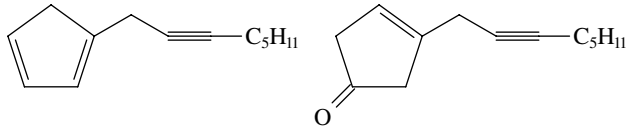


(37) **(38)** **(39)**

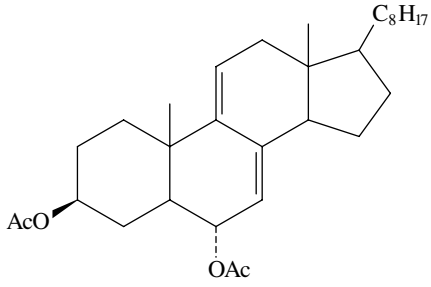
a *trans* over *cis* alkene is significant as was observed in *trans*-2-*cis*-4-hexadiene, where osmylation at the *trans* bond was favored by 15:1. The selective asymmetric dihydroxylation of dienes has recently been applied by others in the very elegant asymmetric syntheses of WCR sex pheromone and antibiotic (−) A26771B[47] and naturally occurring polyethers of the annonaceous acetogenin family[48].

C. Oxidation with Ruthenium Tetraoxide and Chromate Based Oxidants

Both dichromate and ruthenium tetraoxide, but especially the latter, are very strong oxidizing agents and therefore have been usually only used in synthetic procedures requiring double-bond cleavage. Recently, however, a few synthetic procedures have been described in the oxidation of dienes using these oxides. Thus, a 1-alkylated 1,4-cyclopentadiene **40** was oxidized to an enone **41** using the milder oxidizing agent 2-cyanopyridinium chlorochromate[49]. Pyridium dichromate has also been used in the oxidative rearrangement of dienols although the double bonds themselves are not actually oxidized[50]. Ruthenium tetraoxide has been used in the ring contraction of an oxepine to a furan[51]. An interesting use of RuO_4 in the oxidation of the steroidal diene **42** was recently reported where oxidation takes place exclusively at the 9(11) double bond forming a mixture of three separable products[52].



(40) **(41)**



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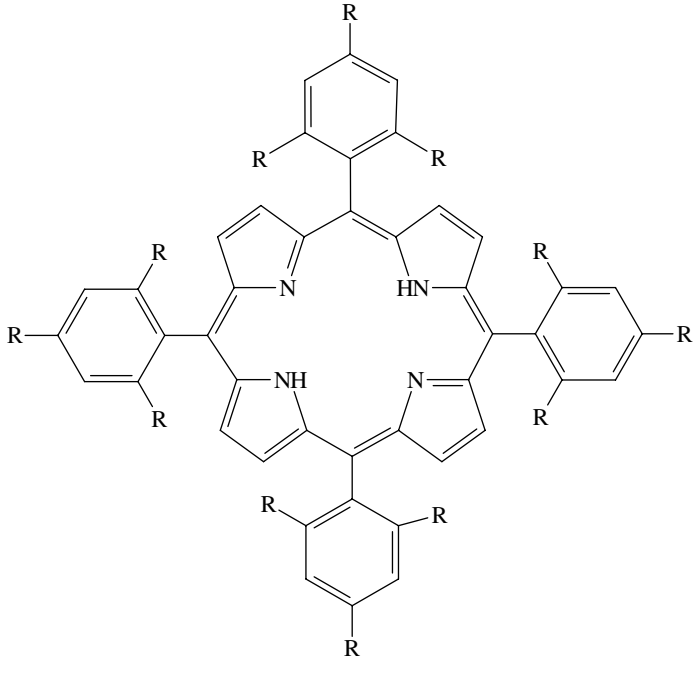
D. Catalytic Oxidation with Metalloporphyrins and Metal Salen Complexes

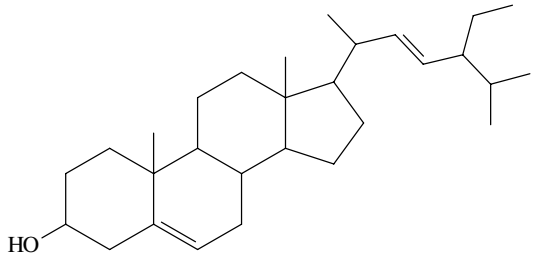
Starting in the early 1980s a great deal of research in the oxidation chemistry of metalloporphyrins became of interest, motivated by a biomimetic approach to the understanding of the unique activity of the cytochrome P-450 enzyme. The initial interest was in the iron porphyrins; however, it became obvious that sometimes, but not always for synthetic purposes, the manganese porphyrins were more effective. The activity of the manganese porphyrins led also to the realization that manganese-salen type compounds would be similarly reactive because of the similar nearly square-planar coordination of the metal in both cases. The complexes in the presence of oxygen donors such as

iodosobenzene, hypochlorite and many others are thought to form highly active intermediate manganese(IV) or more probably manganese(V) oxo intermediates, which can easily react with alkenes to form epoxides in high yields. Turning first to the work with metalloporphyrins, the oxidation of limonene **(2)** led to regioselective epoxidation at the endocyclic position. Endocyclic/exocyclic ratios varied from 7:1[53] to 19.6:1[54] for the manganese and iron porphyrins, respectively. Similar preferred endocyclic oxidation was observed for 4-vinylcyclohexene. In a similar iron-cyclam catalyzed reaction, somewhat lower regioselectivities were observed[55]. In the reaction of 2-methyl-1,3-butadiene (isoprene), there was also a preference, though significantly lower, for epoxidation at the more substituted double bond[53]. The oxidation of the trimethylsilylated derivative of geraniol **(3)** yielded the 6,7-epoxygeranyl–$OSiMe_3$ and only traces of the 2,3-epoxygeranyl–$OSiMe_3$ compound[53]. The reactivity of *cis* vs *trans* olefins is also of importance. Oxidation of *cis, trans, trans*-1,5,9-cyclododecatriene **(25)** showed little preference for either geometry in nonsterically hindered porphyrin ligands although *cis*-stilbene is much more reactive than *trans*-stilbene[54,56]. However, using a more sterically crowded porphyrin ligand, very significant *cis/trans* regioselectivity was observed. The synthetic manipulation of the porphyrin ligand was further used in comparison of epoxidation of dienes with manganese porphyrins. As steric crowding at the manganese center was increased by use of tetraphenyl- < tetramesityl- < tetra(triphenyl)phenyl porphyrin ligands **(43)**, R = H, Me, Ph, respectively, the natural tendency towards epoxidation at the more substituted double bond could be inverted[57]. Dramatic effects were observed for 1,4- and 1,3-hexadiene, 4-vinylcyclohexene and limonene **(2)**. Another approach to obtain regioselectivity in a porphyrin-mediated epoxidation was to prepare a vesicular assembly and positioning



(43)

the metal active site in the center of the lipid bilayer[58]. Then using the hydrophobic/hydrophilic orientation of a substrate within such a biomimetic membrane, regioselectivity of epoxidation of selected substrates such as steroids and fatty acids could be controlled. In this way the normal epoxidation of stigmasterol **(44)** at the Δ^5-double bond in homogeneous solution was reversed to selective epoxidation in the side chain[59]. Similarly, the epoxidation of the Δ^{12}-double bond was preferred over the Δ^9 double bond in linoleic acid **(45)**, otherwise equally reactive in homogeneous solution.



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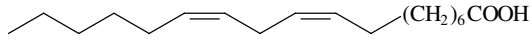
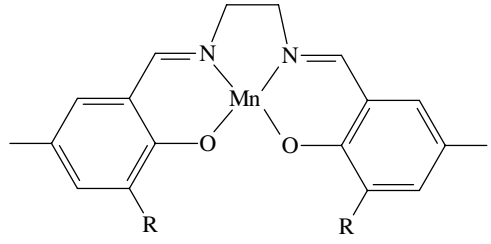


(45)

The regioselectivity of epoxidation of 1,3-conjugated dienes using manganese salen complexes **46** (R = H or *t*-Bu) was compared to that using the mangenese porphyrins[60]. Similar regioselectivities were found in four different dienes (isoprene, 2,4-dimethyl-1,3-pentadiene, 1,3-hexadiene and 1,4-diphenyl-1,3-butadiene). A very significant stride was also made recently in the use of a chiral Mn(salen) compound **(47)** for asymmetric catalytic epoxidation of non-functionalized alkenes[61]. This method utilizes steric control in the approach of the prochiral double bond to the metal-oxo site, forcing preferred epoxidation at one face of the double bond and therefore formation of epoxides in significant enantiomeric excesses. Jacobsen and his coworkers found early on that in the epoxidation of 1,3-cyclohexadiene and the *tert*-butyl ester of 2,4-hexadienoic acid enantiomeric excesses of up to *ca* 60% could be obtained[62]. In a later and much more complete study[63]



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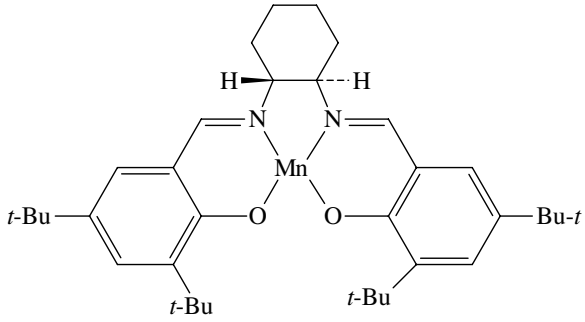

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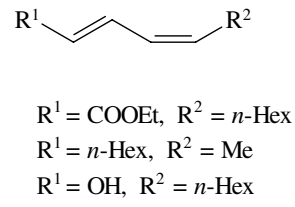


(48)

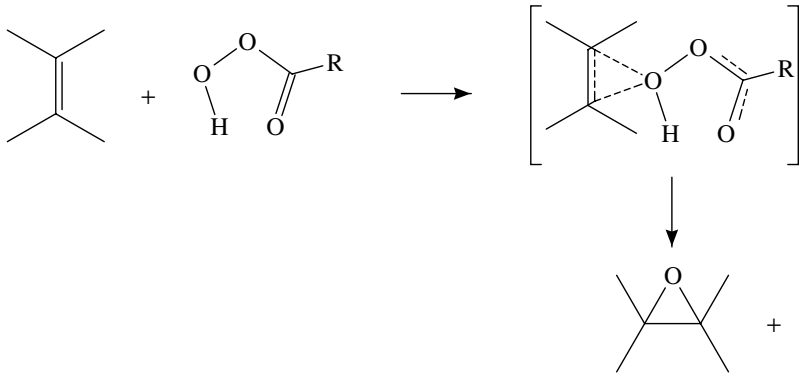
on a series of *E, Z*-conjugated dienes **48**, they found that epoxidation at the *Z* double bond was much preferred. *E*-Epoxides were formed in excess over the *Z*-isomers although ratios varied significantly with no apparent reason. Enantioselectivities were moderate to high. Other substrates such as 3-methylenecyclohexene, 1,3-cyclohexadiene and 1,3-cycloheptatriene were also epoxidized with high enantioselectivities[64]. It is important to note at the conclusion of this section that both the manganese porphyrins and salens react preferably at *cis* vs *trans* double bonds in contrast to what was found for permanganate and osmium tetraoxide. In this sense, these former compounds react in a manner similar to the peroxo compounds to be discussed below.

E. Miscellaneous

Selenium dioxide is also an oxygen donor to alkenes. In this case, however, the initial reaction of the double bond is with the selenium center followed by two pericyclic steps. After hydrolysis of the organo-selenium intermediate, the result is a hydroxylation at the allylic carbon position[65]. Thus, limonene **(2)** yields racemic *p*-mentha-1,8(9)-dien-4-ol[66]. The high toxicity of selenium intermediates and prevalence of many rearrangements has limited the widespread use of the reagent in synthesis.

III. OXIDATION WITH PEROXO COMPOUNDS

The susceptibility of a nucleophilic double bond to an electrophilic oxygen found in peroxo compounds to yield epoxides as products is a very common reaction that was first discovered by Prileschajew at the beginning of the century[67]. For much of this period the epoxidation reaction had been carried out using organic peracids as the epoxidizing agent. Much of the early research has been detailed in a very extensive and encompassing review[68] and later on in a book by Swern[69]. In the earliest years, epoxidation reactions were generally carried out using peracetic, performic, perbenzoic and perphthalic acids, although often the reaction conditions were such that the epoxide was not isolated as primary product. Usually the epoxide would react further with the acid to form glycol monoesters or with water to form diols. Later on, greater control and understanding of the reaction conditions allowed preparation of epoxides in higher yields. The oxygen transfer mechanism is generally considered to be concerted as first proposed by Bartlett (equation 9)[70]. The epoxidation of dienes as a distinct class of compounds with peracids has not been specifically reviewed, but many examples have been given in the early manuscripts[68,69].



(9)

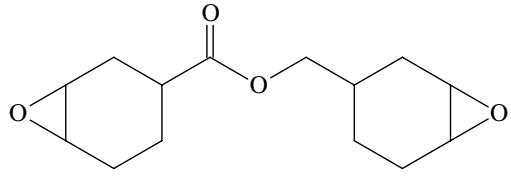
Although the use of peracids in alkene oxidation is simple, it has several drawbacks, especially in large-scale and industrial situations. As indicated above reaction control *vis a vis* selectivity can be problematic; however, additionally and perhaps more seriously, peracids are dangerous and explosive compounds which introduce stringent safety considerations when carrying out such reactions[71]. One possible remedy that is being explored is the use of safer peroxygen compounds. Another possible approach in remediation of this concern is to use alkylhydroperoxides and hydrogen peroxide as oxidants. These compounds are significantly safer and practically inert to double bonds. Their use, however, requires catalytic activation which is generally achieved by use of high-valent (d^0) transition metals with high Lewis acidity and low oxidation potentials. Most commonly used are Ti^{IV}, V^{V}, W^{VI}, Mo^{VI}[72] and, more recently, Re^{VII} compounds[73]. In the activation process it is commonly accepted that a M−OOH peroxo intermediate (sometimes termed an inorganic peracid) is formed which is the real epoxidizing agent. Oxygen transfer takes place by a heterolytic cleavage of the O−O bond in a manner similar to peracid oxidation. Thus, reagents prepared by mixing metal oxides such as WO_3, V_2O_5 and MoO_3 with hydrogen peroxide yield what were originally termed Milas reagents[74]. These original reagents are poor epoxidizing agents and have not been realized at large scales. However, much recent research is being aimed at improving catalytic hydrogen peroxide activation due to its great perceived ecological and economic advantages. Similarly, there have been considerable efforts in the activation of alkylhydroperoxides, most prominently *t*-BuOOH. This activation was first realized by Hawkins in 1950[75] and since has been investigated by many groups. As in the case of organic peracids, there has been no systematic review on the catalytic oxidation of dienes with hydroperoxides.

A. Oxidation with Organic Peracids

The most widely accepted method for epoxidation of alkenes remains oxidation with organic peracids. The early work (up to 1970) in this field shows that a large number of dienes and polyenes were oxidized in this manner[69]. The most commonly used peracids are peracetic, monoperphthalic and perbenzoic acids which are most dominant in industrial applications. On the other hand, in laboratory procedures *m*-chloroperbenzoic acid, MCPBA, is often used, with trifluoroperacetic acid cited in more difficult transformations. Recently, the transportation of *m*-chloroperbenzoic acid has been restricted and the use of other peroxygen agents has been gaining acceptance as a general alternative. Among the substrate types epoxidized it would be especially worthy to point out polyunsaturated

steroids, fatty acids, terpenes and diesters as well as many simpler di- and poly-ene hydrocarbons. The easiest way to summarize the vast pre-1970 literature (over 600 substrates) would be to note the following general conclusions which may serve as a guideline for reactivity in polyfunctionalized compounds. First and foremost, reactions are most strongly affected by the nucleophilicity of the double bond. Therefore, the higher the alkyl substitution at the double bond the higher the reactivity. On the other hand, the presence of electron-withdrawing groups such as carbonyl, carboxylic acids and esters strongly decreases the likelihood of reaction at proximate double bonds. Furthermore, *cis*-alkenes are more reactive than *trans*-alkenes, strained double bonds are more reactive than alkenes without strain, cycloalkenes react more easily than dialkyl substituted alkenes and aryl substituents have little effect. Finally, in conjugated dienes, the epoxidation of the second double bond is slower than the epoxidation at the first double bond. Using these guidelines, the expected regioselectivity in a diene epoxidation can be easily determined. In addition, almost without exception, the epoxidation is stereospecific, i.e. *cis*-double bonds yield *cis*-epoxides whereas *trans*-double bonds yield *trans*-epoxides[76]. In certain cases neighboring groups may effect direction of the peracid attack at the double bond by steric interaction.

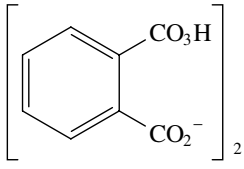
As the oxidation of alkenes with organic peracids is so prevalent, little has been researched over the past two decades at an academic level, especially as concerns epoxidation of di- and poly-enes. It is important, however, to point out that organic peracids have, despite safety considerations, been applied in a number of industrial applications[77]. As concerns polyunsaturated substrates, the most important are the epoxidized vegetable oils (naturally occurring mixtures of unsaturated triglycerides) which are important stabilizers and plasticizers for PVC. Synthetic polymers such as polyisoprenes and polybutadiene containing various percentages of 1,4-*cis*, 1,4-*trans* and 1,2-vinyl olefinic units are available which can be epoxidized easily to a level of 6–8% oxirane oxygen. More recently natural rubber has been epoxidized to form a new polymer, epoxidized natural rubber ENR. Both types of the epoxidized polymers may compete with natural rubber in non-tire applications. An interesting monomeric diepoxide is **49**, which is both a thermosetting and UV curable cross-linking agent used in the electronics industry.



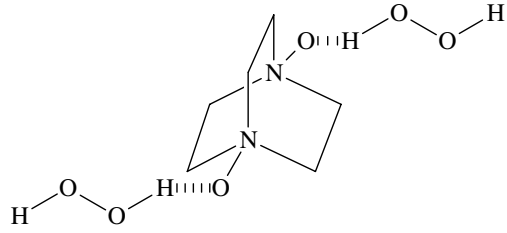
(49)

B. New Peroxygen Reagents

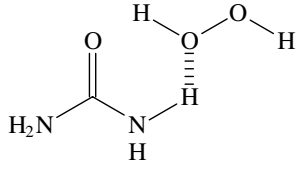
Safety considerations concerning the organic peracids described above have led to a search for possible new peroxygen agents with reduced hazard in their use. Despite this trend MCPBA is still often used in the laboratory. For example, one may note its use in the triepoxidation of barrelene[78]. Some recently developed organic peroxygen compounds include magnesium monoperoxyphthalate hexahydrate, MMPP **(50)**, DABCO-di-*N*-oxide-di-perhydrate **(51)** and urea hydrogen peroxide, UHP **(52)**. The oxidation of 1,2-dimethylcyclohexa-1,4-diene **(53)** and 4,7-dihydroindane **(54)** with MMPP[79] proceeds in an identical manner to that with MCPBA[80], i.e. epoxidation at the more electron-rich double bond is preferred. Similar preference for epoxidation at the more substituted double bond was observed in the reaction of **55** carried as one of the stages in the synthesis of the quinone antibiotic frenilicin[81].



$Mg^{2+}\cdot 6H_2O$



(50) **(51)**



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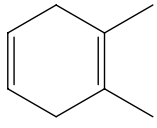
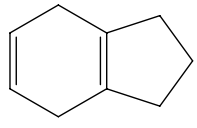
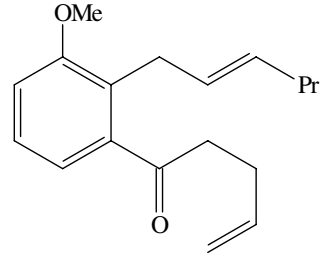
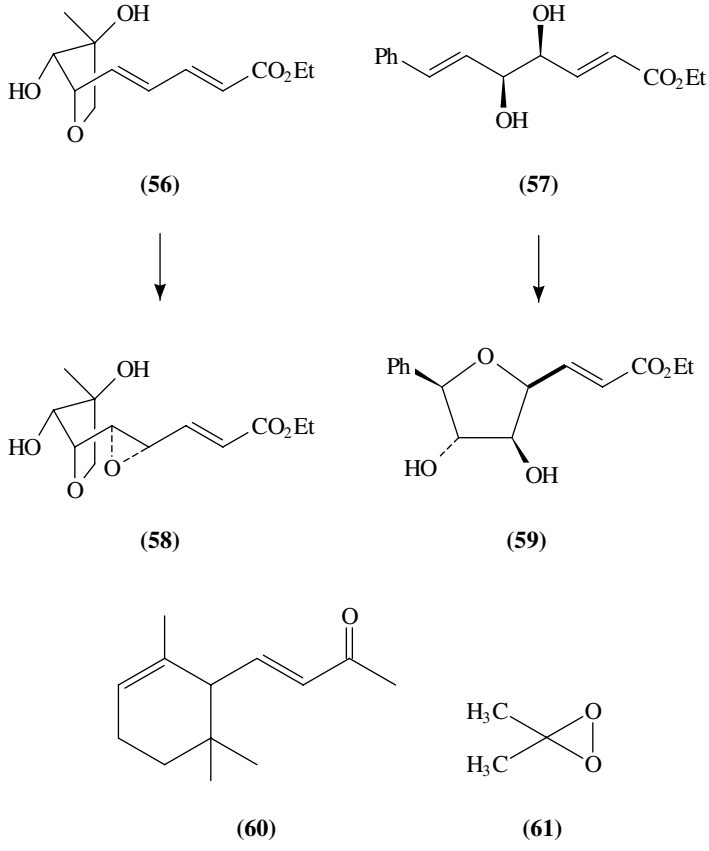






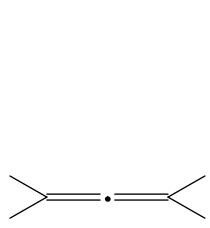
(53) **(54)** **(55)**

Epoxidation of limonene **(2)** with both MMPP and UHP proceeded preferentially at the endocyclic double bond with a 4:1 ratio of regioisomers being observed[82]. The presence of electron-withdrawing groups also has in general the predictable effect. Therefore, geranyl acetate (**3** with OH replaced by OAc) is epoxidized mostly at the 6,7-double bond with both UHP and MCPBA[83]. Notably, this selectivity can be reversed by using an emulsion technique where the more hydrophobic 6,7-double bond is kept from the water-dissolved oxidant in the hydrocarbon or oil phase. Selectivity of 93% to the 2,3-epoxide was obtained[84]. Normal regioselectivity was obtained in the epoxidation of the substituted diene esters **56** and **57** with MMPP. The former yielded the α-epoxide, **58**, exclusively vs 3:1 mixture of α versus β-epoxide with 3,5-dinitroperbenzoic acid[85], whereas the latter gave, upon acid-catalyzed cyclization, a tetrahydrofuran intermediate **59** as a key step in the total synthesis of (+)-altholactone (equation 10)[86]. Worth noting also is the good diastereofacial selectivity obtained with MMPP, 3.5:1, in favor of the β-face vs poor selectivity with MCPBA. In the oxidation of α-ionone **(60)** with UHP, the endocyclic double bond was exclusively epoxidized[78]. This selectivity could be inverted by using basic conditions where a nucleophilic HOO^- species is formed and is known to attack the more electrophilic double bond[87].



Another interesting new class of peroxygen compounds relevant to the oxidation of alkenes are the dioxiranes, especially the dimethyldioxirane **(61)** only recently isolated[88]. Although almost no specific research has been carried out in diene oxidation, research into the oxidation of various alkenes has revealed that the dioxirane reagent is less sensitive to substitution effects than peracids, thereby leading to greater reactivity with less nucleophilic substrates[89]. One important example worth pointing out is the epoxidation of allenes, **62**, to the corresponding diepoxides, **63**[90,91]. An interesting comparison may be made when investigating similar oxidations with MCPBA[92]. In certain cases formation of a monoepoxide may be followed by a cyclization reaction[93]. Another highlight in the use of dimethyldioxirane is the epoxidation of aflatoxin B_1 to form the 8,9 epoxide, **64**, a well-known carcinogen which could not be prepared by other methods[94].

Inorganic peroxygen compounds have also been mentioned as possible organic peracid substitutes. Most noteworthy are potassium monopersulfate, oxone, as a triple salt $2KHSO_5 \cdot KHSO_4 \cdot K_2SO_4$, sodium perborate and sodium percarbonate. The direct use of oxone has been limited because of the high acidity of this reagent, although it is most often used in the presence of ketones to form dioxiranes as discussed above[95]. 4-Vinylcyclohexene was predominately oxidized at the endocyclic double bond with this



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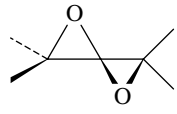

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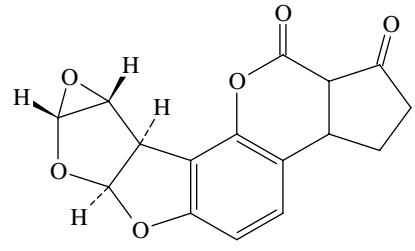
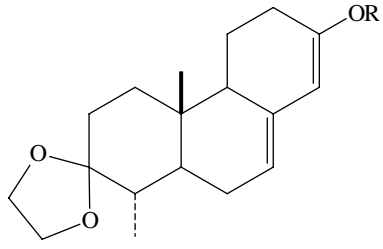


(64)

reagent[96]. In a somewhat unusual reaction oxone gave higher yields than MCPBA in the oxidation of the dienyl ethers **65** (R = Me, Et), a key step in the total synthesis of bruceantin[97]. A 2-nitrobenzenesulfonyl peroxide is active in diene epoxidation at −30 °C with normal regioselectivity[98]. Sodium perborate has been used to epoxidize the tricyclic diene **66** at a 50% yield to the diepoxide[99]. Oxidation of the α, β-enone **67** to **68** at high yields would seem to indicate that the perborate has a reactivity profile more similar to basic hydrogen peroxide[100]. In summary, in recent years we have seen the advent of new peroxygen reagents, developed to overcome inherent safety problems in the use of organic peracids. Selectivity profiles are often near to those found for the peracids.



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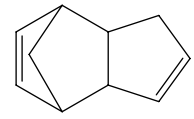

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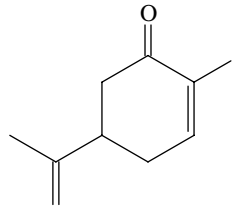

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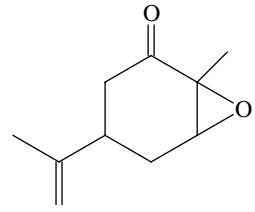


(68)

C. Catalytic Activation of Hydroperoxides

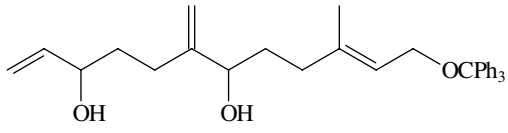
As stated above, one of the alternatives to using organic peracids for the oxidation of alkenes is the use of hydroperoxides[72]. Since the latter are practically inert to double

bonds, it is necessary to activate the hydroperoxide with high-valent transition metals. Use of main group oxides such as selenium dioxide has also been documented. The majority of research has been in the use of *tert*-butyl hydroperoxide and aqueous hydrogen peroxide. Although the exact mechanism of oxygen transfer is not known for all cases, one may generalize by saying the reaction proceeds by formation of a complex between the metal center and the hydroperoxide forming a so-called 'inorganic peracid'. The oxygen transfer occurs via heterolysis of the oxygen–oxygen bond aided by polarization of electron density to the high-valent metal. As concerns synthetic applications, it is important to point out that as the oxidation potential and Lewis acidity of the metal catalysts increase, the selectivity of the reaction often is decreased, due to homolysis of the hydroperoxide. This leads both to non-productive decomposition of the hydroperoxide and often unwanted side reactions due to the intermediate radical oxygen species formed.

1. Alkyl hydroperoxides

In agreement with the electrophilic nature of the metal-hydroperoxide intermediate, the rate of epoxidation increases with the nucleophilicity of the double bond and therefore closely parallels reactivity of organic peracids. The first in-depth study[101] with *tert*-butylhydroperoxide (TBHP) as oxidant with homogeneous vanadium and molybdenum compounds as catalysts revealed that the latter are more effective than the former by approximately two orders of magnitude. However, in the case of allylic alcohols this trend is reversed (see below). For example, oxidation of limonene[102] **(2)** and 4-vinylcyclohexene[96] exclusively yielded the epoxide at the endocyclic double bond with $Mo(CO)_6$ as catalyst. Similarly, 1,5-cyclooctadiene and *cis, trans, trans*-1,5,9-cyclododecatriene both yielded monoepoxides with the same catalyst, the latter preferably at the *cis*-double bond. Conjugated dienes such as 1,3-butadiene and isoprene[103] reacted more slowly. The latter reaction was not regioselective. Other molybdenum complexes have also been used[104]. Early on it was also found that functional groups such as acetates could bring about preferential attack at the double bond from the face of the molecule containing the functional groups, leading to excess formation of stereoisomers, in contrast to what was observed for organic peracids[105].

The strong rate acceleration observed in allyl alcohol oxidation with vanadium compounds, usually $VO(acac)_2$, despite the electron-withdrawing effects observed in peracid epoxidation, was attributed to the strong coordination of the alcohol ligands to the metal. This use of $VO(acac)_2$ and TBHP was utilized to selectively epoxidize both geraniol and linalool at the double bond allylic to the alcohol group with very high selectivity, in contrast to what was found with organic peracids[106]. The principle of preferred oxidation at an allyl alcohol double bond was further utilized almost immediately. Examples include the oxidation of the multifunctionalized alcohol, **69**, to the diepoxide, **70**, in the synthesis of a juvenile hormone[107], and regioselective epoxidation of **71** to **72** (equation 11)[108]. The reactions are also stereospecific to *syn* addition. Therefore, the regioselectivity along with the stereospecificity of addition was also used in the epoxidation of 1,5-cyclohexadiene-4-ol[109] and the cyclic dienol, **73**, which led to **74** via transannular rearrangement of the initially formed *syn*-epoxide (equation 12)[110]. The stereoselectivity of the epoxidation was also applied in the preparation of the antibiotic methyl pseudomonate A[111]. Homoallylic alcohols can also be epoxidized very effectively[112]. In compound **75** having both an endocyclic and an exocyclic homoallylic double bond, the former was oxidized much more easily to yield **76** (equation 13)[113].



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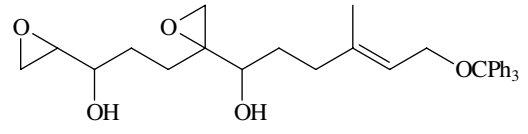

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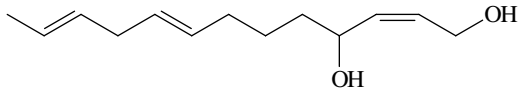

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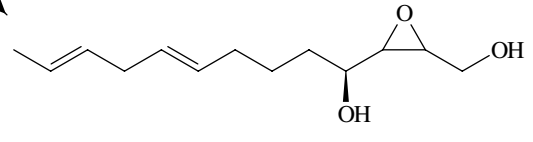

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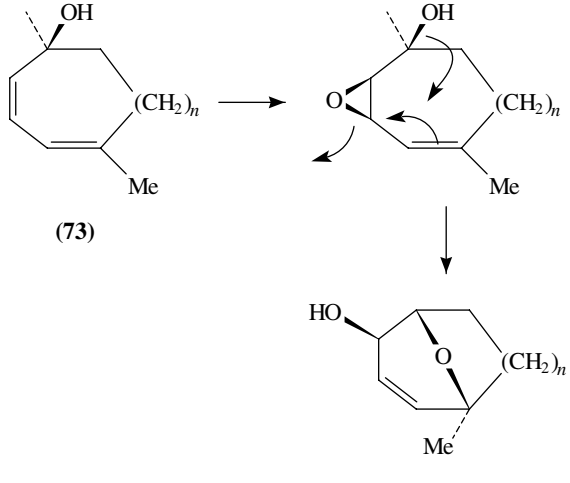

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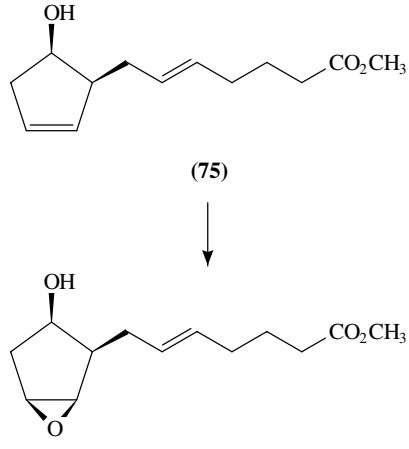
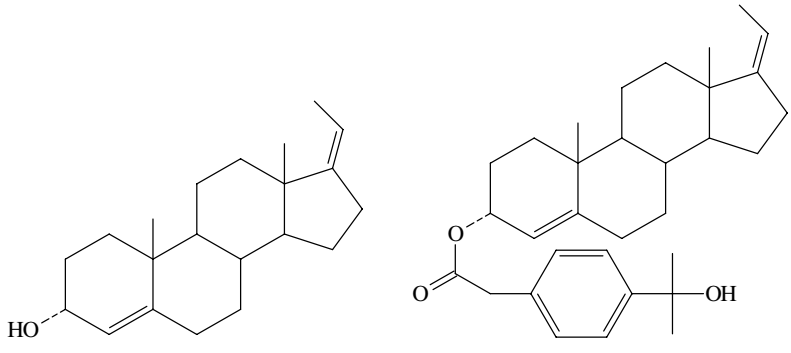


(75) **(76)** (13)

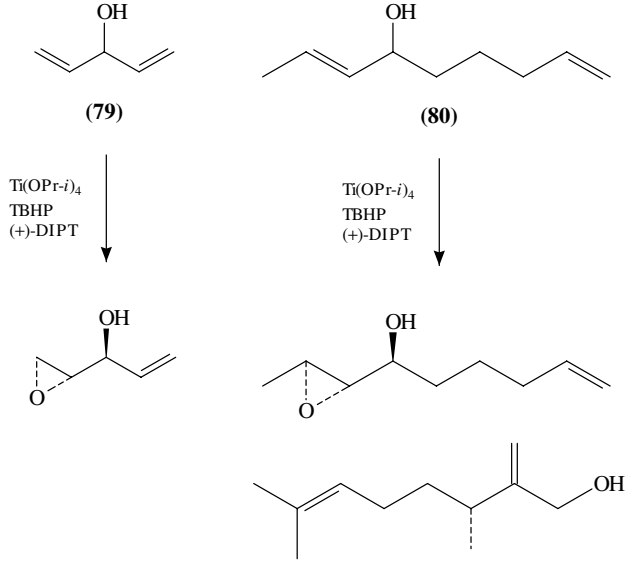
A very interesting way to control alkene epoxidation was introduced by Breslow and Meresca[114]. In the steroid diene, **77**, epoxidation takes place exclusively at the 4,5 double bond using $Mo(CO)_6$ and TBHP. However, by attaching a template, as in **78**, to the alcohol, the regioselectivity could be inverted so that epoxidation takes place only at the 17,20 double bond. It was concluded that the appendage did not act as a steric shield, but the remote tertiary alcohol moiety was transformed *in situ* to a hydroperoxide resulting in the observed selectivity by intramolecular epoxidation. This approach was then extended to other functionalized polyenes, such as farnesol and geranylgeraniol[115].



(77) **(78)**

The use of alkylhydroperoxides as epoxidizing agents for allylic alcohols under catalytic conditions was soon expanded into enantioselective epoxidation with use of the more mild titanium alkoxides in the presence of chiral tartaric esters[116]. As concerns the epoxidation of functionalized dienes, these now so-called Sharpless conditions [$Ti(OPr^i)_4$, dialkyl tartrate, TBHP] have been utilized to enantioselectively epoxidize 1,4-pentadiene-

3-ol[117] **(79)**, 2,8-nonadiene-4-ol[118] **(80)** (equation 14), geraniol and linalool at the allylic position[119] as well as many others which have been complied in a recent review[120]. Steric factors may also play a role in the enantioselective formation of epoxy alcohols. Therefore, in the case of the optically active alcohol **81**, use of (+) diisopropyl tartrate, (+)-DIPT, yields the desired epoxy alcohol in a 92% ee ('matched pair') whereas with (−) diisopropyl tartrate, (−)-DIPT, only a 50% ee was observed in a 'mismatched pair' (equation 15)[121]. The triene **82** was also epoxidized with very high enantioselectivity[122]. Other important epoxy alcohols formed include squalene oxide analogs[123], intermediate in the synthesis of marmine[124] and virantmycin[125]. Recent examples of inverse enantioselectivity[126] and the use of different chiral auxiliaries have been reported[127].



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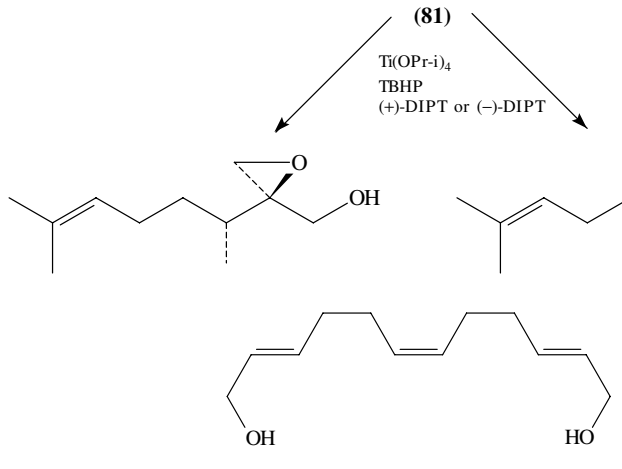
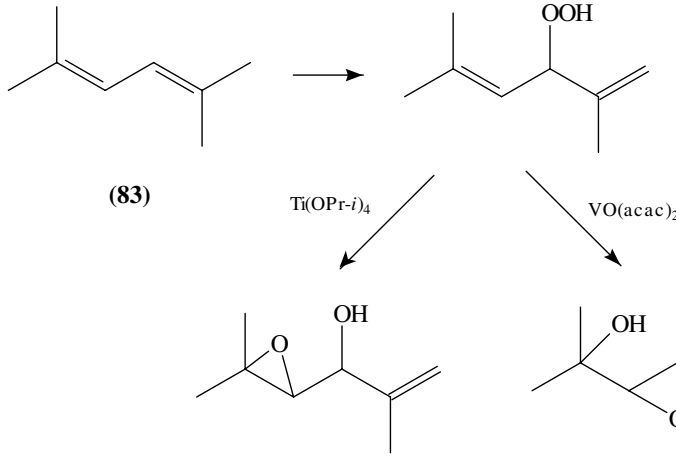


(15)

A further interesting extension of the allyl alcohol epoxidation reaction is the metal-catalyzed direct hydroxy-epoxidation of alkenes. In such a reaction an ene reaction with singlet oxygen, $^1O_2$, or Schenk reaction forming an allylic hydroperoxide is combined with metal-catalyzed intramolecular epoxidation to form epoxy alcohols[128]. For example, with 2,5-dimethyl-2,4-hexadiene **(83)** two different isomers, **84** and **85**, were obtained with $Ti(OPr\text{-}i)_4$ and $VO(acac)_2$, respectively (equation 16)[129]. Similar reactions were also carried out on dicyclopentadiene[130] and α-ionone **(60)**[131]. Recently, a large pore bifunctional titanium-aluminosilicate was used to epoxidize and then cyclize linalool **(86)** to a mixture of furan and pyran derivatives in one step (equation 17)[132]. Other titanium-substituted silicates have also been used for the epoxidation of limonene[133].



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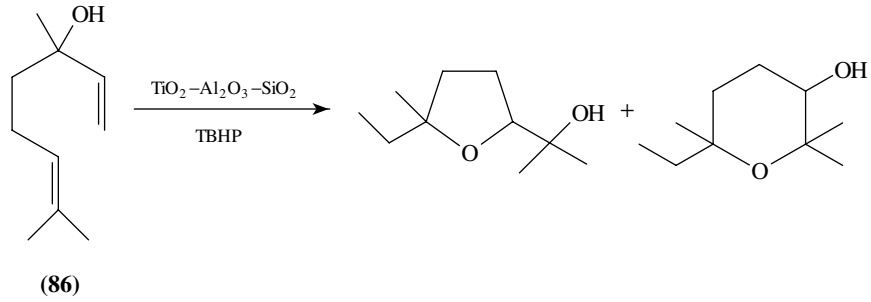
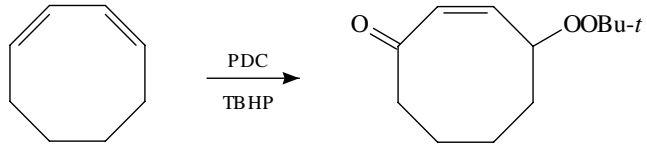


(17)

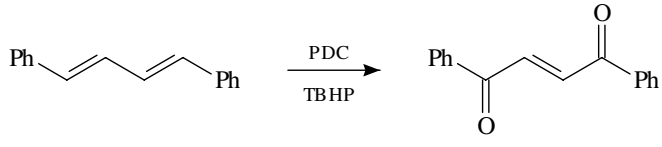
Towards the end of this section it may be worthwhile to point out some new reactions with high-valent metals and TBHP. The first is a pyridinium dichromate PDC–TBHP system[134]. Nonsubstituted or alkyl-substituted conjugated dienes, such as 1,3-cyclooctadiene **(87)** and others (also linear dienes), yield keto allyl peroxides **88** (equation 18), whereas phenyl-substituted dienes such as 1,4-diphenylbutadiene **(89)** gave diketo compounds, **90** (equation 19). In further research into a GIF-type system[135] with iron and TBHP, limonene gave a mixture of products with carvone as the major product. The mechanism is thought to proceed initially by formation of a Fe(V)–carbon

intermediate, followed in the presence of air to a peroxo intermediate, from which products are formed[136].



(18)

(87) **(88)**

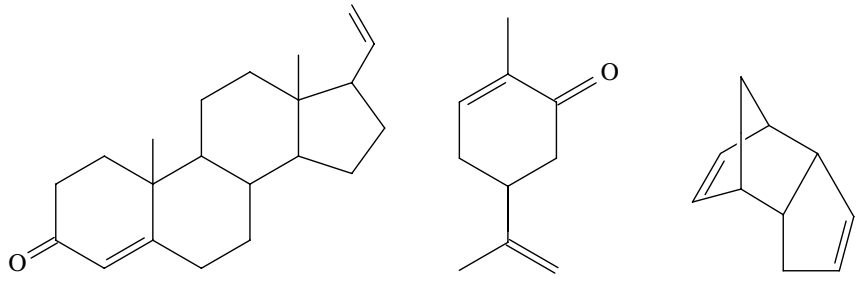


(19)

(89) **(90)**

2. Hydrogen peroxide

The use of hydrogen peroxide in catalytic oxidation of dienes is highly desirable from an economic and ecological point of view. However, there are relatively as yet few results in this still rather virgin field, especially compared to the significant success that has been obtained with TBHP and other alkyl hydroperoxides. Some of the earlier results showed that 1,5,9-cyclododecatriene, 1,4-cyclooctadiene and 1,3-cyclooctadiene could all be epoxidized in the range of 80–90% epoxide vs diol selectivity with simple oxides such as WO_3, MoO_3 and V_2O_5[137]. More recently, peroxotungstates of the type $\{PO_4[W(O)(O_2)_2]_4\}^{3-}$ have been used to oxidize 4-vinylcyclohexene exclusively at the endocyclic double bond and the steroid 4,20-pregnadiene-3-one **(91)** at the 20,21 double bond[138]. Another pertungstate salt which has been used advantageously is the $W_2O_{11}{}^{2-} \cdot 2Ph_3PCH_2Ph^+$ compound[139] which has been shown to catalyze the oxidation of limonene, geraniol, nerol and carvone **(92)**. For limonene the endocyclic position is



(91) **(92)** **(93)**

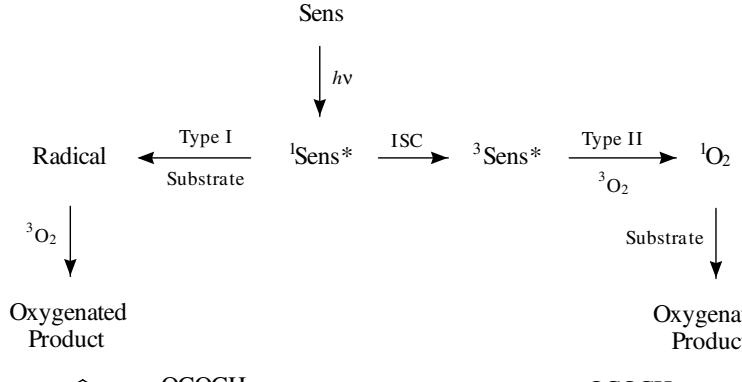
highly preferred, for nerol and geraniol the allylic position is most reactive whereas, in carvone, the α-keto group causes strong deactivation of the neighboring double bond leading to epoxidation at the 9,10 position. Use of the phosphotungstate, $PW_{12}O_{40}^{3-}$, leads to a mixture of mono- and di-epoxides in the epoxidation of the tricyclic **93**[140]. Similarly, $PMo_{12}O_{40}^{3-}$ has been used in the oxidation of dienes with one allylic alcohol unit. The α-epoxy alcohols are the preferred products[141]. Recently, our group has also used a manganese-substituted polyoxometalate as catalyst for diene epoxidation with hydrogen peroxide[142].

IV. OXIDATION WITH OXYGEN

The oxidation of organic compounds with molecular oxygen is a highly desirable goal stemming from its availability. From a thermodynamic point of view combustion products are of course always to be preferred, therefore specific methods and catalysts must be found to bring about selective reactions. Molecular oxygen is a triplet in its ground state making the direct reaction with the majority of organic substrates which are singlets, among them of course dienes and polyenes, a disallowed process. Only upon the input of a large amount of thermal energy, as in gas-phase reactions, can one bring about oxidation of organic substrates, but this has never been successfully done with dienes or polyenes. The use of molecular oxygen, therefore, in essence requires indirect methods for its activation and use in synthetic organic chemistry. In this section, we will discuss these methods. The first possibility is to excite the ground state molecular oxygen to an excited state forming singlet oxygen, $^1O_2$. This is commonly done with light radiation using photosensitizers[143]. The singlet oxygen thus formed is highly reactive with organic substrates and has been especially and successfully used in the formation of numerous endoperoxides from conjugated dienes[143]. A second method commonly employed to use molecular oxygen in organic chemistry is to form hydrocarbon radicals[144]. These radicals react at a diffusion-controlled rate with molecular oxygen, forming peroxides. These intermediates can propagate a radical chain reaction, termed autooxidation, by formation of more hydrocarbon radicals and intermediate hydroperoxides. Initial formation of hydrocarbon radicals occurs occasionally due to thermal carbon–hydrogen bond disassociation, although for most practical applications thermally sensitive initiators are employed. Alternatively, photoactivation as well as use of catalysts of sufficient oxidation potential may be considered in order to initialize radical formation. A third method to utilize molecular oxygen is to form metal–dioxygen bonds which, under appropriate conditions, form highly active metal-oxo intermediates[145]. In nature, monooxygenase enzymes such as cytochrome P-450 or methane monooxygenase utilize reducing agents in order to split the oxygen–oxygen bond. Dioxygenases are also known. Although many enzymatic systems have been discovered, they are as yet relatively poorly understood and have not been translated by comparable synthetic or biomimetic systems to diene oxidation. A fourth way to use molecular oxygen is as the secondary oxidant in a catalytic cycle. In such a cycle a primary oxidant, often a metal catalyst, is used to carry out the original oxidative transformation of the organic substrate. The reduced primary oxidant or metal catalyst can then be reoxidized by molecular oxygen. The most important prototype of this reaction is the palladium-catalyzed oxidation of alkenes, commonly termed the Wacker process or reaction[146]. A fifth and final method for employing molecular oxygen is to pass it between two electrodes at high voltages thereby producing ozone, O_3. The latter is a highly potent oxidizing agent[147].

A. Singlet Oxygen

Singlet oxygen may be produced chemically by reaction of hydrogen peroxide and hypochlorite. The most useful procedure, however, is via sensitized photooxidation (equation 20). Light absorption of the sensitizer leads to formation of a sensitizer in the excited singlet state. In some cases, especially with electron-poor aromatics and ketones, a type I photooxidation will take place whereby electron transfer between the substrate and the excited state singlet sensitizers will yield a radical ion. The latter will react with ground triplet oxygen. These types of reactions will be discussed in the next section. More commonly, the excited singlet sensitizer, most commonly rose bengal, methylene blue and porphyrins, undergoes intersystem crossing to the triplet state and then reacts in a type II photooxidation with ground state oxygen to form singlet oxygen, which then reacts with the organic substrate to form product. The reaction of singlet oxygen with conjugated dienes forms endoperoxides as the initial product by a Diels–Alder type reaction where singlet oxygen reacts as a dienophile[148]; the reaction of **94** to **95** (equation 21) is simply a fairly recent example[149]. Reactions are most efficiently selective to the endoperoxides at low temperatures in halogenated or deuterated solvents.



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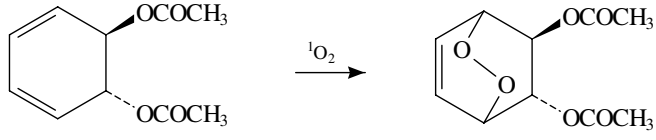
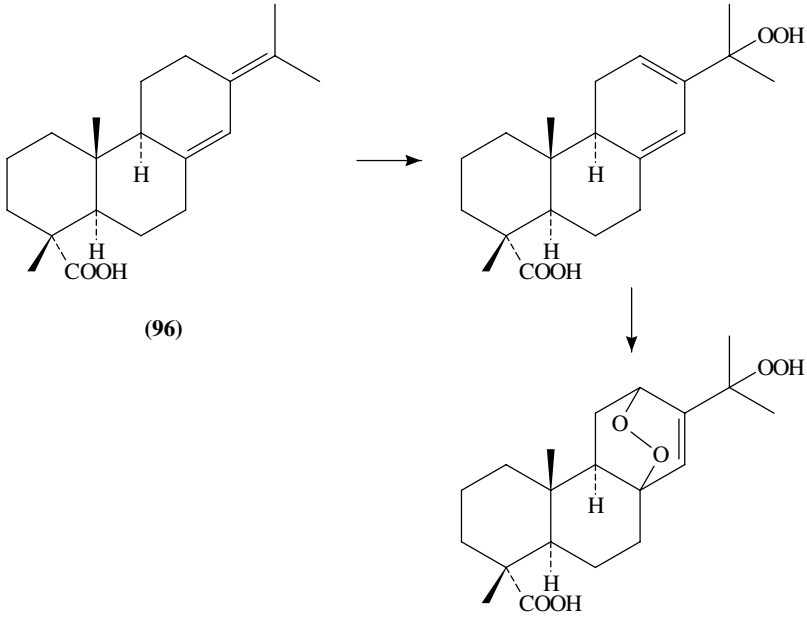


(21)

(94) **(95)**

Kinetic measurements showed the following relative rates for oxidation with singlet oxygen with representative conjugated dienes: 1,3-cyclooctadiene < 2-*cis*-4-*trans*-hexadiene < 2-*trans*-4-*trans*-hexadiene ~ 1,3-pentadiene < 1,3-cycloheptadiene < 1,3-cyclohexadiene < 1,3-cyclopentadiene[150]. The slow reactions of the eight-membered and larger rings are attributed to the lack of planarity of the diene[151]. The slower rate of addition for acyclic dienes vs cyclic dienes often causes formation of byproducts such as dioxetanes and hydroperoxides in the reaction of the former, which are rarely observed in the latter. An interesting example showing both formation of the hydroperoxide in acyclic dienes and endoperoxide formation in cyclic hexadienes was observed in the oxidation of neoabietic acid **(96)** to the endoperoxide **97** (equation 22)[152].



(96) (22)

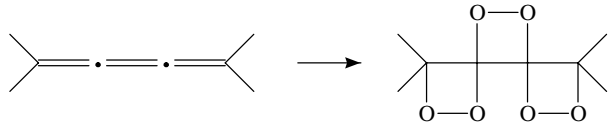
(97)

The literature on the oxidation of dienes with singlet oxygen is very voluminous and only recently both the mechanistic and synthetic aspects of this reaction have been very thoroughly reviewed and therefore will not be repeated here[153]. It is worth pointing out that the stable endoperoxides formed in the addition of singlet oxygen to conjugated dienes may be manipulated in many ways to form further interesting products, for example by reduction[154] or rearrangement[155]. Products which may be obtained include acids, ketones and aldehydes, alcohols, epoxides and others depending on the specific additional conditions applied during or after the singlet oxygen reaction.

Non-conjugated dienes react differently with singlet oxygen. In such substrates each alkene reacts as a separate entity with allylic hydroperoxides being the predominant product via the Schenk reaction[156]. Regioselectivities in such reactions vary to a great degree. The general rule of thumb is that the hydroperoxide is most easily formed at the allylic hydrogen orthogonal to the alkene plane[157] due to the electronic requirement for overlap between p orbitals of the developing double bond in the transition state[158]. It has been shown that functional groups may affect regioselectivity, for instance in the oxidation of α, β-unsaturated ketones[159]. Stereoselectivity in reactions of non-conjugated dienes with singlet oxygen is a newly found phenomenon. In connection with the synthesis of calcitriol (dihydroxyvitamin D_3) both remarkably high regio- and stereoselectivities were observed[160]. A further investigation has shown that the selectivities obtained are due to a combination of electronic and steric effects where addition of carboxylic acid substituents lead to selectivity[161].

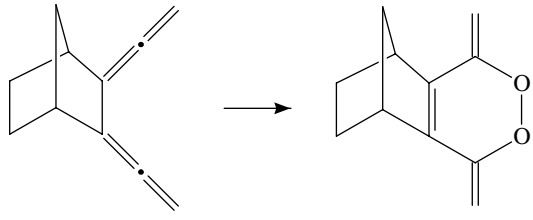
Finally, another interesting use of singlet oxygen in the oxidation of dienes concerns the reactivity of allenes. Besides the formation of endoperoxides by addition to dienes and hydroperoxide formation via the ene reaction, singlet oxygen reacts with electron-rich

alkenes to form dioxetanes. Allenes react in this manner[162]. Thus, the triene **98** yields **99** (equation 23)[163]. Similarly, an adamantane disubstituted allene also yields the same type of product[164]. Dioxetane formation was also observed in the reaction of the norbornene derivative **100** to yield **101** (equation 24)[165].



(23)

(98) **(99)**

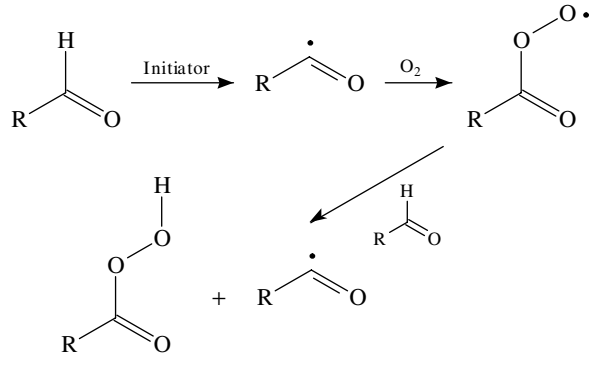


(24)

(100) **(101)**

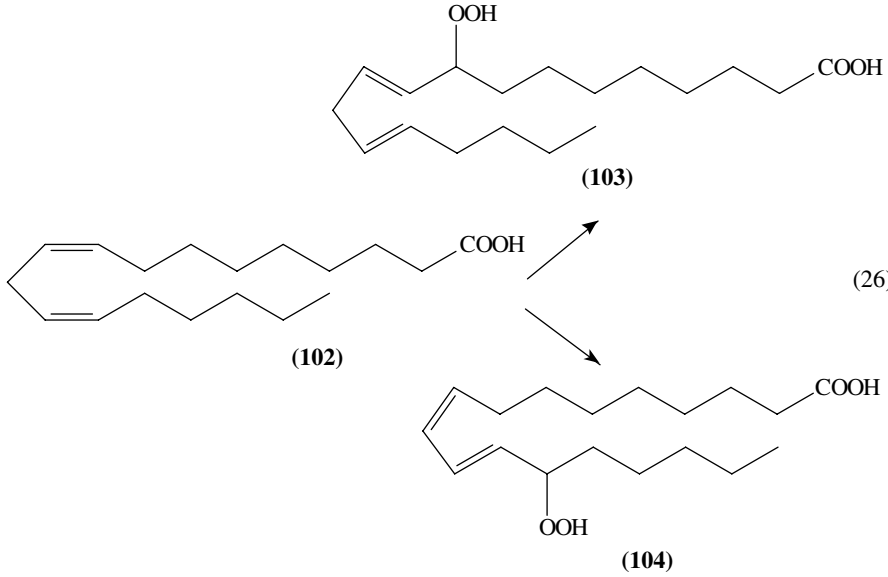
B. Triplet Ground State Oxygen

As stated above, reaction of triplet ground state molecular oxygen with a singlet organic substrate requires formation of a radical (atom transfer) or cation radical (electron transfer) from the former to an initiator or catalyst. This type of chemistry has been realized in a variety of ways. One common scheme is to mix an aldehyde, alkene and dioxygen often in the presence of a catalyst[166]. Since aldehydes are relatively sensitive to hydrogen abstraction, peracids are easily formed in this manner (equation 25). The peracids may then quickly react with the alkenes, also dienes and polyenes, in the reaction mixture to form epoxides. Although these are technically reactions with molecular oxygen, the reactivity and mechanism is more similar to that of organic peracids. A recent example of the use of this technique is in the oxidation of 3-hydroxy-7-methyl-1,6-octadiene to the expected epoxide at the nonallylic position[167]. There has been no further systematic study of diene oxidation using these systems.



(25)

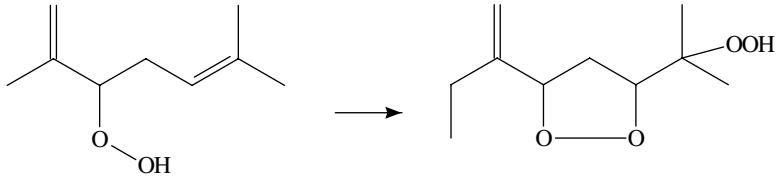
Reaction of molecular oxygen with radicals formed directly from dienes is a subject of chemical, medicinal and biological interest[168]. The polyenes of most interest are the fatty acids, linoleic acid (*cis,cis*-9,12-octadecadienoic acid), γ-linolenic acid (*cis,cis,cis*-6,9,12-octadecatrienoic acid), α-linolenic acid (*cis,cis,cis*-9,12,15-octadecatrienoic acid), arachidonic acid (*cis,cis,cis,cis*-5,8,11,14-eicosatetraenoic acid) and polyenes from the prostaglandin family of compounds. The polyunsaturated acids are important components of membranes and the prostaglandins are important regulatory compounds. The autooxidation of these compounds has often been associated with aging and disease. Using linoleic acid as a model it has been found that carbon–hydrogen bond strengths are 82, 87 and 95 kcal mol^{-1} for the bisallylic, allylic and nonallylic secondary carbons, respectively[169]. Therefore, autooxidation using free radical initiators will predominantly, but not only, yield hydroperoxides at the bisallylic positions. A report on a unified mechanism of polyunsaturated acid autooxidation including kinetic measurements has been carried out for linoleic[170] and triene and tetraene acids[171]. Enzymatic oxidation using lipoxygenase enzymes, however, yields specific products. Thus, for example, using maize lipoxygenase, hydrogen abstraction at the bisallylic position of linoleic acid **(102)** is accompanied by isomerization of the double bond and stereospecific formation of 9-*d*-hydroperoxy-*trans,cis*-10,12-octadecadienoic acid **(103)**. Soybean lipoxygenase will similarly yield the hydroperoxide at the C-13 carbon, i.e. 13-*l*-hydroperoxy-*cis,trans*-9,11-octadecadienoic acid **(104)** (equation 26)[172].



(26)

In the case of arachidonic acid, lipoxygenase enzymes will yield hydroperoxyeicosatetraenoic acids (HPETEs), which may then be enzymatically manipulated to leukotrienes by controlled dehydration or to endoperoxide prostaglandins such as PGG_2 by cyclooxidation[173]. The non-enzymatic reaction of diene hydroperoxides, for example **105** to form the hydroperoxide-endoperoxide **106**, has been studied (equation 27). Many additional substrates have been studied including 1-hydroperoxy-3,5-hexadiene and 1-hydroperoxy-4,8-undecadiene[174]. Similarly, the reaction of the fatty acid hydroperoxides under acid conditions (Hock rearrangement) gives both carbon–carbon bond cleavage and

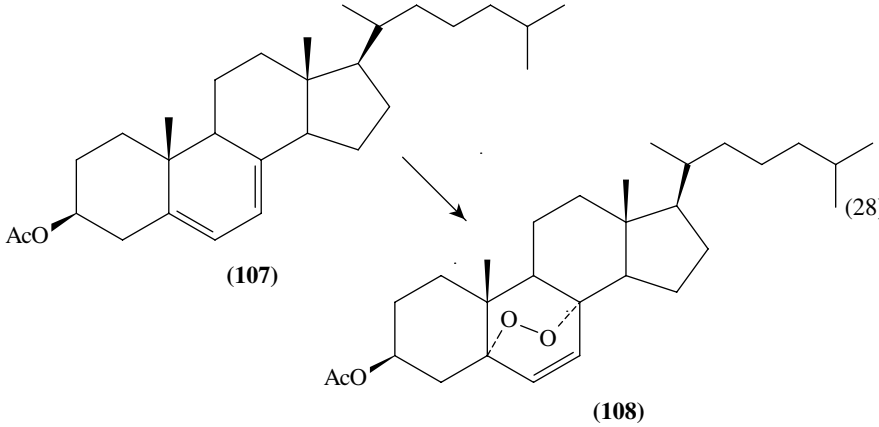
ether formation[175], e.g. colneleic acid[176] via intermediate epoxides. These product types are associated with formation of organic volatiles in food degradation.



(27)

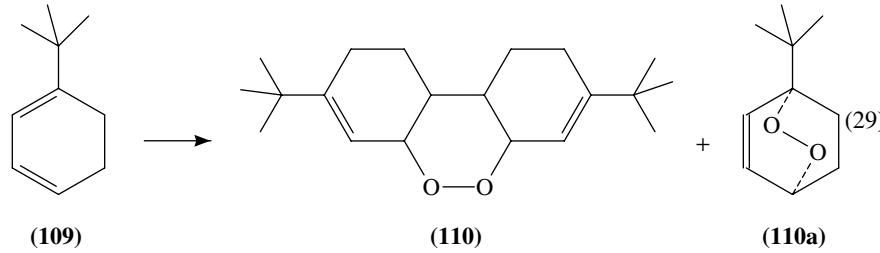
(105) **(106)**

Another interest in the use of triplet oxygen lies in the oxidation of dienes with photochemical activation (Type I, above) with formation of endoperoxides as products. The first example of this reaction was observed in the early 1970's. Thus, reaction of ergosteryl acetate **(107)** in the presence of trityl tetrafluoroborate[177] and Lewis acids[178] in the presence of light yielded the endoperoxide **108** (equation 28). With certain Lewis acids this reaction could be thermally, rather than photochemically, activated. Cation radicals were shown to be the intermediate active species, as was borne out by a comparative oxidation of the isomeric lumisteryl acetate which was inactive under these conditions but reacted easily with singlet oxygen[179]. This reaction was later extended to other substrates. Thus, the intermediacy of cation radicals was also indirectly observed by the fact that the *t*-butyl substituted 1,3-cyclodiene **109** gave a 'dimeric' product **110** (equation 29) via the cation radical intermediate in addition to the usual endoperoxide **110a**[180].



(28)

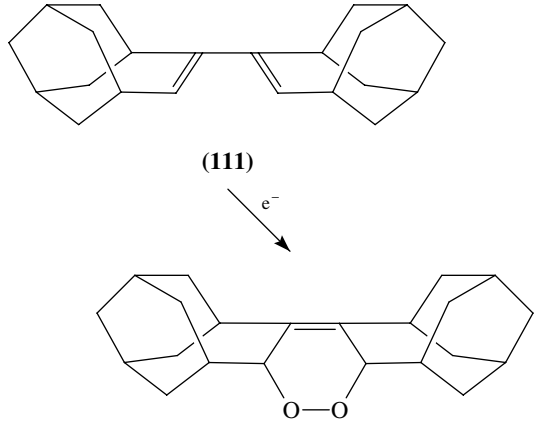
(107) **(108)**



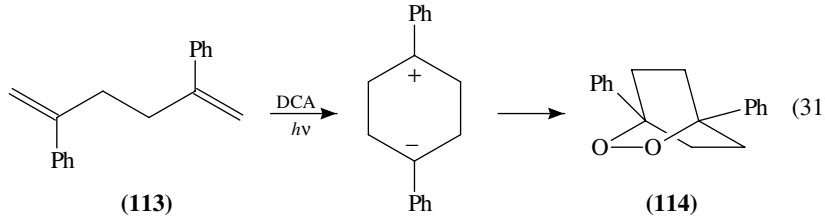
(29)

(109) **(110)** **(110a)**

In an electrochemical transformation of **111**, **112** was obtained as product (equation 30)[181] and 9,10-dicyanoanthracene (DCA) was used to photochemically initiate the reaction of 2,5-diphenyl-1,5-hexadiene **(113)** to **114** (equation 31)[182].



(111) **(112)** (30)

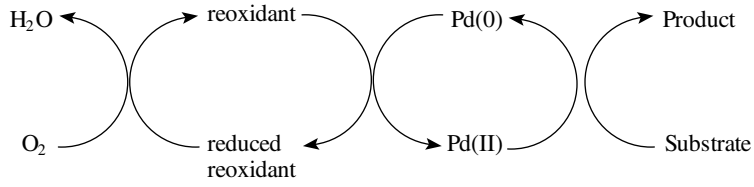


(113) **(114)** (31)

Above, we have discussed some methods for the use of triplet oxygen via interaction with organic radical intermediates. There is a natural interest in the 'activation' of molecular oxygen using transition metal complexes[183]. Excluding examples where the function of the transition metal, most often cobalt, is to form free radicals, the nonradical activation of molecular oxygen is a poorly developed field. As concerns diene oxidation, two rather exceptional examples are worth pointing out. The first is the use of a μ_3-oxo triiron catalyst in the presence of molecular oxygen to epoxidize geraniol acetate at the 6,7 position only, as found for peracid epoxidation[184]. The mechanism is unknown although the interim formation of a radical could not be discounted. Although dioxygen complexes of transition metals are often unreactive, a rhodium complex, $[(COD)_2Rh(O_2)]_2$ (COD = 1,5-cyclooctadiene), heated without any additives in benzene, resulted in oxidation of the 1,5-cyclooctadiene ligand to a mixture containing mostly cyclooctanone and cyclooctanone-4-ene[185]. Addition of $^{18}O_2$ showed that this was an intramolecular reaction.

Although there are indeed only few reported methods of direct activation of molecular oxygen via transition metals, there are many reports of indirect oxidation. The majority of this research is based on palladium-based oxidation as summarized in equation 32. The palladium complex catalyzed oxidation reactions have been reviewed previously[186] and also only very recently[187] and in this book the palladium catalyzed oxidation of dienes and polyenes will be discussed separately and therefore will not be discussed

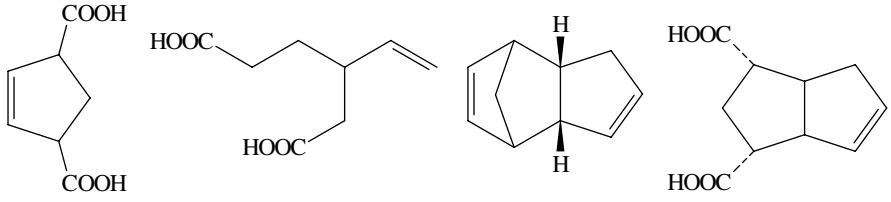
further[188]. Molecular oxygen has also been used as a secondary oxidant in other metal-catalyzed systems. As concerns the subject of this review, it is possible to oxidatively dehydrogenate cyclic dienes to the corresponding aromatic products using the polyoxometalate, $H_5PV_2Mo_{10}O_{40}$, as catalyst. In such a way anthracene is obtained from 9,10-dihydroanthracene and *p*-cymene is the product of limonene dehydrogenation. In the latter case, dehydrogenation is preceded by isomerization of the exocyclic double bond[189].



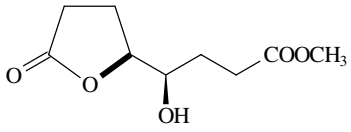
(32)

C. Ozone

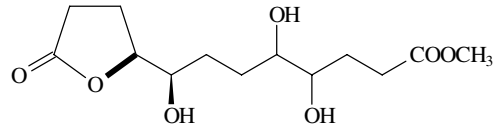
Ozonolysis as used below is the oxidation process involving addition of ozone to an alkene to form an ozonide intermediate which eventually leads to the final product. Beyond the initial reaction of ozone to form ozonides and other subsequent intermediates, it is important to recall that the reaction can be carried out under reductive and oxidative conditions. In a general sense, early use of ozonolysis in the oxidation of dienes and polyenes was as an aid for structural determination wherein partial oxidation was avoided. In further work both oxidative and reductive conditions have been applied[190]. The use of such methods will be reviewed elsewhere in this book[191]. Based on this analytical use it was often assumed that partial ozonolysis could only be carried out in conjugated dienes such as 1,3-cyclohexadiene, where the formation of the first ozonide inhibited reaction at the second double bond[192]. Indeed, much of the more recent work in the ozonolysis of dienes has been on conjugated dienes such as 2,3-di-*t*-butyl-1,3-butadiene[193], 2,3-diphenyl-1,3-butadiene[194], cyclopentadiene[195] and others[196,197]. Polyethylene could be used as a support to allow ozonolysis for substrates that ordinarily failed, such as 2,3,4,5-tetramethyl-2,4-hexadiene, and allowed in addition isolation of the ozonide[198]. Oxidation of nonconjugated substrates, such as 1,4-cyclohexadiene and 1,5,9-cyclododecatriene, gave only low yields of unsaturated dicarboxylic acids. In a recent specific example 1,4-cyclohexadiene yields mostly malonic acid or esters as product depending on the solvent[199]. In oxidative ozonolysis use of a emulsion with aqueous hydrogen peroxide allowed higher yields[200]. Later on, use of silver oxide allowed formation of **115** from norbornadiene[201] and **116** from vinylcyclohexene[202]. Treatment of the dicyclopentadiene **(117)** gave the dicarboxylic acid **118**[203]. Use of selenium dioxide after the ozonolysis of 1,4-cyclohexadiene and 1,5,9-cyclododecatriene yielded stereospecific formation of lactones **119** and **120**, respectively[204]. Reductive ozonolysis has been useful in formation of



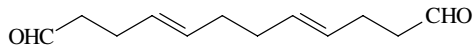
(115) **(116)** **(117)** **(118)**



(119)



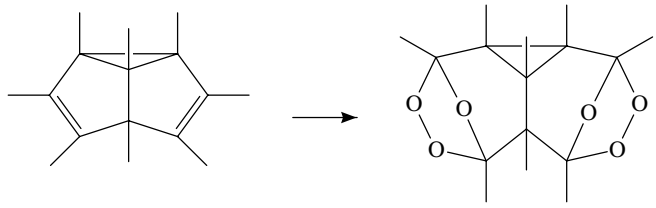
(120)



(121)

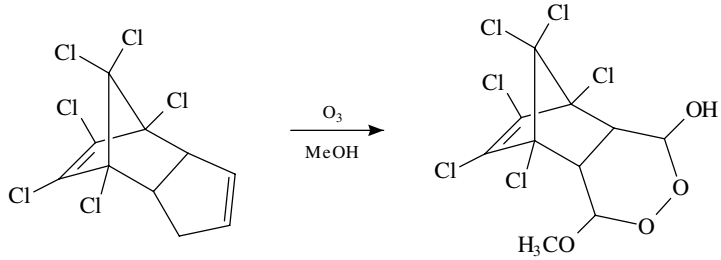
unsaturated dialdehydes, ketones and even alcohols. For example, the intermediate monoozonide of 1,5,9-cyclododecatriene could be catalytically reduced with H_2 to yield the dialdehyde **121**[205]. Other similar reactions have been reviewed[206]. Ozonolysis of di-vinyl ethers yielded keto-ethers or keto-alkenes, depending on the solvent[207].

Reaction of ozone with a double bond is not surprisingly a function of the nucleophilicity or electron density of the double bond. Therefore, in ozonolysis of octamethylsemibullvalene[208] **(122)** as well as for hexamethylbicyclo[2.2.0]-2,5-hexadiene[209] and octamethyltricyclo-octadiene[210] the diozonides, e.g. **123**, are formed as the major product (equation 33). On the other hand, for hexachlorobicyclopentadiene[211] **(124)**, hexachlorobicycloheptadiene[212] and 2-chloro-3-methyl-1,3-butadiene[213] attack takes place at the nonchlorinated double bond only to form the ozonide **125** (equation 34).



(33)

(122) **(123)**



(34)

(124) **(125)**

Finally, there has also been research into the ozonolysis of allenes. Thus sterically hindered allenes react by transfer of one oxygen atom, forming a mixture of reaction products[214]. Recently, the ozonolysis of a cyclopropylallene has been shown to yield a diastereomeric mixture of cyclopropyl esters[215].

V. SUMMARY AND CONCLUSIONS

In the review presented above, we have tried to point out the major pathways for oxidation of dienes and polyenes useful for organic synthesis. It is apparent that the many different methods bring about different product types allowing great flexibility in the functionalization of dienes and polyenes. Emphasis has been placed on the synthetic aspects with the adjutant kinetic and mechanistic questions receiving less attention, the latter often reviewed in connection with alkene oxidation, wherein dienes and polyenes are a specific subgroup. Not discussed were the many possibilities for oxidizing substrates containing both dienes and other functional groups where, in fact, the other functionality is reactive and the diene inert. An attempt has been made to give a complete spectrum of samples reported in the literature, although it is certain that some examples have surely missed our attention. This is true especially concerning specific examples mentioned, among many others, in papers dealing with the oxidation of monoalkenes and also for examples reported in the patent literature. There are other reports which were beyond the scope of this paper. For example, isoprene (2-methyl-1,3-butadiene) is a natural hydrocarbon emitted from plants at a level of 4.4×10^6 ton year^{-1} in the USA alone. Research has been carried out on the reaction of isoprene with several oxidants such as ozone[216,217], the hydroxyl radical and atomic oxygen simulating its reaction in the troposphere[218]. This type of research has even been expanded to other substrates, including other terpenes[219].

It would appear that the oxidation of dienes and polyenes has reached a stage of maturity in the context of available oxidants as to the type of transformations and product types accessible. Future work with known oxidants and oxidation systems, however, will surely enable advances in the synthesis of complex organic molecules. On the other hand, new oxidants and oxidation systems will certainly also find their way to application in transformation of dienes and polyenes.

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CHAPTER **21**

Synthesis and transformation of radialenes

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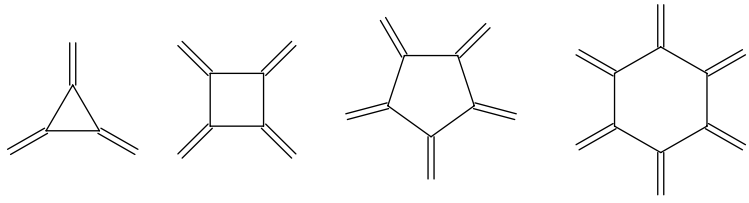
I. INTRODUCTION

A. Nomenclature and Classification

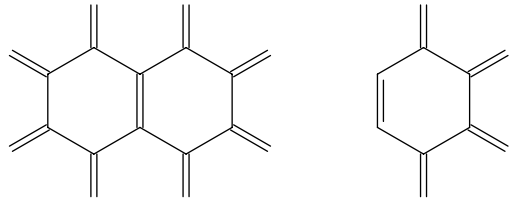
Radialenes are alicyclic compounds in which all ring carbon atoms are sp^2-hybridized and carry as many exocyclic double bonds as possible. The general term for the parent

molecules is [*n*]radialenes where $n \geqslant 3$ and stands both for the ring size and the number of double bonds involved. Thus the hydrocarbons **1–4**, with the general formula C_nH_n ($n = 3,4,5,6$) are [3]-, [4]-, [5]-, and [6]radialene.



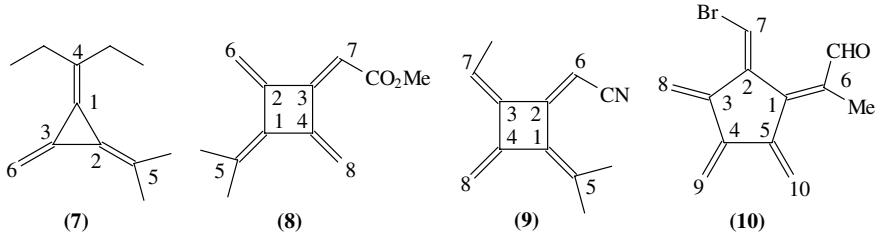
(1) **(2)** **(3)** **(4)**

It is obvious that these compounds have in common an uninterrupted cyclic arrangement of cross-conjugated π-systems. Compound **5** likewise contains the maximum number of exocyclic double bonds at a perimeter consisting only of sp^2-hybridized carbon atoms. Thus, our definition allows one to call it a radialene, i.e. naphtharadialene; on the other hand, it excludes hydrocarbons such as **6** [3,4,5,6-tetrakis(methylene)cyclohexene]. Although in the latter molecule all carbon atoms are indeed sp^2-hybridized, the number of exocyclic double bonds has not reached its maximum. In **5**, however, the number of double bonds cannot be increased further.



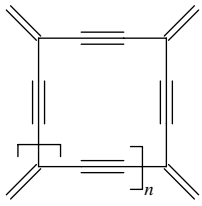
(5) **(6)**

It is of course possible to name individual radialenes according to IUPAC rules [e.g. per(methylene)cycloalkanes **1–4**]. However, the descriptiveness of the term 'radialene' may some day pave its way into the 'official' nomenclature. For substituted [*n*]radialenes we have proposed[1] a 'pragmatic' numbering system, in which an 'inner ring' is numbered first, followed by an 'outer ring'. The numbering of substituents should follow IUPAC rules. Thus, the hydrocarbon **7** is 4,4-diethyl-5,5-dimethyl[3]radialene, the ester **8** should be called 7-methoxycarbonyl-5,5-dimethyl[4]radialene, the nitrile **9** which can exist in four diastereomeric forms is (6*Z*,7*Z*)-6-cyano-5,5,7-trimethyl[4]radialene and the difunctionalized [5]radialene **10** is (7*E*,6*Z*)-7-bromo-6-formyl-6-methyl[5]radialene.

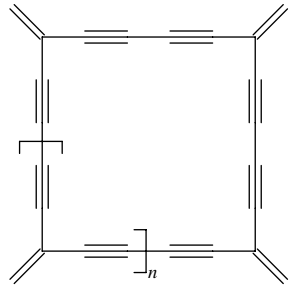


(7) **(8)** **(9)** **(10)**

We are aware that these simple rules must and will be extended as the structural complexity of the known radialenes evolves. Unfortunately, however, the 'catchiness' of the term radialene has led to its inflationary use in recent years. Although we think it is justified to call molecules such as **11** and **12** 'expanded' [4]- ($n = 1$) and [6]radialenes ($n = 3$) — by widening our above definition, since sp-hybridized carbon atoms are 'allowed' — we hesitate to call compounds of the type **13** heteroradialenes.



(11)



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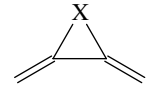
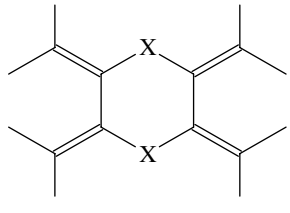


X = SiR_2, NH, PH, S, ···

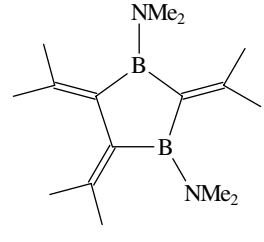
(13)

If one were to call compounds **13** radialenes, one would have to include molecules such as **14** and **15** as well. Although this has been done in the chemical literature we prefer to regard these latter unsaturated ring systems as polyalkylidene heterocycles. One reason for this is that they are lacking the characteristic cross-conjugation encountered in the radialenes (see above).



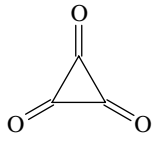
X = SiR_2, SnR_2, BR

(14)

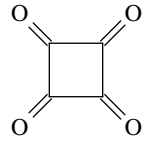


(15)

On the other hand, radialenes whose methylene groups have been replaced partially or totally by heteroatoms or heteroorganic groups — as examples, the (unknown) 'oxocarbons' **16** and **17** may be quoted as well as the tetraaza[4]radialene **18** and 'mixed' systems such as **19–21** — are clearly covered by the above definition if 'sp^2-hybridized carbon atom' is replaced by the appropriate isovalent group. Such heteroradialenes, however, will



(16)



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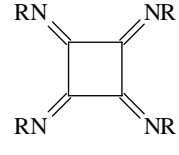

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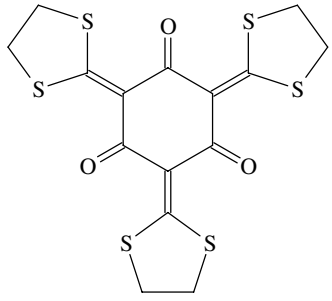
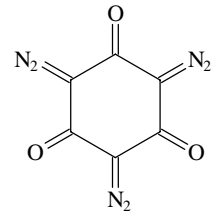


(19)



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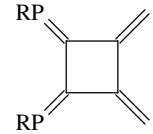


(21)

not be presented here in detail, since this volume deals with the chemistry of C=C double bond systems.

B. Significance of the Radialenes

Among the olefins — and unsaturated systems in general — the radialenes were the last to attract the interest of the chemists. Although the number of publications dealing with these cross-conjugated molecules has been growing rapidly during the last decade, they still cannot compete in importance with many of the other classes of dienic and polyenic π-systems discussed in this Volume. In fact, it appears likely that they will always play a specialized role among the numerous unsaturated hydrocarbon systems and their derivatives. However, many of the reactions employed to prepare the radialenes are useful in other fields of synthetic chemistry, the structural data obtained are of importance in comparsion to those of other π-structures, and for the development of computational methods the radialenes are also important reference structures. The radialenes are hence not only of importance for their own sake.

The last review on radialenes — which is also the first ever published and still the only available one — was published by the authors just a few years ago[1]. This, of course, raises the question of whether the present summary is really necessary. We believe it is — not only for the sake of completeness but also since especially during the last five-year period there has been significant progress in the radialene area. The main reason for this lies outside of radialene chemistry and has to do with the development of fullerene chemistry on the one hand, and various attempts to synthesize novel carbon allotropes and networks on the other. For example, C_{60} may be regarded as a cyclic dodecamer of (the still unknown) [5]radialene hydrocarbon — the six-membered ring of the former being produced 'automatically' when the hydrogen atoms of the latter are 'removed' (on paper). Correspondingly, partial structures of C_{60} containing five-membered rings may be regarded as derivatives of [5]radialene also. The so-called 'exploded' radialenes (see below) are other examples of the extension of a basic radialene structural element to a larger molecular framework or scaffold.

C. Scope of the Review

Since our earlier review[1] appeared not so long ago, it makes no sense to repeat here all facets of the radialene family. Therefore, we focus here on the synthesis and chemical transformation of the radialenes, and we suggest the reader consult our earlier review for information on structural and spectroscopic data as well as the use of radialenes as building blocks for organic conductors and organic ferromagnets, as these topics will not

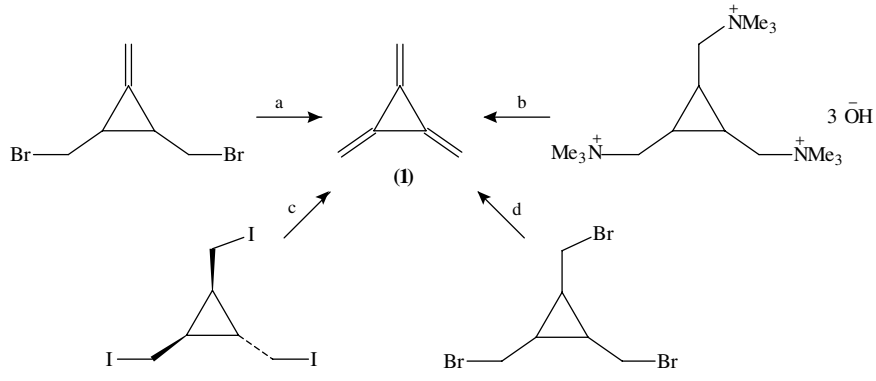
be discussed in this chapter any more. We have tried to include in the present review the material published in the primary literature until the end of 1995. Besides using our own literature files we carried out both a Chemical Abstract and Beilstein Crossfire™ literature search.

II. SYNTHESIS AND TRANSFORMATION OF RADIALENES

A. [3]Radialenes

The parent [3]radialene **1** has been generated from variously functionalized cyclopropane precursors by classical β-elimination reactions (Scheme 1)[2–6]. All these reactions have been carried out as gas-phase reactions, and the radialene has been collected at $-63\,^{\circ}C$ or below. At $-78\,^{\circ}C$, the pure compound is stable for several days, but polymerization occurs when the vapor is exposed to room temperature as well as in carbon tetrachloride at 273 K[2], or in contact with oxygen[3].

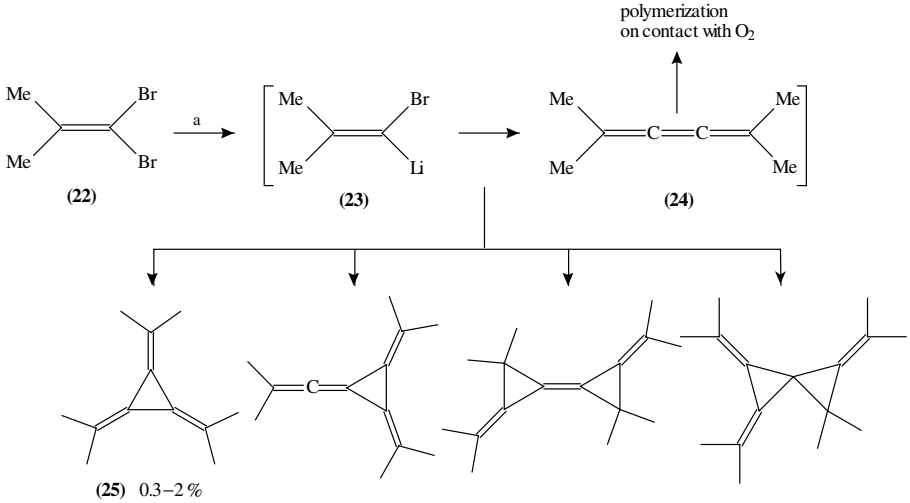
Attempts to prepare **1** from some other precursors were largely unsuccessful: *N*, *N′*, *N″*-(cyclopropane-1,2,3-trimethyl)-tris(dimethylamine oxide) decomposed unspecifically above $250\,^{\circ}C$[3] and pyrolysis of 1,2,3-tris(acetoxymethyl)cyclopropane gave mainly benzene[3]; its gas-phase pyrolysis at 570–580 °C produced a mixture of at least fifteen compounds containing perhaps a small amount of **1**[7].



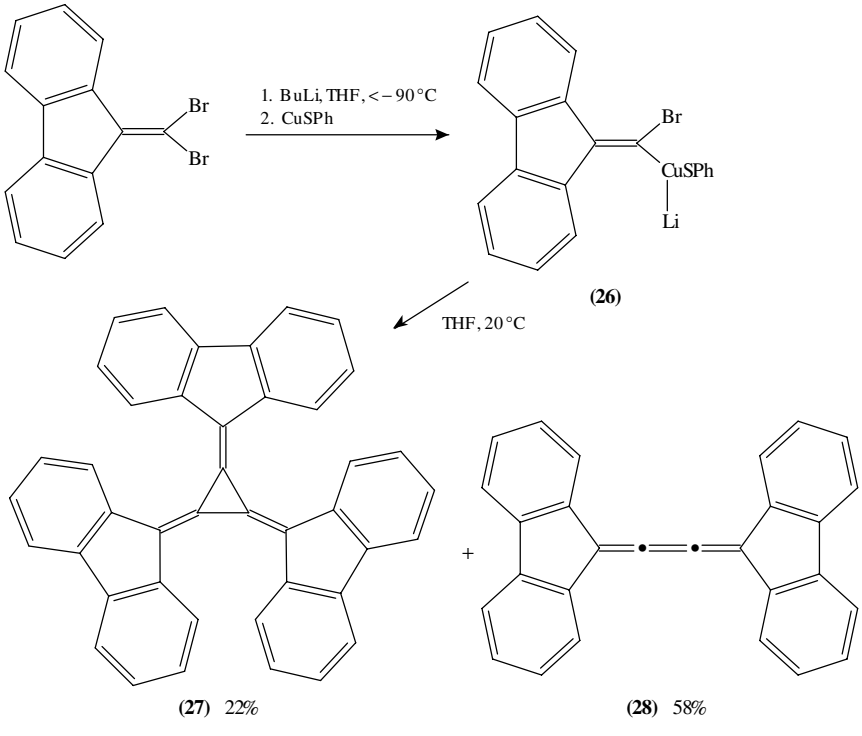
SCHEME 1. Reagents: (a) KOH, 150 °C, 47% yield[2]; (b) 160–170 °C, 4.5 Torr, 1.5% yield[3,4]; (c) KOH, 140 °C, *ca* 20% yield[3,4]; (d) powdered KOH, CaO, 150 °C, 1 Torr, no yield given[5,6]

Various alkyl- and aryl-substituted [3]radialenes could be prepared from 1,1-dihaloalkenes using organometallic pathways. Hexamethyl-[3]radialene **(25)**, the first [3]radialene to be synthesized, was obtained in a very low yield by treatment of 1,1-dibromo-2-methyl-1-propene **(22)** with butyllithium[8,9]. The lithium carbenoid **23** and the butatriene **24** are likely intermediates of this transformation (Scheme 2), the former being the source of an unsaturated carbene moiety which is transferred onto the latter. However, the outer double bonds of **24** are more readily cyclopropanated than the central one.

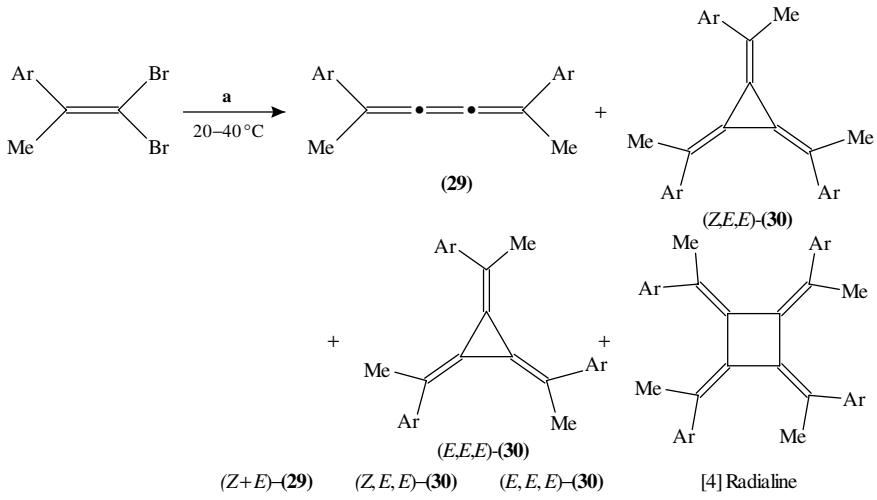
It appears that neither the lithium carbenoid pathway nor the cyclopropanation of butatrienes are general routes to [3]radialenes. More successful is the cyclotrimerization of 1,1-dihaloalkenes via copper or nickel carbenoids, provided the substituents at the other end of the C=C double bond are not too small. Thus, tris(fluoren-9-ylidene)cyclopropane **27** was formed besides butatriene **28** from the (1-bromo-1-alkenyl)cuprate **26** generated *in situ* from (9-dibromomethylene)fluorene (Scheme 3)[10]. The cuprate complexes formed



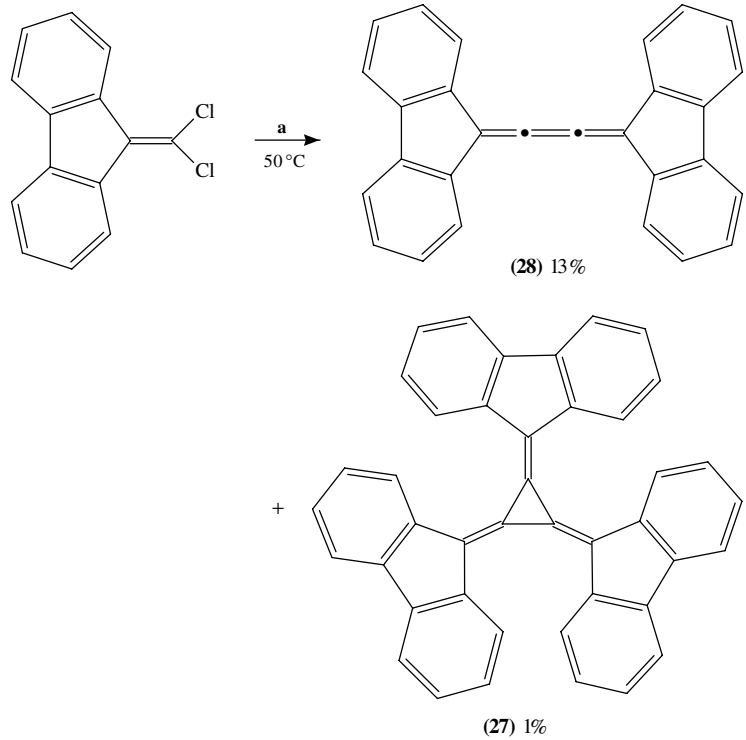
SCHEME 2. Reagents: (a) 2 equiv. of **22**; 1. BuLi (1.25 equiv.), THF, −110 °C; 2. −110 °C → −65 °C; 3. BuLi (0.75 equiv.), −65 °C → 20 °C



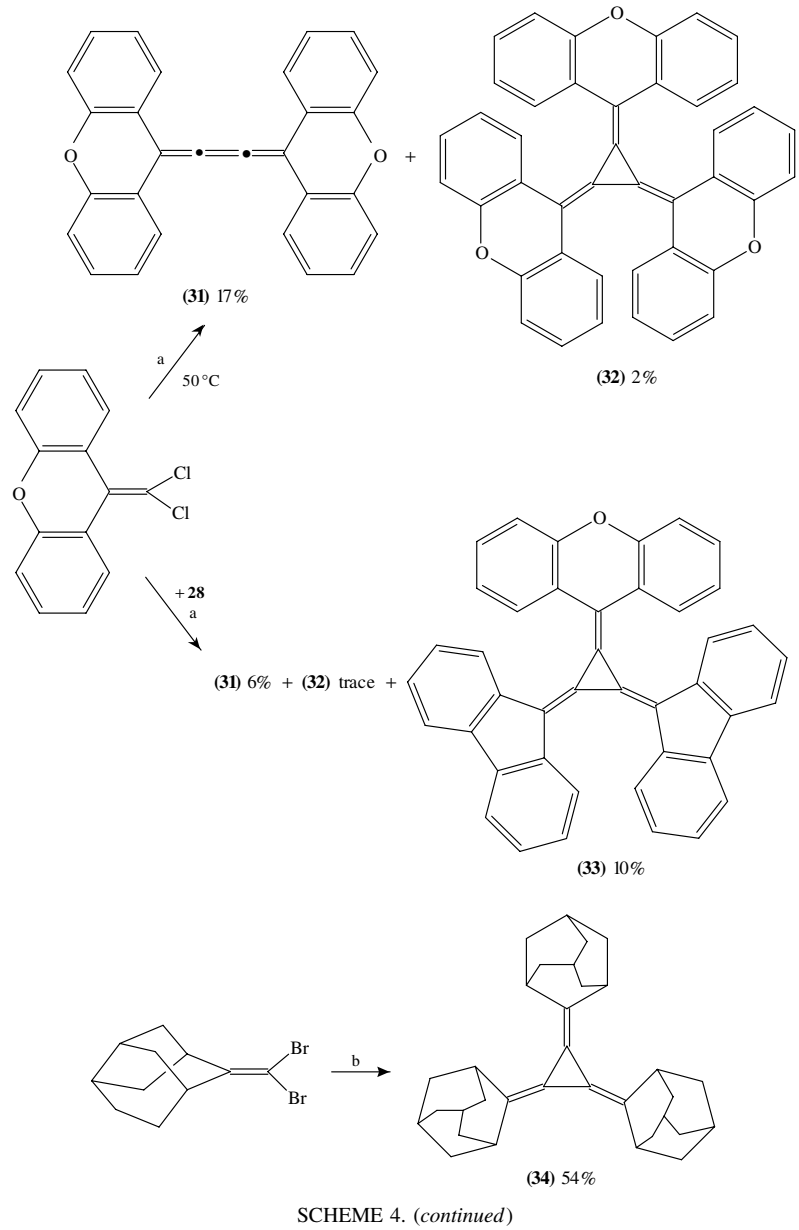
SCHEME 3



	(Z+E)–(29)	(Z, E, E)–(30)	(E, E, E)–(30)	[4] Radialine
(a) Ar = Ph	5%	22%	7%	trace
(b) Ar = 4-ClC_6H_4	3%	43%	12%	–
(c) Ar = 4-NCC_6H_4	14%	53%	5%	trace



SCHEME 4. Reagents: (a) Ni (5–10 equiv.), THF, ultrasound; (b) NiI_2, Li, 4,4′-di-*tert*-butylbiphenyl, THF, 50 °C



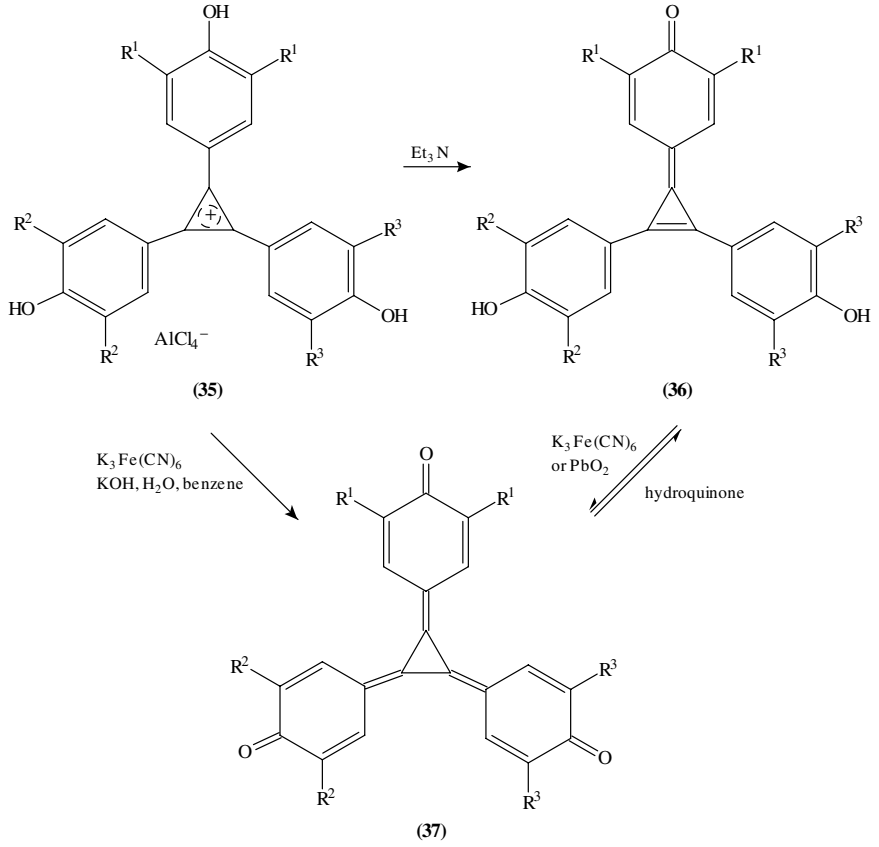
SCHEME 4. (*continued*)

with $CuI{\cdot}PBu_3$ or $CuBr{\cdot}Me_2S$ gave the radialene in only 2–3% yield together with **28** (76–85%), and with CuCN only traces of **27** were found. Furthermore, decomposition of the cuprate obtained with $CuI{\cdot}PBu_3$ in the presence of butatriene **28** did not result in an improved yield of **27** which suggests that the cumulene is not an intermediate in the radialene formation, in contrast to the lithium carbenoid pathway shown in Scheme 2.

While no [4]- and [5]radialenes were formed in the decomposition of cuprate **26**, the analogous cuprate generated from 1,1-dibromo-2,2-diphenylethene led to the corresponding [4]radialene, and [4]- and [5]radialenes were obtained from the cuprate derived from **22** (see Section II.B and II.C). These findings point to a steric influence on these cyclooligomerization reactions, with sterically demanding substituents favoring the formation of [3]radialenes.

The most recent strategy to prepare [3]radialenes is the treatment of 1,1-dihaloalkenes with activated nickel. Thus, the aryl-substituted [3]radialenes (*Z*,*E*,*E*)-**30** and (*E*,*E*,*E*)-**30**, **27** and **32** were obtained together with the corresponding butatrienes (**29**, **28**, **31**) from the 1,1-dibromo- or 1,1-dichloroalkenes with the help of nickel activated by ultrasound (Scheme 4)[11]. It is worth mentioning that the mixed-substituted radialene **33** was produced, when the nickel carbenoid derived from 9-(dichloromethylene)xanthene was generated in the presence of butatriene **28**[11].

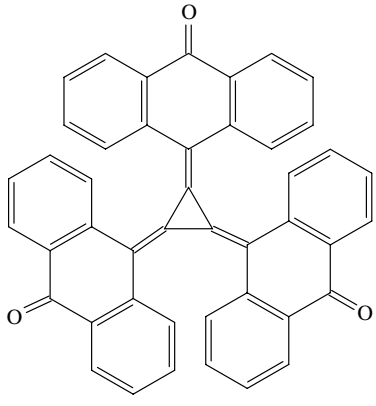
Treatment of 2-(dibromomethylene)adamantane with Ni(0) generated from $NiBr_2$-$(PPh_3)_2$, Zn and PPh_3 in DMF gave the corresponding butatriene as the main product, but no tris(2-adamantylidene)cyclopropane **34**. However, when the activated nickel was generated from NiI_2 and Li powder with 4,4′-di-*tert*-butylbiphenyl as electron carrier



SCHEME 5. **35–37**: **(a)** $R^1 = R^2 = R^3 =$ Me; **(b)** $R^1 = R^2 = R^3 =$ *i*-Pr; **(c)** $R^1 = R^2 = R^3$ *t*-Bu; **(d)** $R^1 = R^2 =$ *t*-Bu, $R^3 =$ Me; **(e)** $R^1 = R^2 =$ *t*-Bu, $R^3 =$ *i*-Pr; **(f)** $R^1 =$ *i*-Pr, $R^2 = R^3 =$ *t*-Bu

in THF, radialene **34** was the sole product in 54% isolated yield (Scheme 4)[12]. These results show that the success of the Ni(0)-mediated cyclotrimerization reactions depends on many factors, including the nickel activation, as well as electronic (cf **30a–c**; electron-withdrawing aryl substituents give better yields) and steric factors (successful formation of **34** as opposed to [4]- and [5]radialene formation from 1,1-dibromo-2-methylpropene, see Sections II.B and II.C).

A variety of functionalized [3]radialenes have been prepared starting from the appropriately substituted cyclopropanes or cyclopropenes. West and Zecher have pioneered the chemistry of [3]radialenes with quinoid substituents. The general strategy of this synthesis is outlined in Scheme 5[13]. A tris(4-hydroxyphenyl)cyclopropenylium



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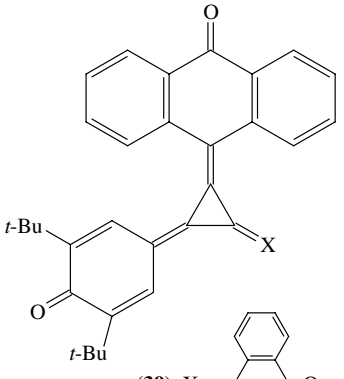
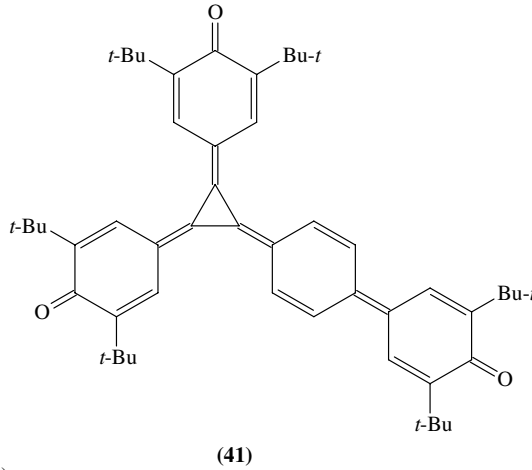


(39) X = (9-anthron-10-ylidene)



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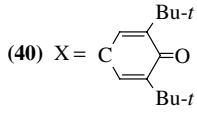
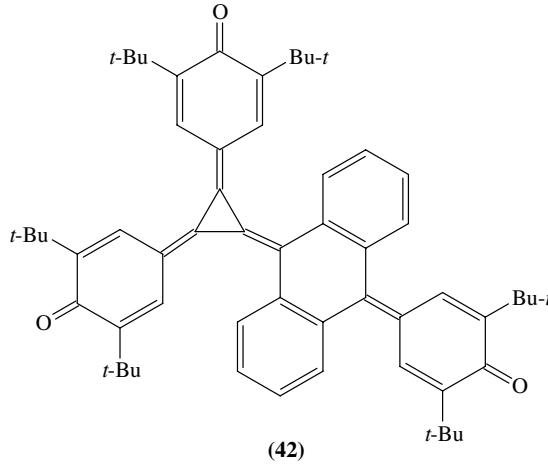


(40) X =

salt **35**, which is obtained from the trichlorocyclopropenylium salt $CCl_3^+ \cdot AlCl_4^-$, is deprotonated to give a methylenecyclopropene **36**. Oxidation of the latter provides the desired tris(quino)cyclopropane **37**. The deprotonation/oxidation sequence can also be carried out in a two-phase system as a one-pot reaction.

The thermal stability in air of the deeply colored radialenes **37** increases with the efficiency of steric shielding of the carbonyl groups. Thus, **37a** was only detected in solution by its UV/Vis spectrum, whereas **37b** and **37c** are reduced to their precursors, **36b** and **36c**, when heated in air at 133 and 280 °C, respectively. In solution, this reduction is readily accomplished with hydroquinone[13].

Various other [3]radialenes bearing quinoid substituents have been synthesized analogously, for example **38**[14], **39**[14], **40**[15], **41**[16], **42**[15], and the rather unstable **43**[17]. In contrast to most other tris(quino)cyclopropanes, reduction of tris(anthraquino)cyclopropane **38** does not succeed with hydroquinone, but requires more forcing conditions (Sn/HCl or Zn/HCl). Compound **44** represents the only tropoquino-substituted [3]radialene known so far[18]; the black-blue crystals of this strongly electron-accepting radialene are stable to air and light.



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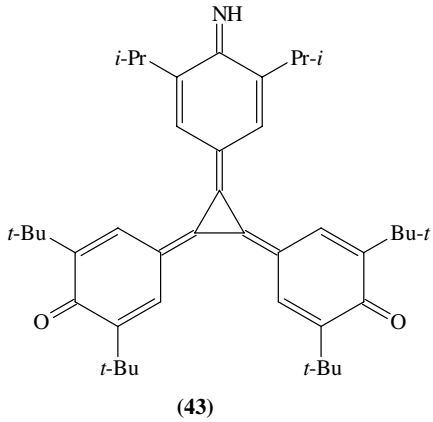

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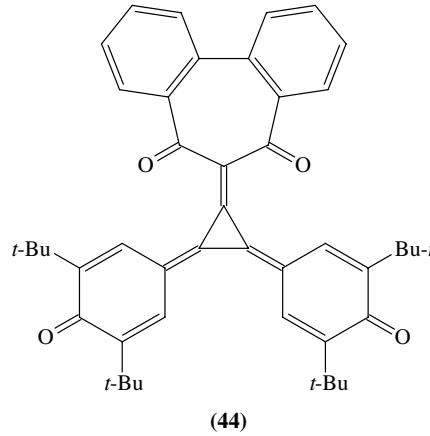
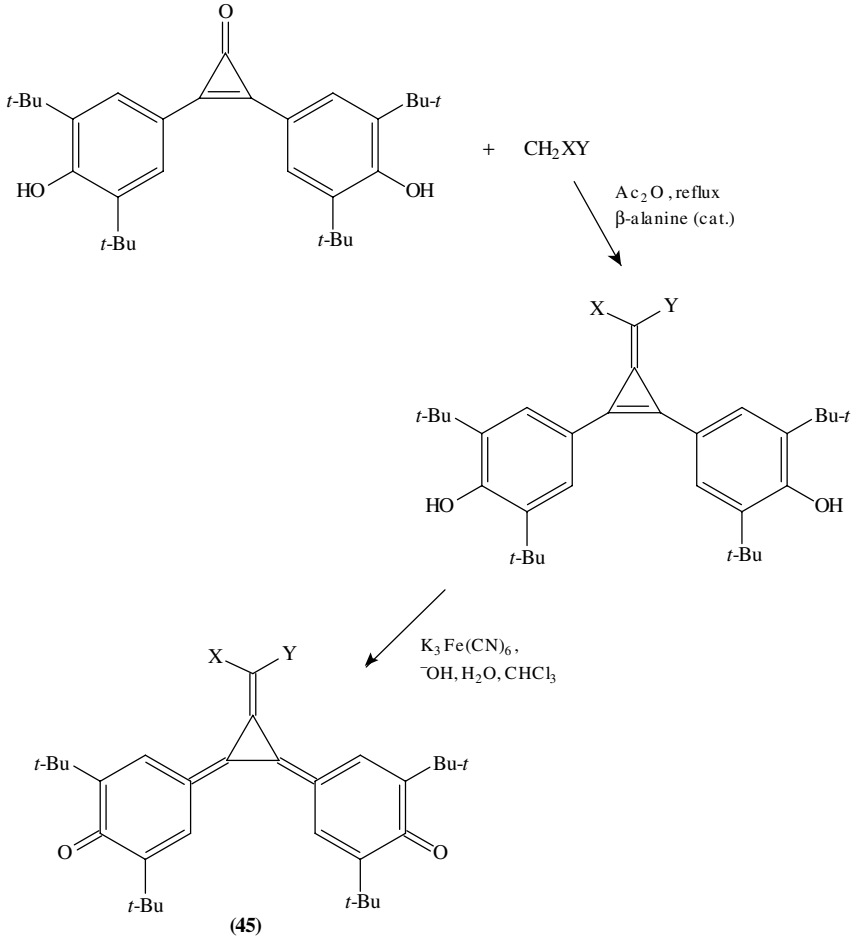
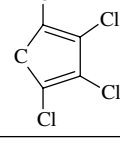
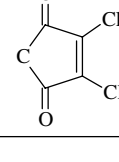
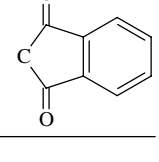


(44)

[3]Radialenes which are structurally related to **44**, i.e. cyclopropanes bearing two quinoid and another acceptor-substituted methylene substituent, were obtained by condensation of bis(4-hydroxyphenyl)cyclopropenones with active methylene compounds, followed by oxidation (Scheme 6)[19]. Radialenes **45a–f** are brilliantly colored solids that are blue or blue-violet in solution but appear metallic gold or red in reflected light. Instead



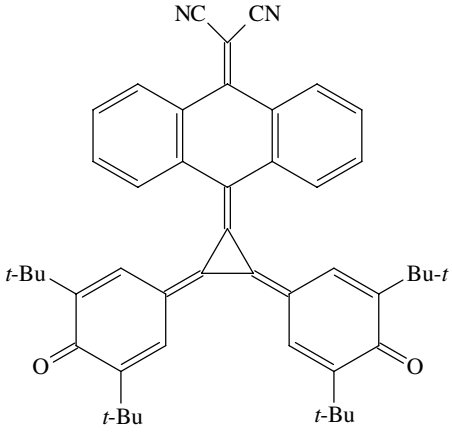
(45)

(45)	(a)	(b)	(c)	(d)	(e)	(f)
CXY	$C(CN)_2$		$C(COMe)_2$			

SCHEME 6

of active methylene compounds, arenologous malononitriles such as 9-anthryl-, 2-thienyl- or 2-selenienyl-malononitrile can be employed in the condensation step which gives access to the [3]radialenes **46**[20], **47**[21] (R = *t*-Bu: quite stable in the solid state and in solution; R = Me: stable in solution at room temperature) and **48**[22].

Tetrachlorocyclopropene is another building block for [3]radialenes (Scheme 7). Its reaction with anions of active methylene compounds such as malononitrile



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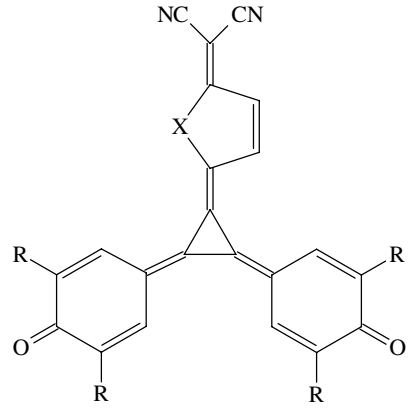
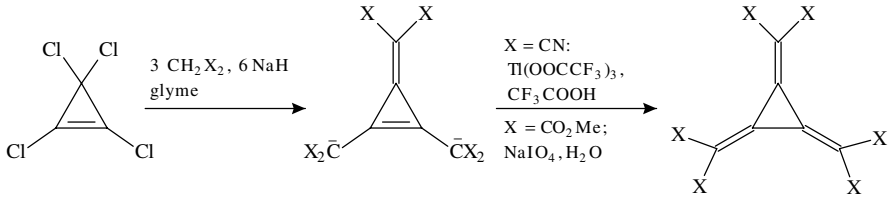
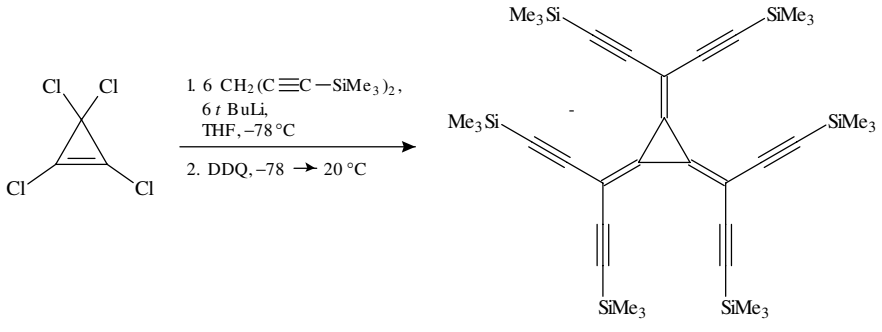


(47) X = S; R = *t*-Bu, Me
(48) X = Se; R = *t*-Bu



(49)

(50) X = CN
(51) X = CO_2Me



(52) 5 %

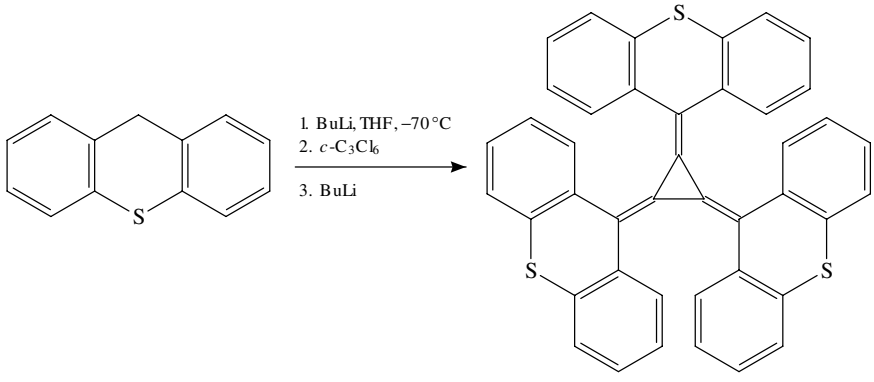
SCHEME 7

and dimethyl malonate yields the dianions **49**, which could be isolated as tetrabutylammonium or sodium salts[23]. Subsequent oxidation of the respective salts provides hexacyano[3]radialene **(50)** and hexamethoxycarbonyl[3]radialene **(51)**[24,25]. Hexakis(trimethylsilylethynyl)[3]radialene **(52)** was prepared analogously, but without isolation of the intermediate dianionic salt[26a]. The corresponding (i-Pr_3Si)-derivative could not be obtained in this manner, probably because of steric overcrowding.

In contrast to **51**, hexacyano[3]radialene **(50)** proved difficult to obtain in pure form. Freshly prepared samples are bright-yellow, but turn brown on exposure to air and blue on contact with many solvents. Potassium bromide and sodium iodide reduce **50** to the radical anion and the dianion, respectively[24].

Radialene **52** has been envisaged as a precursor to hexaethynyl[3]radialene, a potential building block for carbon networks. However, desilylation under very mild conditions led to an unstable product of so far unknown identity. In this context, it should be mentioned that according to thermochemical calculations, the still unknown hexaethynyl[3]radialene has an increased conjugation energy with respect to vinylacetylene, probably because of partial relief of strain in the radialene core[26b]. A remarkable aspect of **52** is its color: the crystals are deep-red and a hexane solution has a purple color. In this respect, **52** differs from the yellow radialenes **50** and **51** and resembles [3]radialenes such as **27** and **38**, which have much more extended π-systems.

The condensation of hexachlorocyclopropane with three equivalents of the active methylene compound thioxanthene has been used for the synthesis of the electron-rich, blue [3]radialene **53**[27] (equation 1).

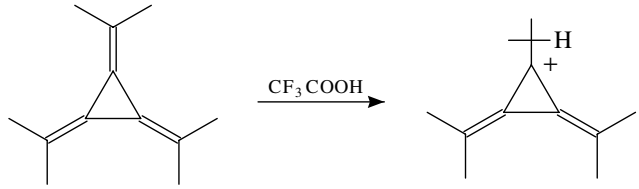


(53) 21% (1)

[3]Radialenes have not received much attention with regard to the classical chemical transformations of polyolefins. While the parent [3]radialene **(1)** is difficult to handle because of its extreme oxygen-sensitivity and its propensity to polymerize under various conditions (see above), increasing substitution of the skeleton leads to a kinetic stabilization, but at the same time it renders intermolecular addition reactions more difficult. Catalytic hydrogenation of **1** with Pd/C as catalyst furnishes a mixture of 3-methylpentane and 3-methyl-2-pentene; with $Rh-Al_2O_3$ as catalyst, however, 3-methylpentane, all-*cis*-1,2,3-trimethylcyclopropane, 2-ethyl-1-butene, and (*E*)- and (*Z*)-3-methyl-2-pentene (in a 6:2:1:7:3 ratio) were found[3]. The hydrogenation products from hexamethyl[3]radialene **(25)** (H_2, Raney–Ni, EtOH, consumption of 2.94 equivalents of H_2) have not been identified[9].

In trifluoroacetic acid, **25** is protonated to form the cyclopropylium cation **54** (UV/Vis: $\lambda_{max} = 480$ nm) (equation 2)[28]. Protonated **1** could not be prepared cleanly in the same

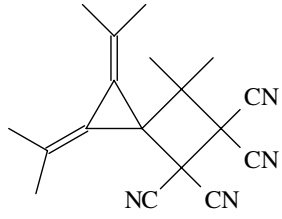
manner due to the extreme propensity of this radialene to undergo cationic polymerization[28]. The remarkable stability of **1** towards dilute mineral acids is worth mentioning, however.



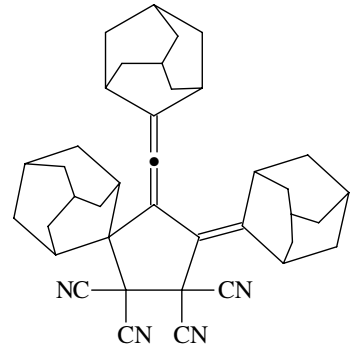
(2)

(25) **(54)**

Hexamethyl[3]radialene **(25)** does not undergo Diels-Alder-reactions with the typical electron-poor dienophiles, probably because of the full substitution at the diene termini. With TCNE, however, a violet-blue charge-transfer complex is formed which disappears within 30 min at room temperature to form a 1:1 adduct (82% yield) to which structure **55** was assigned[9]. Similar observations were made with tris(2-adamantylidene)cyclopropane **(34)**, but in this case cycloaddition product **56** (81% yield) was identified; its allenic moiety is clearly indicated by IR and ^{13}C NMR data[12].



(55)

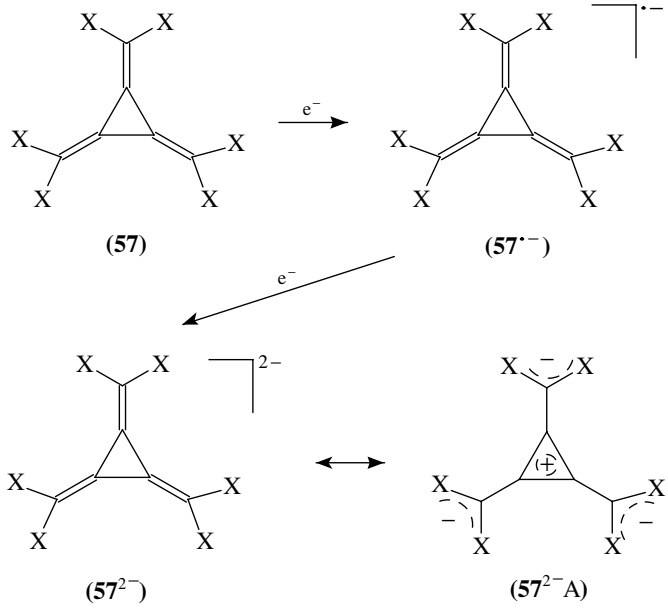


(56)

Virtually all of the [3]radialenes known so far have been evaluated with respect to their reduction/oxidation properties. Electron-donating [3]radialenes can be oxidized to the radical cation and the dication, electron-accepting ones are reduced to the radical anion and the dianion, depending on the substituents. The parent [3]radialene **(1)** has been transformed into the molecular ion only by photoionization in the gas phase[6]. For its permethylated derivative **25**, the ionization potential has also been determined from the photoelectron spectrum[29]; furthermore, the radical cation (formed by γ-irradiation in an organic matrix at 77 K, characterized by the UV/Vis spectrum[28]) and the radical anion (formed by K in DMF at $-70\,^{\circ}C$; characterized by ESR spectrum[30]) have both been generated. Tris(2-adamantylidene)cyclopropane **(34)** undergoes a rather easy, irreversible one-electron oxidation in acetonitrile–dichloromethane solution[12]. The cyclic voltamogram of tris(thioxanthen-9-ylidene)cyclopropane **(53)** in dichloromethane consists of two pairs of reversible waves at $+0.67$ and $+0.80$ V vs Ag/AgCl, corresponding each to a one-electron oxidation[27]. The radical cation $\mathbf{53}^{\bullet+}$ and the dication $\mathbf{53}^{2+}$ were also generated by

chemical oxidation with thallium(III) trifluoroacetate and characterized by their UV/Vis and ESR spectra. The dark-blue salt $\mathbf{53}^{2+} \cdot 2\ CF_3COO^-$ could be isolated; analysis of its ESR spectra at various temperatures points to the existence of a triplet state that is only 0.07 eV higher in energy than the singlet ground state[27]. So far, **53** is the [3]radialene with the best electron-donating qualities.

[3]Radialenes with electron-accepting substituents **(57)** are typically reduced in two one-electron steps via the radical anion $\mathbf{57}^{\bullet -}$ to the dianion $\mathbf{57}^{2-}$ (equation 3). MO calculations and ^{13}C NMR data for $\mathbf{27}^{2-}$[31], $\mathbf{33}^{2-}$[31], $\mathbf{50}^{23}$ and $\mathbf{51}^{23}$ suggest that resonance structure $\mathbf{57}^{2-}$ **A**, with a cyclopropenylium core and negative charges delocalized in the electron-accepting substituents, contributes considerably to the ground states of the dianions $\mathbf{57}^{2-}$. Experimentally determined bond geometries of such dianions are not yet available. However, X-ray crystal structure analyses of several transition metal salts formally containing the radical anion $C_6(CN)_6^{\bullet -}$ $(\mathbf{50}^{\bullet -})$[32–34] reveal the bond length equalization between the ring and exocyclic C–C bonds in these [3]radialene anions [12 individual values; average bond length of C–C (ring): 1.393 ± 0.028 Å; exocyclic C–C: 1.375 ± 0.031 Å].

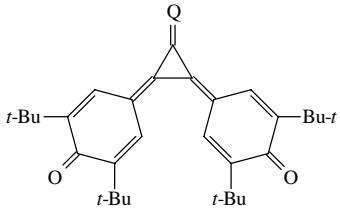


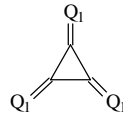
(3)

X = electron-accepting group

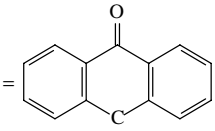
Hexacyano[3]radialene **(50)** is a very powerful electron acceptor according to both experiment[23,24,35] and MNDO calculations of LUMO energy and adiabatic electron affinity[25]. The easy reduction to the stable species $\mathbf{50}^{\bullet -}$ and $\mathbf{50}^{2-}$ by KBr and NaI, respectively, has already been mentioned. Similarly, the hexaester **51** is reduced to $\mathbf{51}^{2-}$ by LiI[24]. Most [3]radialenes with two or three quinoid substituents are reduced in two subsequent, well-separated, reversible one-electron steps. As an exception, an apparent two-electron reduction occurs for **46**[20]. The reduction potentials of some [3]radialenes of this type, as determined by cyclic voltammetry, are collected in Table 1. Due to the occurrence of the first reduction step at relatively high potential, all these radialenes

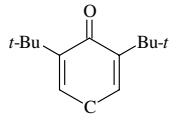
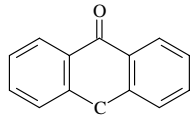
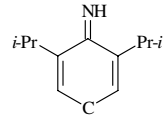
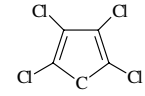
TABLE 1. Reduction potentials of [3]radialenes ($E_{1/2}$, V) with quinoid substituents and of some related compounds, as determined by cyclic voltammetry (in CH_2Cl_2 vs SCE)

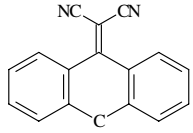
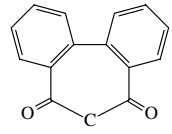
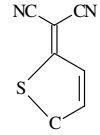
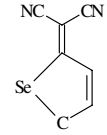




(38)



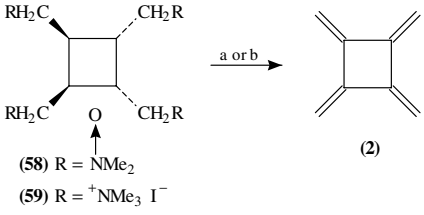
Compound	**37c**	**39**	**43**	**45a**	**45d**
Q				$C(CN)_2$	

Compound	**46**	**44**	**47**	**48**
Q				

Compound	$E^1_{1/2}$	$E^2_{1/2}$	Reference
37c	+0.05	−0.27	36
38	+0.02	−0.28	14
39	+0.02	−0.27	14
43	−0.08	−0.51	17
45a	+0.30	−0.24	19
45d	+0.25	−0.14	19
46	0.00	−0.04	20
44	+0.17	−0.20	18
47	+0.20	−0.12	21
48	+0.19	−0.13	21
TCNQ	+0.22	−0.36	21
DDQ	+0.57	−0.32	35b
Chloranil	0.00	−0.78	35b

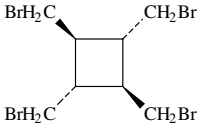
represent strong oxidants. For example, the oxidizing power of **44**, **45a**, **45d**, **47** and **48** is comparable to that of TCNQ, whereas in most other cases the first reduction step is comparable to that of chloranil, and the second one to that of DDQ. As we have mentioned already, these radialenes in general are indeed reduced quite easily to the corresponding bis(4-hydroxyaryl)cyclopropenes (e.g. **37** ⟶ **36**). In several cases, persistent radical anions have also been generated by chemical reduction and characterized spectroscopically. For example, reduction of **47** with LiI provides $\mathbf{47}^{\bullet-}$ quantitatively[21], and radical anion $\mathbf{46}^{\bullet-}$ can be obtained by treatment of the radialene with Na/K alloy[20].

Because of the stability of their reduced forms, in combination with remarkable and reversible color changes, these quinoid radialenes have been suggested as materials for electrochromic display devices[18,35b].



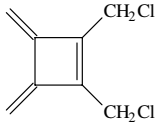
(58) R = NMe_2
(59) R = $^{+}NMe_3\ I^{-}$

(2)



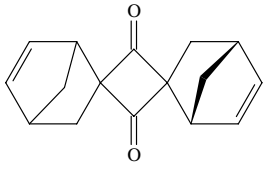
2

(60)



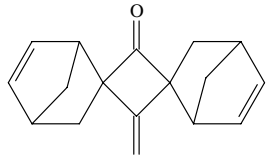
$Zn, BuOCH_2CH_2OCH_2CH_2CH_2OBu, 50°C$, 77% → **2**

(61)



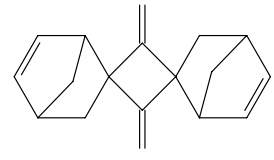
(62)

$Ph_3P{=}CH_2$



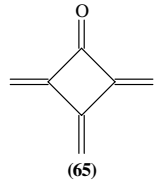
(63)

$Ph_3P{=}CH_2$



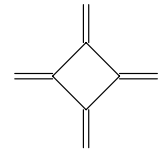
(64)

680 °C, 5×10^{-5} Torr



(65)

680 °C, 5×10^{-5} Torr



(2)

SCHEME 8. Reaction conditions: (a) 250 °C, vacuum, 1–2% yield; (b) 115 °C, no pure product; (c) NaOEt, EtOH, 0 °C, <50% yield; (d) solid KOH, 150 °C

The two-step reduction of tris(9-fluorenylidene)cyclopropane **27**[31] and of hexakis(trimethylsilylethynyl)cyclopropane **52**[26a] requires increasingly more negative potentials than in the cases listed in Table 1; this is, of course, a consequence of the presence of less electron-accepting substituents. Nevertheless, dianion $\mathbf{27}^{2-}$ has been generated by reduction with sodium or lithium; the lithium salt could be kept in THF solution for up to one year at 20 °C without detectable decomposition[31].

Electron-rich and electron-poor [3]radialenes have received much attention as components of molecular π donor–acceptor complexes; for information on this subject, see elsewhere[1,21,22].

B. [4]Radialenes

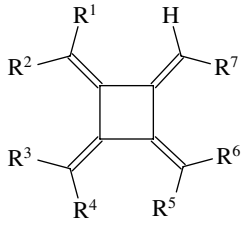
[4]Radialenes represent the biggest and best known subset of the radialene family; this is not surprising in view of the fact that more methods to prepare them exist than for any other class of radialenes. The major strategies are the transformation of appropriate cyclobutane derivatives, the thermal or Ni(0)-catalyzed cyclodimerization of butatrienes or higher cumulenes and the cyclotetramerization of (1-bromo-1-alkenyl)cuprates.

Cyclobutane derivatives are involved in all known syntheses of the parent [4]radialene (Scheme 8). The first approaches used β-elimination reactions on compounds **58**[36], **59**[36] and **60**[36–38] to introduce all four exocyclic C=C bonds in one operation.

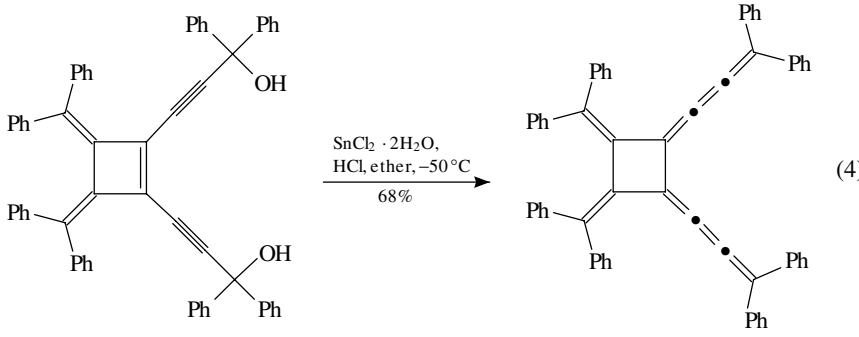
A more recent approach is the reductive 1,4-dechlorination of 1,2-bis(chloromethyl)-3,4-dimethylenecyclobutene **(61)**, which is prepared in five steps from 1,5-hexadiyne in good overall yield[39]. Finally, **2** has been generated by flash vacuum pyrolysis of **64** in a twofold retro-Diels-Alder reaction[40]. Dispiro compound **64** is prepared from the cyclobutane-1,3-dione **62** in two Wittig olefination reactions via **63**; notably, the thermal fragmentation of **63** provides the radialene-like trimethylencyclobutanone **65**, a compound which polymerizes already at −95 °C.

Radialene **(2)** can be stored at −78 °C, but undergoes dimerization and polymerization reactions in solution at room temperature; neat **2** may even start to burn at this temperature[39]. It is also very sensitive towards oxygen; exposure to air leads to an intractable material containing up to 40% oxygen.

[4]Radialenes bearing four to seven phenyl substituents have been prepared from 3,4-bis(diphenylmethylene)cyclobutane-1,2-dione **(66–68)** and 2,3-bis(diphenylmethylene)-4-benzylidenecyclobutan-1-one (**69**, **70**), respectively, by standard synthetic operations[41]. While octaphenyl[4]radialene could not be prepared analogously[41], a cumulenic homologue thereof **(72)** was obtained (equation 4) by reductive 1,8-elimination from **71**, which itself came from a palladium-catalyzed cross-coupling reaction of 1,2-bis(diphenyl)methylene-3,4-dibromocyclobutene and 3,3-diphenylpropynol[42].



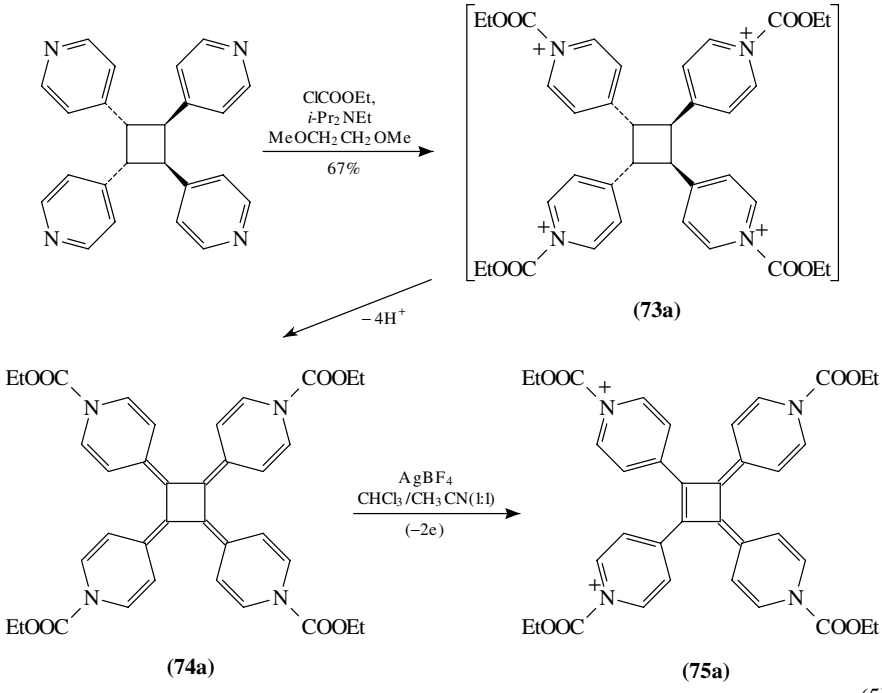
$R^1 - R^4 = Ph,\ R^5 - R^7 = H$ **(66)**
$R^1 - R^6 = Ph,\ R^7 = H$ **(67)**
$R^1 - R^7 = Ph$ **(68)**
$R^1 - R^4 = Ph,\ R^6 = Ph,\ R^5 = R^7 = H$ **(69)**
$R^1 - R^4 = Ph,\ R^6 = R^7 = Ph,\ R^5 = H$ **(70)**



(4)

(71) **(72)**

When 1,2,3,4-tetrakis(4-pyridinyl)cyclobutane is treated with ethyl chloroformate in the presence of ethyldiisopropylamine, radialene **74a** is formed and can be isolated as red crystals. Addition of $AgBF_4$ to a red solution of **74a** results in an immediate color change to deep blue caused by the formation of the dicationic species **75a** (equation 5)[43]. Undoubtedly, the tetrapyridiniocyclobutane **73a** is an intermediate in the formation of **74a**. By way of contrast, the fourfold deprotonation of the analogous tetrakis(*N*-methyl-4-pyridinyl)cyclobutane **(73b)** did not succeed in the presence of oxygen. Treatment with NaH/EtOH in the presence of oxygen produced the dication **75b**, which could be reduced to the [4]radialene only electrochemically[44]. Deprotonation of **73b** with sodium hydride



(73a)

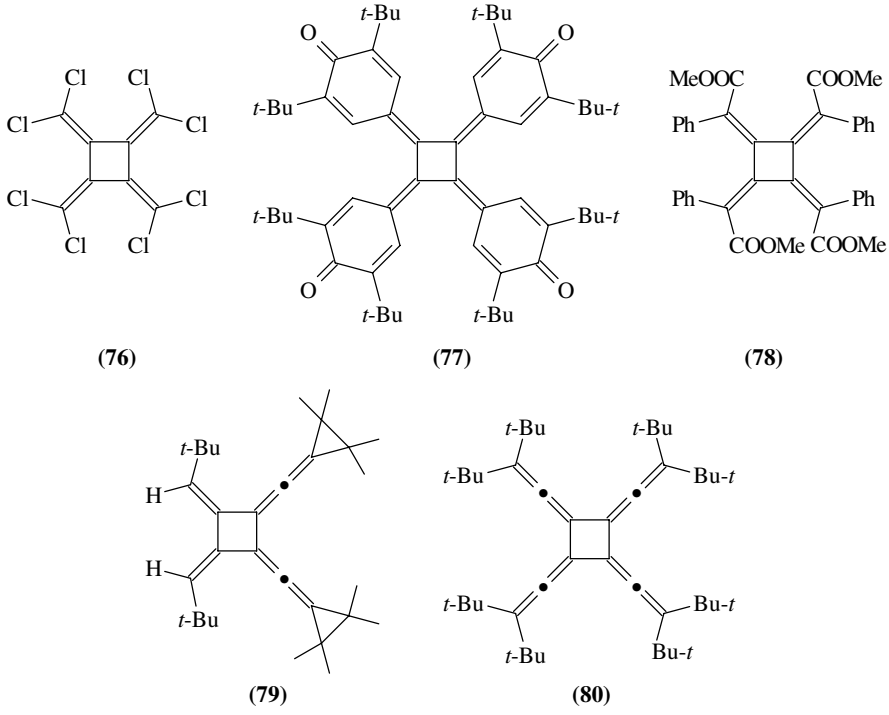
(74a) **(75a)**

(73b) – (75b): NMe instead of NCOOEt

(5)

in dimethylacetamide under an argon atmosphere gave a red solution, which had a similar absorption spectrum as radialene **74a** and turned blue on admission of air with formation of dication **75b**.

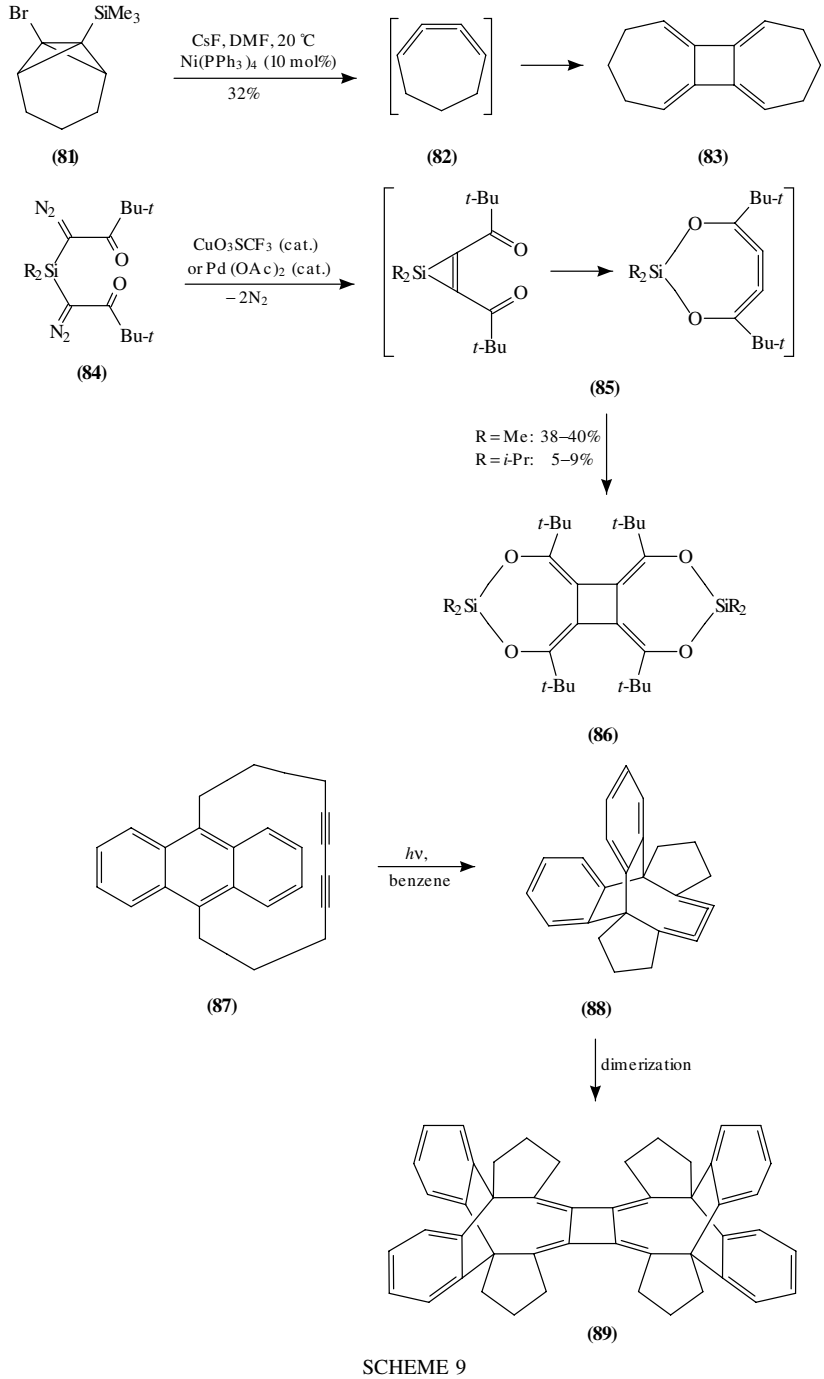
The thermally or photochemically induced (2 + 2) cyclodimerization of butatrienes across the central C=C double bond, or of higher cumulenes at an inner double bond, appears as a reasonable route to [4]radialenes. However, success and failure of this approach have been reported about equally often. Butatriene itself yields 1,5-cyclooctadiyne and other products, but no [4]radialene, on heating[45]. Silyl-, stannyl- and germyl-substituted butatrienes seem to undergo no thermal dimerization at all[46]. In contrast to earlier assumptions, the photochemical dimerization of tetraphenyl- and tetrakis(4-methoxyphenyl)butatriene as well as the thermal dimerization of 7-(propadienylidene)tricyclo[4.1.0]heptane do not provide the respective [4]radialenes, but occur at one of the terminal C=C bonds to give a head-to-tail dimer in the former case[47] and a head-to-head dimer in the latter[48]. Some [4]radialenes which have been obtained by thermal (100–200 °C) cyclodimerization of [*n*]cumulenes are given below. It appears that only butatrienes bearing electron-withdrawing substituents are able to form [4]radialenes (e.g. **76**[49], **77**[50], **78**[51]). On heating, radialene **79** was obtained from a pentatetraene[52], and **80** from a hexapentaene[53,54], but it must be mentioned that different cyclodimers are formed when these cumulene systems bear other alkyl substituents[48,55,56].



(76) **(77)** **(78)**

(79) **(80)**

1,2,3-Cyclononatriene, the smallest cyclic [3]cumulene isolated so far, polymerizes when its solutions are concentrated[57]. On the other hand, several radialenes have been isolated which represent cyclodimers of seven- and eight-membered 1,2,3-trienes (Scheme 9).


Br
SiMe3
CsF, DMF, 20 °C
Ni(PPh3)4 (10 mol%)
32%
(81)
(82)
(83)
N2
Bu-t
R2Si
O
N2
Bu-t
(84)
CuO3SCF3 (cat.)
or Pd(OAc)2 (cat.)
– 2N2
t-Bu
R2Si
O
t-Bu
Bu-t
R2Si
O
Bu-t
(85)
R = Me: 38–40%
R = i-Pr: 5–9%
t-Bu
t-Bu
R2Si
SiR2
t-Bu
t-Bu
(86)
hν,
benzene
(87)
(88)
dimerization
(89)

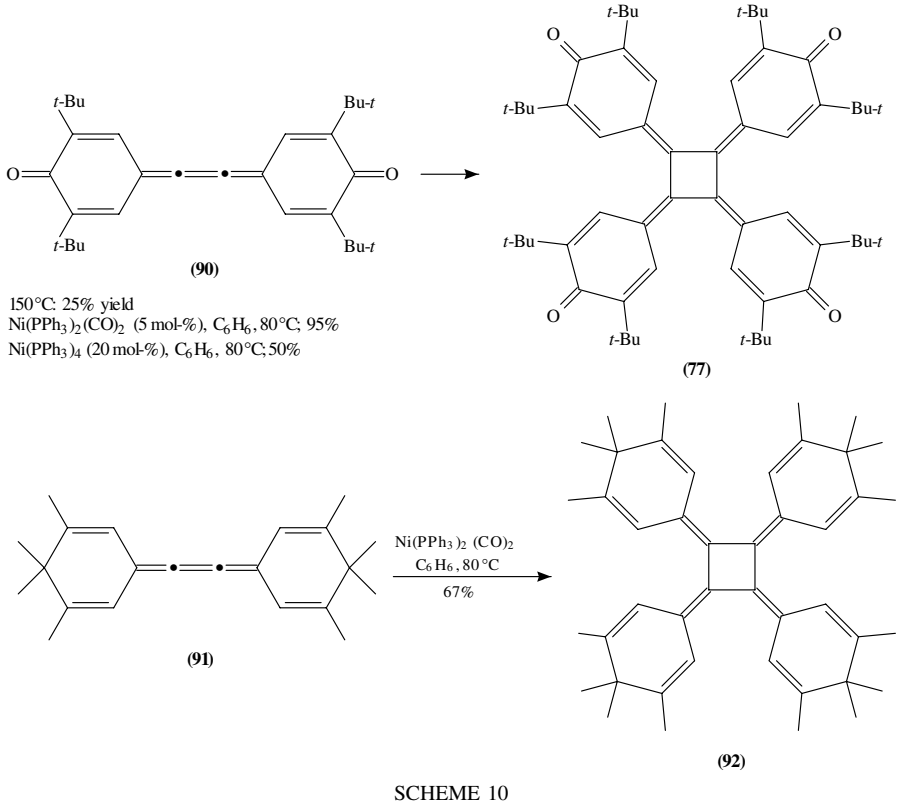
SCHEME 9

The parent 1,2,3-cycloheptatriene **(82)**, generated as a reactive intermediate from tricyclus **81**, can be trapped with various dienes, but it does not dimerize[58]. In the presence of $Ni(PPh_3)_4$, however, the dimer, i.e. radialene **83** is formed[59]. Similar to the parent compound **(2)**, it polymerizes on contact with oxygen within a few hours.

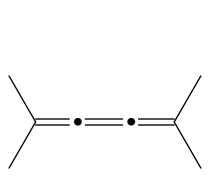
Radialenes **86** were obtained when bis(1-diazo-2-oxoalkyl)silanes **84** were decomposed with copper or palladium catalysts[60,61]. The assumption, that the heterocyclic [3]cumulene **85** is the immediate precursor of **86**, is corroborated by its trapping in a Diels-Alder reaction with furan.

Radialene **89**, a dimer of 1,2,3-cyclooctatriene derivative **88**, was isolated when the [10](9,10)anthracenophane-4,6-diyne **87** was exposed to sunlight[62]. In this case, the intermediate occurrence of **88** could not only be substantiated by isolation of (4 + 2) cycloadducts in the presence of furan or cyclopentadiene, but also by a UV/Vis spectrum obtained at 77 K in an organic glass.

The cyclodimerization of **82** to **83** is an example of a Ni(0)-mediated synthesis of [4]radialenes from [*n*]cumulenes. Applications of this method to butatriene derivatives **90**[50,63], **91**[64] and **93**[65,66] are shown in Scheme 10. The usefulness of Ni(0) catalysis for this transformation was first demonstrated by West and coworkers[63] and later explored in detail by Iyoda and coworkers[42,54,67]. In some cases, Ni(0) catalysis improves the efficiency of the process as compared to the purely thermal reaction (e.g. **90** ⟶ **77**); in other cases, it is a requirement for a successful [4]radialene synthesis (e.g. **82** ⟶ **83**

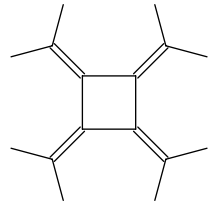


SCHEME 10



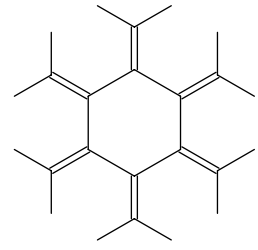
(93)

Ni(0)



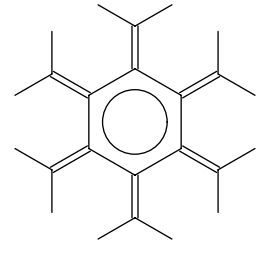
(94)

+



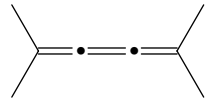
(95)

+



(96)

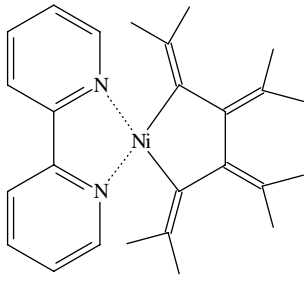
Ni(0) Catalyst	Solvent	Temp.	Yield (%)		
		(°C)	**94**	**95**	**96**
$Ni(PPh_3)_4$	C_6H_6	50	7	–	19
	DMF	50	4	24	21
$Ni(PPh_3)_2(CO)_2$	C_6H_6	80	11	3	35



(93)

80 %

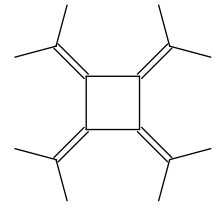
Ni(bpy)(cod),
THF, 5 °C



(97)

maleic anhydride
(2 equiv), THF

79 %



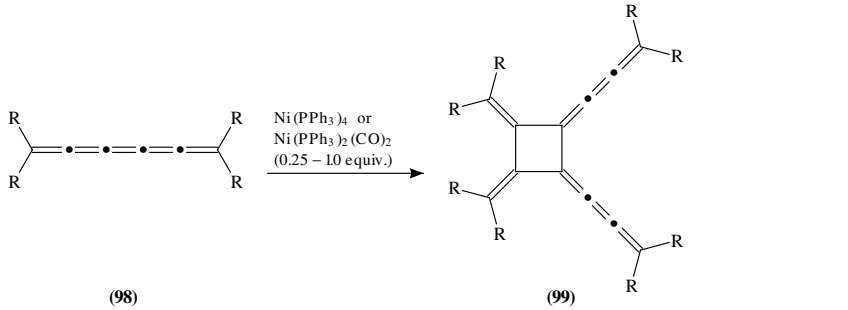
(94)

SCHEME 10. (*continued*)

and **93** ⟶ **94**). On the other hand, tetraphenylbutatriene and 2,5-diphenylhexa-2,3,4-triene could not be cyclodimerized with catalytic $Ni(PPh_3)_4$ in benzene[66]. The examples shown in Scheme 10 also illustrate that different Ni(0) catalysts are in use, especially $Ni(PPh_3)_4$ [conveniently generated by *in situ* reduction of $NiBr_2(PPh_3)_2$, $Ni(CO)_2(PPh_3)_2$ and $Ni(cod)_2$, cod = 1,5-cyclooctadiene].

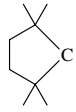
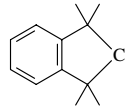
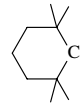
In the case of tetramethylbutatriene, Ni(0) catalyzes not only the cyclodimerization (formation of [4]radialene **94**), but also the cyclotrimerization, leading to [6]radialene **95** and its isomer **96** (see also Section II.D). The product pattern depends to some extent on the nature of the catalyst, but the choice of solvent seems to be more crucial[65,66]. This is illustrated impressively by the $Ni(cod)_2$-catalyzed reaction of **93**, which leads exclusively to the [4]radialene in toluene solution, but to the [6]radialene in DMF[68]. Interestingly, the stoichiometric reaction between **93** and (2,2′-bipyridyl)-(1,5-cyclooctadiene)nickel yields the nickel complex **97**, which has been isolated and characterized by X-ray diffraction[69]. On treatment of **97** with two equivalents of maleic anhydride, reductive elimination of nickel takes place and octamethyl[4]radialene **(94)** is formed in good yield. This reaction sequence sheds light on the mechanism of the Ni-catalyzed reactions mentioned above; further ideas on the mechanism of the cyclodimerization and cyclotrimerization reactions have been developed by Iyoda and coworkers[66].

The Ni(0)-mediated synthesis of [4]radialenes from hexapentaenes has also been investigated[42,54,67]. The regioselectivity of the cyclodimerization and the question of



(98) **(99)**

(100) **(101)** **(102)**

C(R,R)	C(Ar,Ar)				C(*t*-Bu,*t*-Bu)
Products	**99**	**100**	**100**[a]	**101, 102**	**102, 101**[b]
Reference	42	67	54	67	67

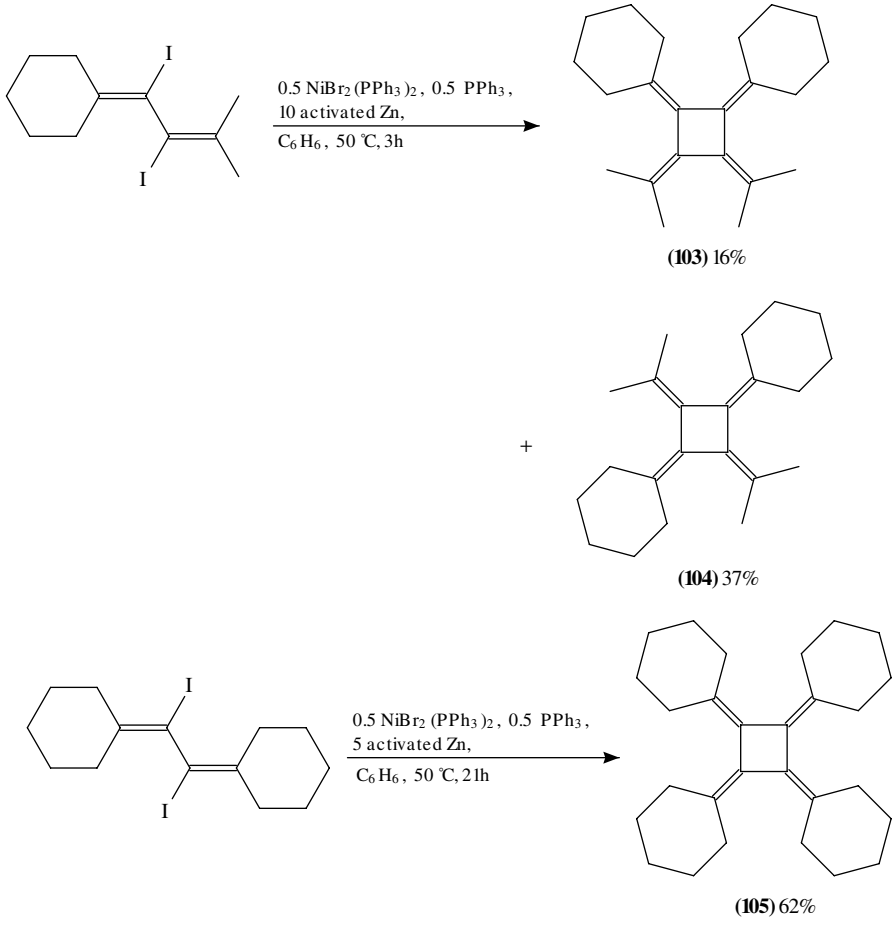
[a] The thermal reaction (270 °C, 5 min) yields 101(51%).

[b] 101(R = *t*-Bu) = 80. The thermal reaction (200 °C, 15 min) also yields 101(90%)[53].

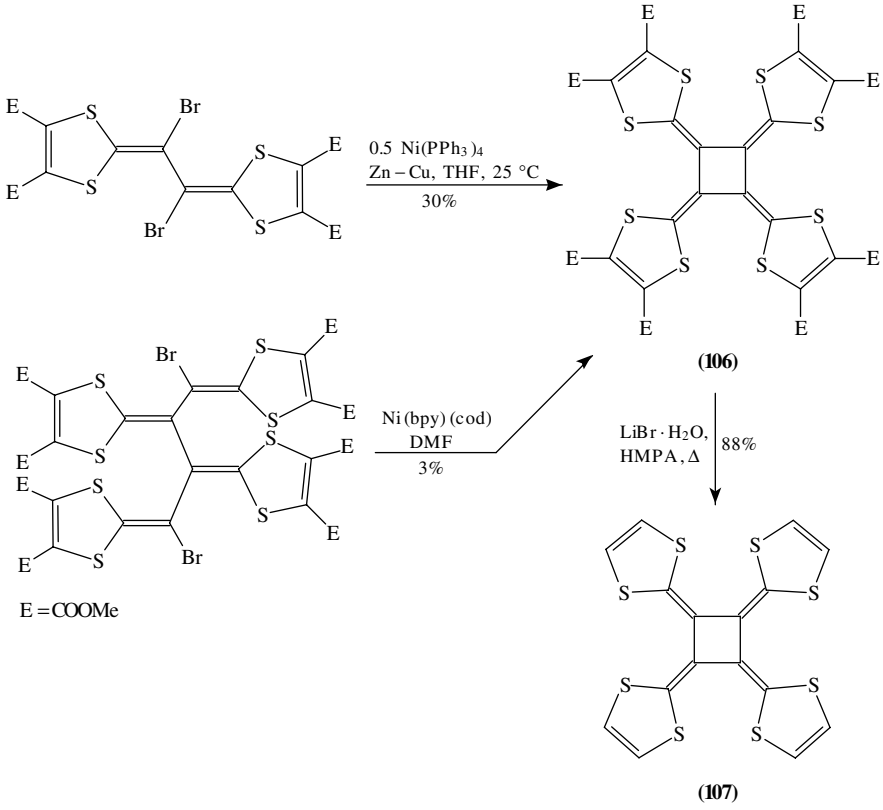
SCHEME 11

whether head-to-head or head-to-tail cycloaddition occurs depends obviously on the steric bulk of the substituents. It appears that cycloaddition across the C2=C3 bond of the [5]cumulene is normally favored, but bulky substituents induce reaction across the central double bond; in the latter case, a carbonyl ligand from the catalyst can be incorporated into the cyclodimer; see Scheme 11.

Zero-valent nickel complexes are known to reduce 1,2-dihalides to olefins and to mediate C,C-coupling reactions of vinyl halides. Based on these facts, Iyoda and coworkers developed a two-step, one-pot synthesis of alkyl-substituted [4]radialenes which starts from 2,3-dihalo-1,3-butadienes and 1,4-dichloro-2-butyne derivatives[65,66] and circumvents the isolation of the butatriene intermediates. Furthermore, the synthesis can be made catalytic in nickel when the Ni(0) complex is generated from $NiBr_2(PPh_3)_2$ with a more than stoichiometric quantity (based on the dihalide) of zinc. Again, the formation of radialene **94** must compete with that of **95** and **96**. With preformed $Ni(PPh_3)_4$ and $Ni(PBu_3)_4$, the [4]radialene is normally favored in benzene solution, but formation of **95** and/or **96** becomes important in the more polar solvents THF and DMF. With a catalyst



SCHEME 12



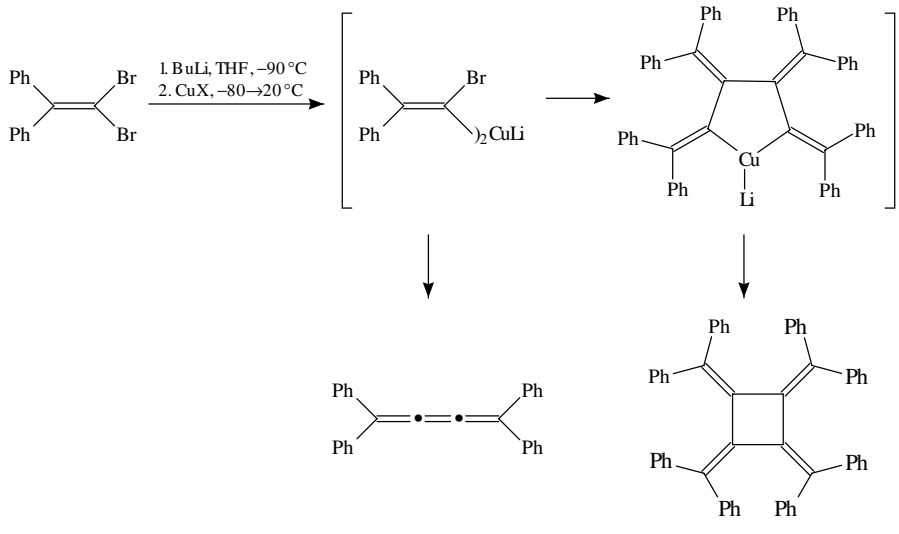
SCHEME 12. (*continued*)

generated *in situ* from $NiBr_2(PPh_3)_2$, Et_4NI and Zn (0.5:2:5 ratio) in THF solution, good yields of **94** can be obtained, and **95** and **96** are only minor products.

The scope of this method is illustrated by the preparation of other peralkylated [4]radialenes, such as **103–105**[66] and the functionalized radialene **106**[70,71] (Scheme 12). Removal of the carboxylate groups from the latter provided the very electron-rich radialene **107**.

As we have mentioned, octaphenyl[4]radialene **109** can be obtained neither by photochemical nor by Ni(0)-catalyzed cyclodimerization of tetraphenylbutatriene. However, **109** has been prepared from 1,1-dibromo-2,2-diphenylethene via organocuprate intermediates (Scheme 13)[72]. The correct choice of the added copper(I) salt is crucial for the success of this transformation, but even then, formation of tetraphenylbutatriene **(108)** from the bis(1-bromovinyl)cuprate intermediate limits the yield of **109**.

When the organocuprate methodology is applied to 1,1-dibromo-2-methylprop-1-ene, octamethyl[4]radialene **(94)** and decamethyl[5]radialene are the major products[73]. While this method does not offer any advantage over the Ni(0)-mediated syntheses of **94** (see above), it constitutes the only known synthesis of the permethylated [5]radialene (see Section II.C). For the sake of completeness, we mention that the Ni(0)-mediated dehydrohalogenation/cyclotetramerization of 1,1-dibromoalkenes is not an efficient route to [4]radialenes[66].



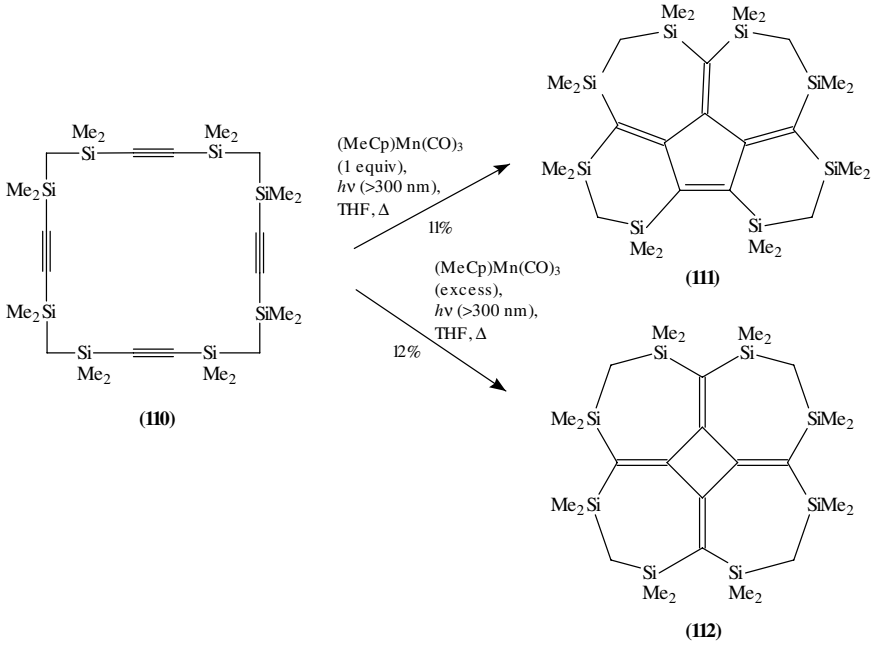
(108) **(109)**

CuX	Ratio alkene : BuLi : CuX	Yield of **108** (%)	Yield of **109** (%)
CuI · PBu_3	2 : 2 : 1	34	40
	4 : 2 : 1	48	29
CuCN	2 : 2 : 1	traces	41
CuI	2 : 2 : 1	Ph—≡—Ph (86%)	

SCHEME 13

An elusive [4]radialene synthesis has been reported by Sakurai. Irradiation of the 1,3,6,8,11,13,16,18-octasilacycloeicosan-4,9,14,19-tetrayne **110** in the presence of an equimolar amount of tricarbonyl(methylcyclopentadienyl)manganese initiates a skeletal rearrangement leading to **111**, whereas in the presence of an excess of the metal carbonyl, [4]radialene **112** is formed (Scheme 14)[74]. Although the mechanistic details of these rearrangements are not known, it is likely that the intramolecular version of the transformation of bis(trialkylsilyl)acetylene into a (2,2-disilylvinylidene)manganese complex is involved.

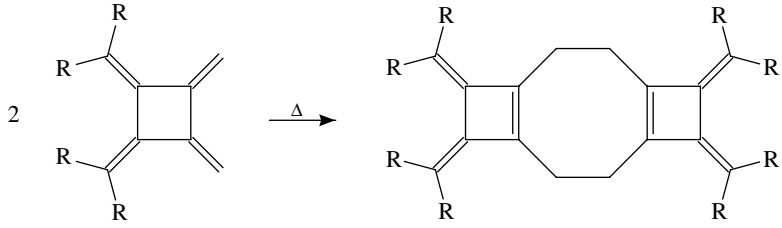
Concerning the transformation of [4]radialenes, the parent compound **(2)** has been studied best, despite its high instability in solution at room temperature or in the solid state (see above). We have already mentioned that **2** can be kept indefinitely at −78 °C, but undergoes dimerization and polymerization in solution at 20 °C. The dimerization leads to cyclooctadiene derivative **113**[36]. Trimethylenecyclobutane behaves analogously[75], and 5,5,6,6-tetraphenyl[4]radialene **66** reacts in the same manner to give **114** at 60 °C in chloroform solution (equation 6)[41]. Since thermal (4 + 4) cycloadditions should not occur in a concerted manner, it has been suggested that this reaction is a stepwise process in which the reacting 1,2-dimethylenecyclobutene unit exhibits 1,4-diradical character[39].



(110) (111) (112)

SCHEME 14

Notably, gas-phase thermolysis of **113** at 220 °C leads back to **2**[76].

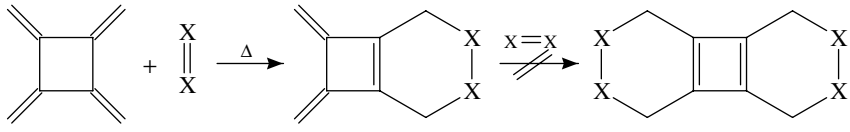


R = H (**2**) (**113**)
R = Ph (**66**) (**114**)

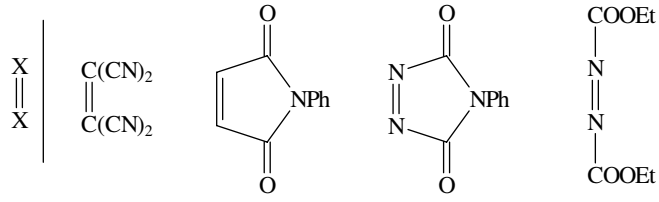
(6)

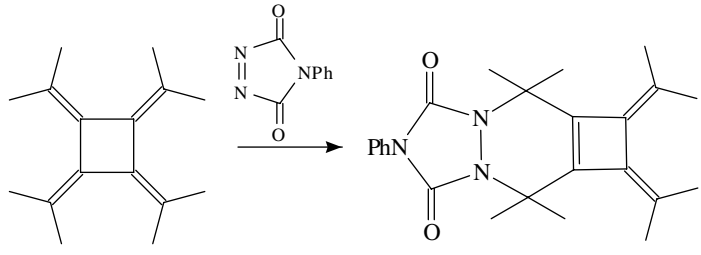
In the gas phase, **2** is a thermally very stable compound up to 850 °C. Pyrolysis at 880 °C/10^{-3} Torr generates styrene (55–62%) and *o*-xylene (6%) along with small amounts of phenylacetylene, benzene, toluene and unidentified hydrocarbons[39]. Cycloaddition reactions with dienophiles were among the first reactivity studies on **2**; they were of course driven by the expectation to generate a cyclobutadiene structure by a twofold (4 + 2) cycloaddition. However, while **2** reacts readily with electron-deficient alkenes such as TCNE[36], *N*-phenylmaleimide[36], 4-phenyl-1,2,4-triazolinedione[39] and diethyl azodicarboxylate[39] to form 1:1 adducts **115**, a second Diels-Alder reaction

producing cyclobutadienes **116** could never be realized with an excess of these powerful dienophiles. Obviously, the activation barrier on the way to the antiaromatic **116** is prohibitive. Octamethyl[4]radialene **(94)** also undergoes but a single (4 + 2) cycloaddition with TCNE[68]. With 4-phenyl-1,2,4-triazolinedione, however, not only the 1:1 adduct **117** but also the dipolar 2:1 adduct **118** is formed; again, the reacting system is reluctant to form a cyclobutadiene.

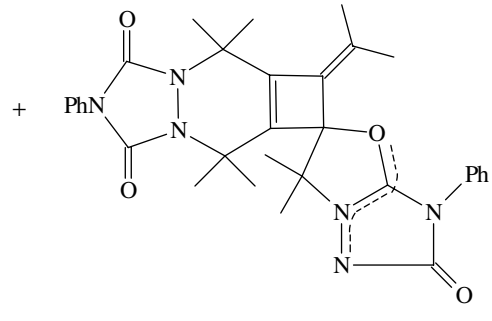


(2) **(115)** **(116)**



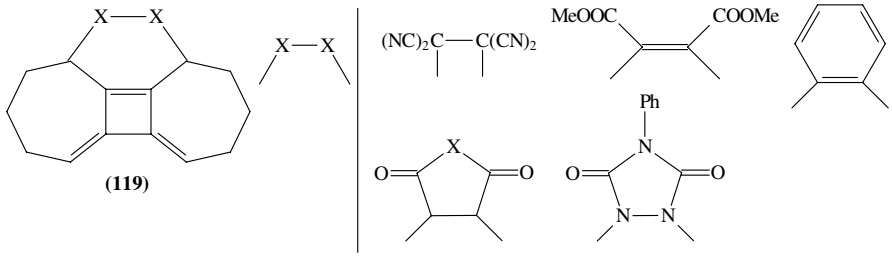


(94) **(117)**



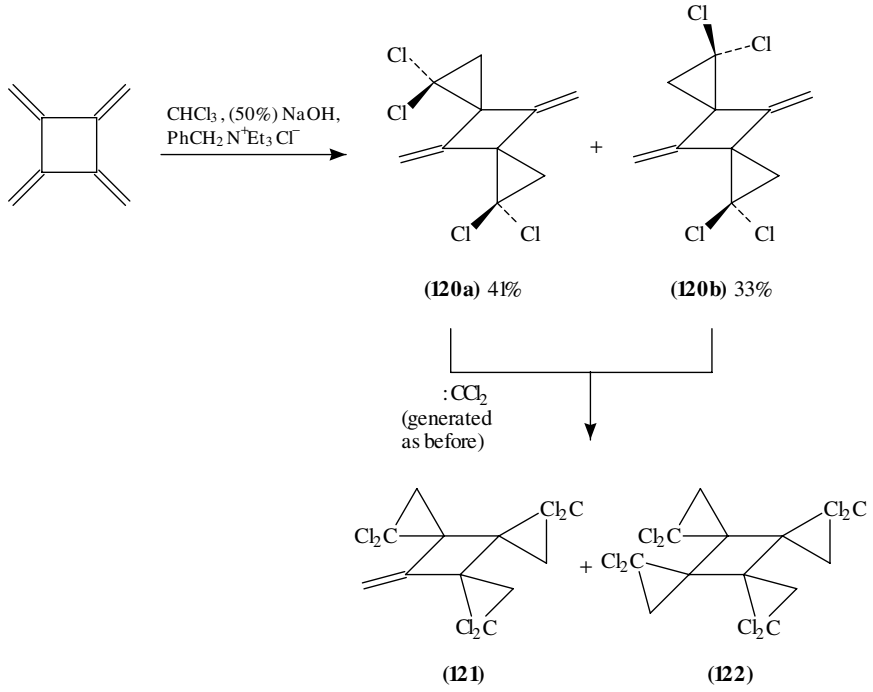
(118)

Diels–Alder reactions of **83** with various dienophiles occur regioselectively to form condensed tetra- or pentacycles of the type **119**[77]. (2 + 1) Cycloaddition reactions between **2** and carbenes are also known[78]. While exposure of **2** to diazomethane in the presence of CuCl leads to a mixture of mono-, di-, tri- and tetracyclopropanated products, transfer of



(119)

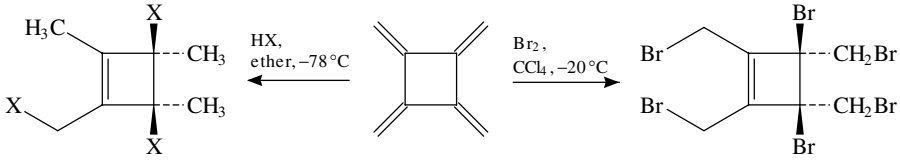
dichloro- or dibromocarbene becomes increasingly more selective. With dichlorocarbene, generated from chloroform under phase-transfer conditions, a diastereomeric mixture of the dispiro compounds **120a** and **120b** is formed. Treatment of this mixture with more dichlorocarbene provides the trisadduct **121** and the octachloro[4]rotane **122** (Scheme 15). In the second carbene transfer step, **120b** is obviously not cyclopropanated further and it can indeed be recovered. Addition of dibromocarbene proceeds slower and in lower yield, and the twofold cyclopropanated products analogous to **120a** and **120b** do not accept another carbene unit.



SCHEME 15

Although **2** was found to be remarkably stable towards dilute mineral acids and strong bases, some electrophilic addition reactions have been realized. With HCl, HBr and Br_2, trisadducts **123** and **124** were obtained (equation 7) which obviously result from one 1,4-

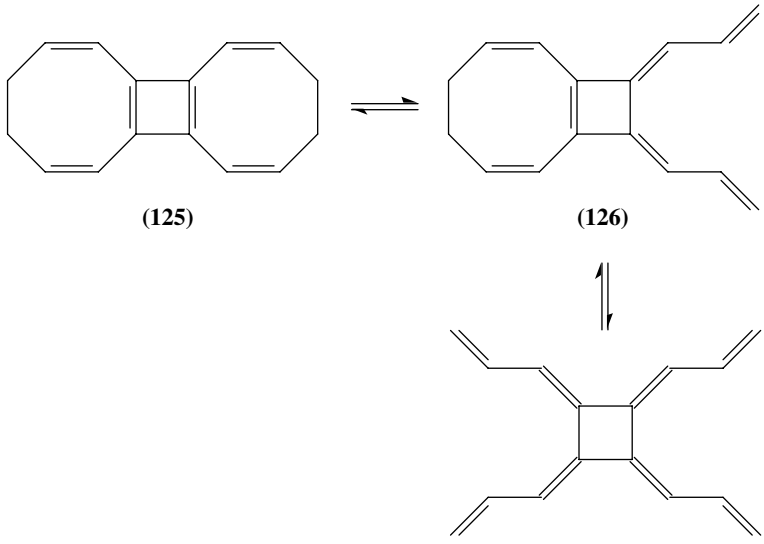
and two 1,2-addition reactions of the electrophile[39]. Again, formation of a cyclobutadiene, this time by a fourfold electrophilic 1,2-addition, is avoided.



(123) **(124)** 68%

X = Cl (68%)
X = Br (50%) (7)

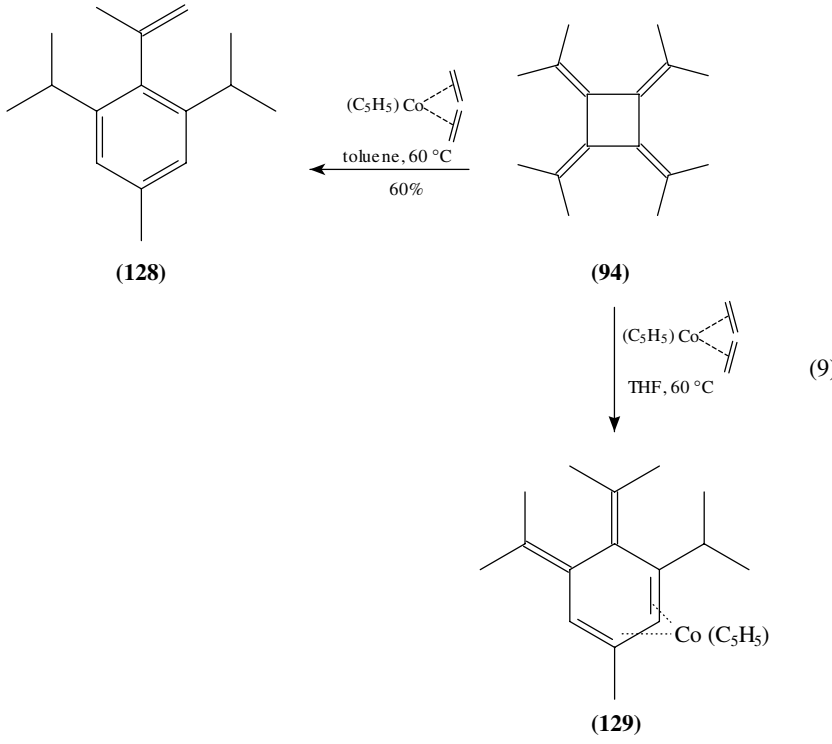
Surprisingly little is known about isomerization reactions of [4]radialenes. 5,6,7,8-Tetravinyl[4]radialene **127** is certainly a unique case since it appears to be in equilibrium with its precursors in synthesis, **125** and **126**, by electrocyclic reactions (equation 8). As **127** has not been isolated in pure form and is unstable with respect to polymerization, no details on this possible equilibrium are known[79].



(125) **(126)** (8)

(127)

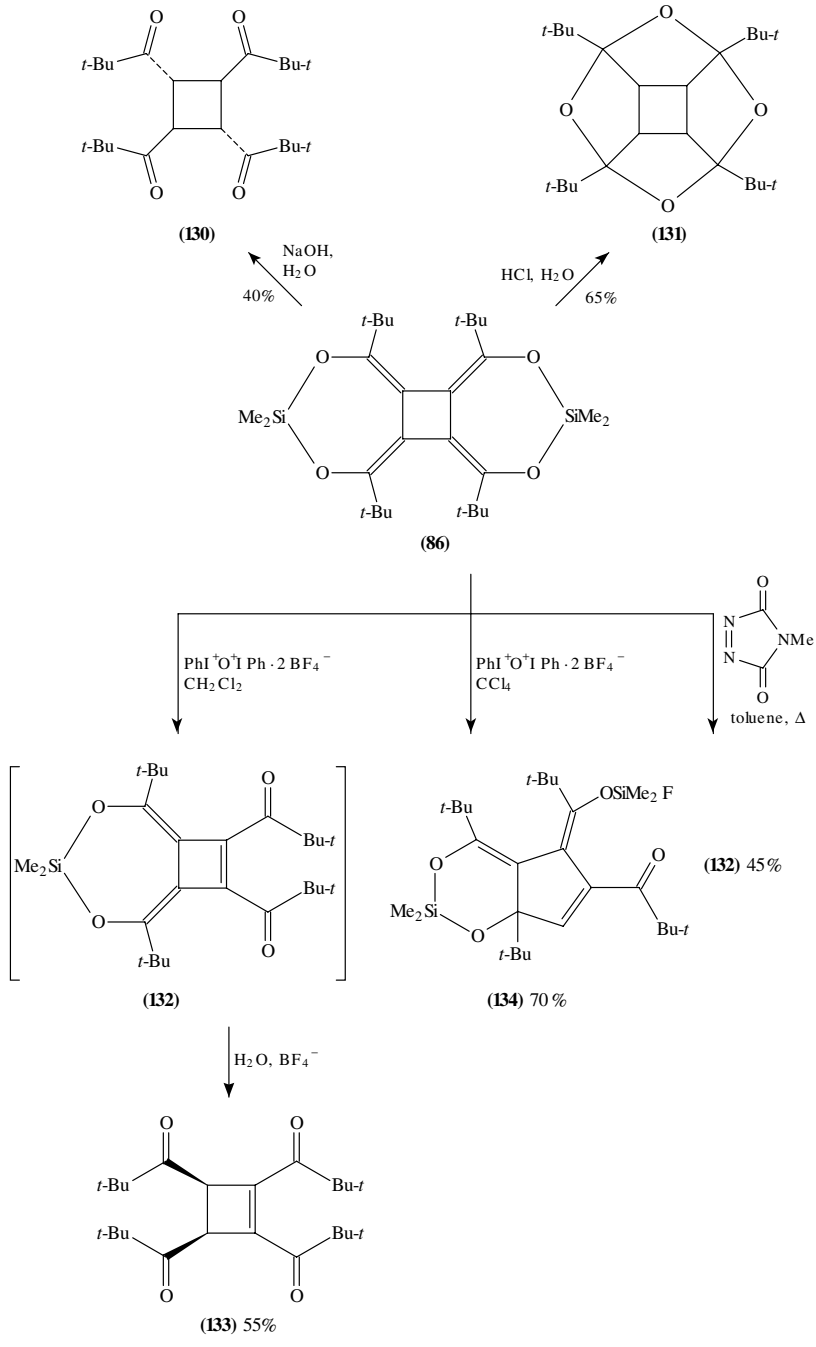
With the transition-metal-assisted ring-opening and isomerization of small rings in mind, it is astonishing that only one such study for a [4]radialene is known. The cobalt(I) complex $(C_5H_5)Co(H_2C{=}CH_2)_2$ catalyzes the isomerization **94** ⟶ **128** in toluene solution, while a stoichiometric reaction takes place in THF solution from which the cyclohexadiene–cobalt complex **129** results (equation 9). The formation of **129** in the latter reaction suggests that this complex is also an intermediate in the catalytic reaction[80]. Notably, permethylated [6]radialene does not react with $(C_5H_5)Co(H_2C{=}CH_2)_2$.



(9)

The functionalized [4]radialene **86** offers opportunities for further transformations by hydrolytic cleavage of the O-silylenol moieties and by oxidative desilylation (Scheme 16). Base- and acid-catalyzed hydrolyses lead to different products (**130** and **131**, respectively)[60]. By analogy with the formation of 1,4-diketones by oxidative coupling of two siloxyalkene molecules, treatment of **86** with the iodonium salt $PhI^{+}-O-{}^{+}I-Ph \cdot BF_4^{-}$ in dichloromethane leads to **132** which is immediately desilylated to provide cyclobutene **133**. If the reaction is carried out in carbon tetrachloride, the bicyclus **134** is obtained. Both the mechanism of this transformation and the influence of the solvent on the result are a matter of speculation[81]. 4-Methyl-1,2,4-triazolinedione, known as a powerful dienophile, does not undergo a Diels–Alder reaction with **86**. This is not unexpected, since the diene units of **86** are far from being planar and are sterically shielded at the termini by the *t*-Bu groups. Similar to the iodonium salt mentioned before, the triazolinedione brings about an oxidative desilylation of **86** leading to **132**[61]. A second transformation of this kind, which would provide tetrapivaloylcyclobutadiene, does not occur.

The redox chemistry of [4]radialenes shows similarities as well as differences with respect to [3]radialenes (see elsewhere[1] for a more detailed comparison). The simplest [4]radialene for which a redox chemistry in solution is known appears to be octamethyl[4]radialene (**94**). It has been converted into the radical anion $\mathbf{94}^{\bullet -}$ (with potassium, [2.2.2]cryptand, THF, 200 K) and into the radical cation $\mathbf{94}^{\bullet +}$ (with $AlCl_3/CH_2Cl_2$, 180 K)[82]. Both species are kinetically unstable, but the radical cation is less stable than the radical anion and disappears even at 180 K within 2 hours, probably by polymerization. For the success of the oxidation of **94** with the one-electron transfer system


(130)
(131)
NaOH, H2O
40%
HCl, H2O
65%
(86)
PhI+O+I Ph · 2 BF4−
CH2Cl2
PhI+O+I Ph · 2 BF4−
CCl4
toluene, Δ
(132)
(132) 45%
(134) 70%
H2O, BF4−
(133) 55%

SCHEME 16

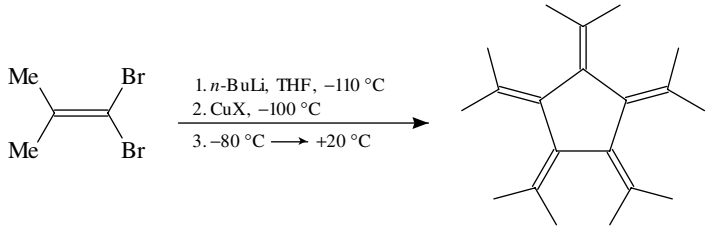
$AlCl_3/CH_2Cl_2$, it is important that the first vertical ionization energy of **94** is lower by more than 1 eV with respect to the parent [4]radialene **2** (7.30[82] vs 8.35[37] eV). The near congruency of the ESR and ENDOR spectra of $\mathbf{94}^{\bullet+}$ and $\mathbf{94}^{\bullet-}$ is a nice experimental proof of the topological prediction based on HMO theory that even-membered [*n*]radialenes have alternant π molecular properties. On the other hand, the corresponding spectra of the radical cation (generated with $Tl(OOCCF_3)_3/CH_2Cl_2$) and radical anion (formed with K, [2.2.2]cryptand) of octaphenyl[4]radialene **(109)** exhibit significant differences[83]; it has been suggested that structural differences of the two charged species account for this phenomenon.

For appropriately substituted [4]radialenes, the range of accessible redox stages is wider than for [3]radialenes. While the latter can accept or give away up to two electrons (Section II.A, Table 1), the possibilities for [4]radialenes range from the dianion to the tetracation (see elsewhere[1] for a compilation). For example, the extremely electron-deficient octacyano[4]radialene, in contrast to the corresponding [3]radialene **50**, could not yet be generated. Its dianion was prepared from 1,2-dichloro-3,3,4,4-tetrafluorocyclobutene and malononitrile and isolated as the tetrabutylammonium salt; only the one-electron oxidation to the radical anion could be achieved electrochemically[84]. Tetra(cyclohexadienylidene)cyclobutene **92** displays a fully reversible electrochemical transition from the dianion to the dication by subsequent one-electron steps[64], and the electron-rich tetrakis(1,4-dihydropyridin-4-ylidene)cyclobutane **74a**[43] and tetrakis(1,3-dithiol-2-ylidene)cyclobutanes **106** and **107**[70] can give away up to four electrons. It should be noted that this electrochemical four-electron oxidation converts the radialenes into energy-rich cyclobutadienes bearing four cationic substituents; these species are either present only in small equilibrium concentration **(74^{4+})** or undergo irreversible transformation (**106^{4+}** and **107^{4+}**).

As in the case of [3]radialenes, the individual redox stages of [4]radialenes may have different colors. Based on these electrochromic properties, the application of **77** as a component in liquid crystal display devices was patented[85].

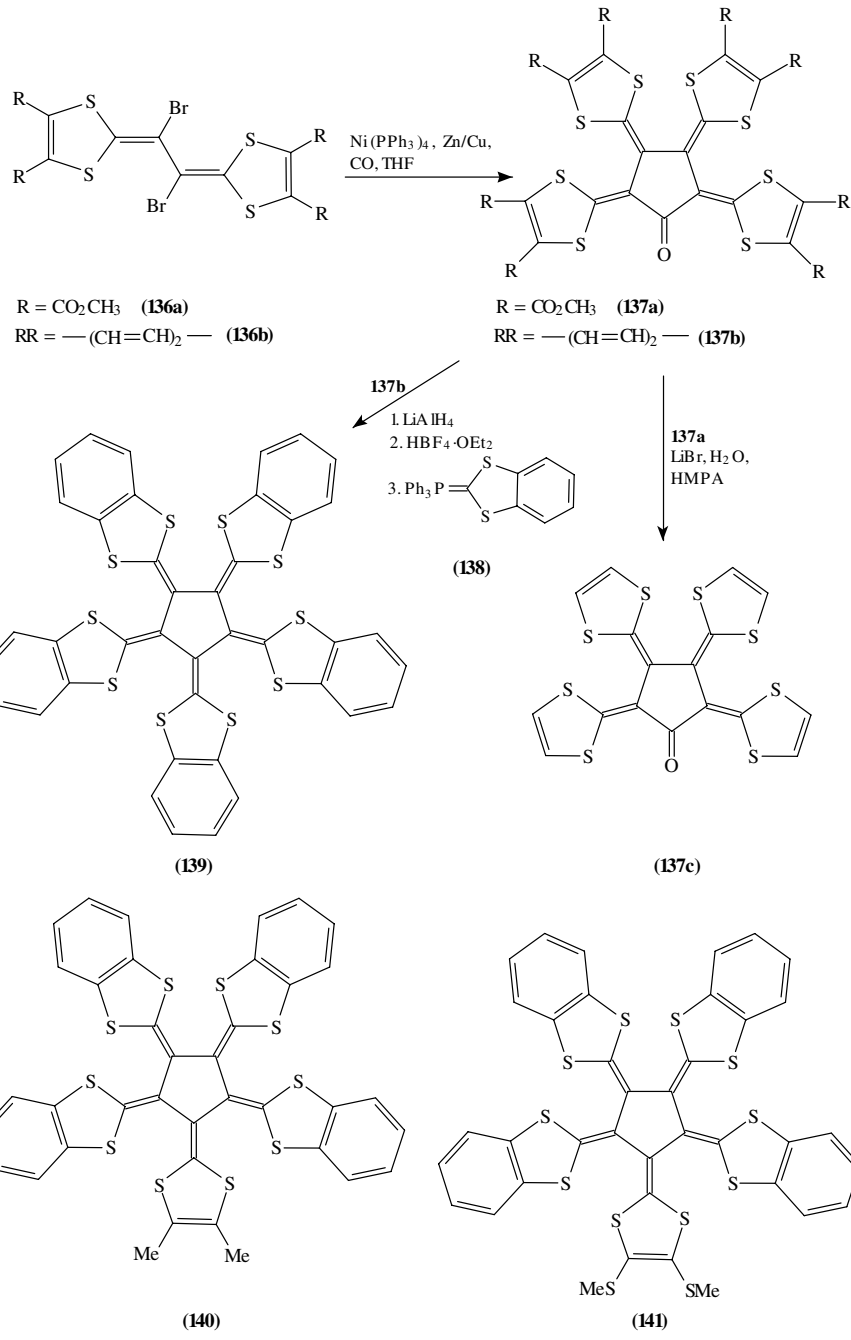
C. [5]Radialenes

Among the series of the parent systems **1–4**, [5]radialene **(3)** is still unknown. The simplest derivative described so far is decamethyl[5]radialene **(135)** which has been obtained from 1,1-dibromo-2-methylpropene **(22)** by low temperature metalation with *n*-butyllithium followed by a metal exchange reaction with nickel[11] or (better) copper[73] salts and the thermal decomposition of the carbenoid thus formed (equation 10). The yield of **135** varies: it is only 14% with $CuBr \cdot SMe_2$, but it more than doubles (32%) when $CuI \cdot PBu_3$ is employed[73]. The formation of **135** is accompanied by di-, tri- and tetramerization of the dimethylvinylidene unit derived from **22** leading to tetramethylbutatriene and the respective permethylated [3]- and [4]radialenes. It is unlikely, though, that this



(10)

(22) **(135)**

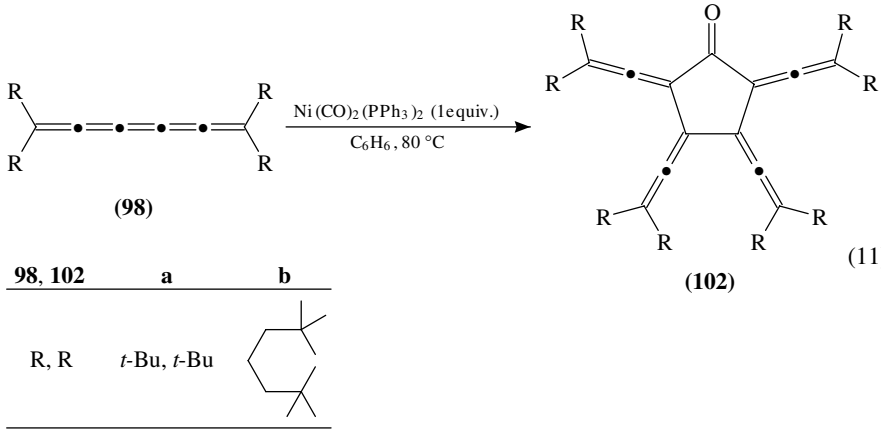

Ni(PPh3)4, Zn/Cu,
CO, THF
R = CO2CH3 (136a)
RR = —(CH=CH)2— (136b)
R = CO2CH3 (137a)
RR = —(CH=CH)2— (137b)
137b
1. LiAlH4
2. HBF4·OEt2
3. Ph3P=
(138)
137a
LiBr, H2O,
HMPA
(139)
(137c)
Me
Me
MeS
SMe
(140)
(141)

SCHEME 17

formally simple approach can be developed into a general method for the preparation of substituted [5]radialenes, since the amount of the [3]- and [4]radialenes produced increases with increasing bulkiness of the substituent (see Sections II.A and II.B).

In another metal-mediated coupling reaction, the highly functionalized dienes **136a** and **136b** were allowed to react with $Ni(PPh_3)_4$ in the presence of excess zinc/copper couple at 50 °C and 1 atm of carbon monoxide to provide the octakis(methoxycarbonyl) **137a** and the tetrabenzo derivatives **137b** in excellent yields (77 and 84%, respectively), (see Scheme 17; compare also Scheme 12 for the formation of the related [4]radialene **106**[86–88]). When **137a** was treated with excess $LiBr \cdot H_2O$ in HMPA at temperatures above 100 °C, the parent system **137c** was obtained in 88% yield[88]. The ketone **137b** was subsequently used to prepare the [5]radialene **139** by a condensation reaction employing the ylide **138**[87,89]. The [5]radialenes **140** and **141** were prepared analogously[89].

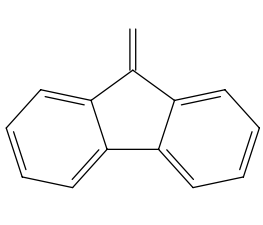
Another [5]radialene ketone, the tetraallene **102a**, has been prepared in 74% yield by treating the [5]cumulene **98a** with stoichiometric amounts of $Ni(CO)_2(PPh_3)_2$[67]; the sterically very shielded ketone **102b** is produced analogously in 32% yield from the corresponding 'terminally bridged' [5]cumulene **98b** (equation 11). In both cases the dimers of the [5]cumulenes, the peralkylated [4]radialenes are formed as well (see Section II.B, Scheme 11).



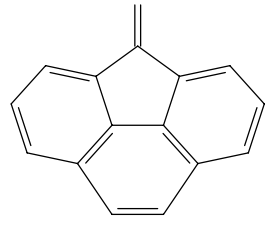
(11)

As already pointed out in the Introduction, [5]radialene **(3)** may be regarded as the 'monomer' of C_{60}[90a]. Likewise, hydrocarbon frameworks containing both six- and five-membered rings may be regarded as subunits of fullerenes if they are arranged in the proper geometric arrangement and are constructed from sp^2-hybridized carbon atoms only. In many of these subsystems — examples are provided by **142–144** — the aromatic character will clearly determine the chemical behavior. In other hydrocarbons, however, the radialenic, i.e. more polyolefinic, character might well begin to take over. This could, for example, be the case for the still unknown [5]radialenes **145** and **146**. For the 'totally benzannelated' compound **147**, corannulene, a tub-shaped molecule, which constitutes one-fourth of C_{60}, several ways of preparation are now known[90b].

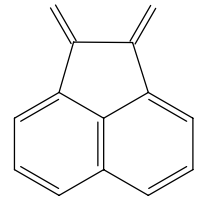
Practically nothing is known about the chemical behavior of [5]radialenes. An exception is the electrochemistry of systems **139–141**. These potent electron-donating molecules show only one pair of reversible waves involving a net transfer of four electrons. In fact, these systems constitute the first examples of a single-wave four-electron transfer with only one macroscopic redox site in an organic redox system[87,89]. The corresponding tetracationic salts could be isolated.



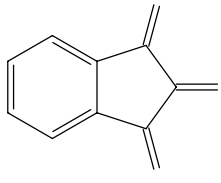
(142)



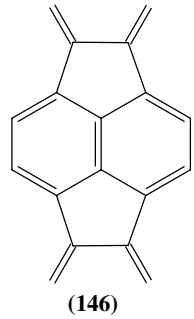
(143)



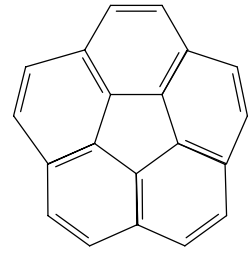
(144)



(145)



(146)

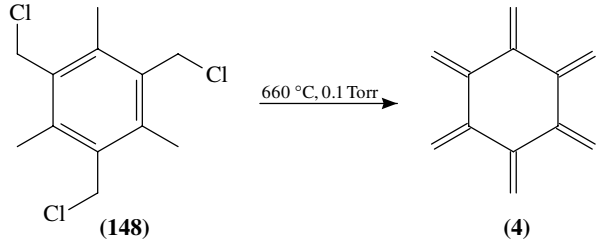


(147)

D. [6]Radialenes

Alkyl derivatives of [6]radialene **(4)** were the first members of this class of polyolefinic compounds ever to be reported (see below).

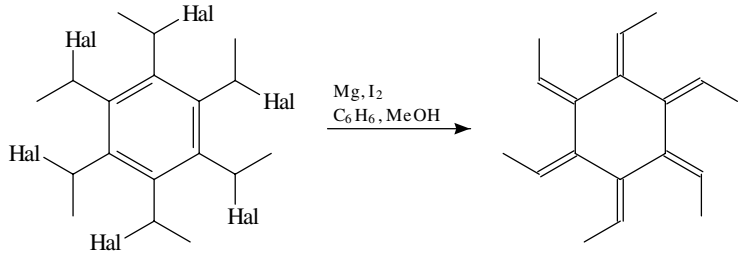
The parent hydrocarbon **4** has been obtained by several routes[91–93], with the thermal dehydrochlorination of the readily available 2,4,6-tris(chloromethyl)mesitylene (**148**, equation 12) being particularly valuable[92]. The yields of this process (close to 50%) are reproducible, making **4** a readily available, albeit difficult-to-handle, highly reactive starting material for further transformations (see below).



(148) **(4)** (12)

The hexamethyl derivative of **4**, all-(*E*)-7,8,9,10,11,12-hexamethyl[6]radialene **(150)**, was the first [*n*]radialene described in the chemical literature. It was prepared in 1961 in 30% yield by treating either the hexabromide or the hexachloride **149** with magnesium in methanol/benzene (equation 13)[94,95]. The analogous hexaethyl[6]radialene was obtained by the same method from the corresponding hexakis(1-bromopropyl)benzene[96]. The two radialenes mentioned, which according to X-ray structural analysis[97] possess the so-called bucket wheel configuration, are the main elimination products. They crystallize particularly well and can hence be isolated easily. Besides these products there are other

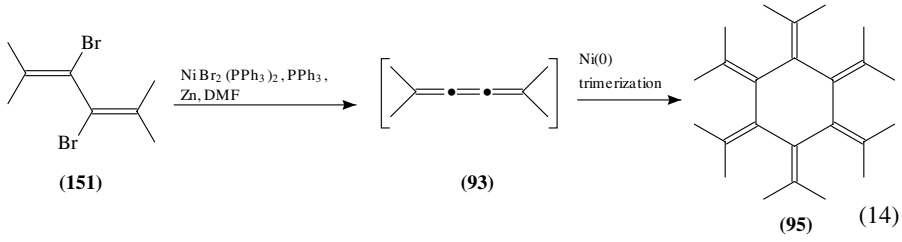
diastereomers formed as well in low concentration.



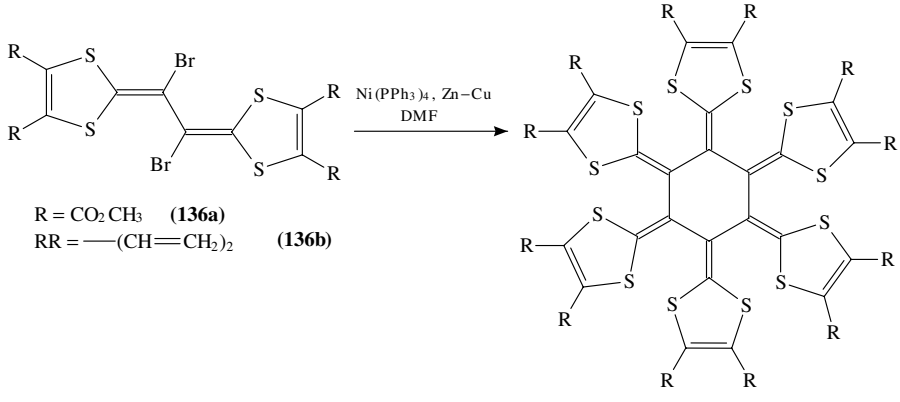
(149) (150) (13)

Hal = Cl, Br

Dodecamethyl[6]radialene **(95)** is obtained when *in situ* produced tetramethylbutatriene **(93)** is trimerized with a Ni(0) catalyst after debromination of the dibromide **151** with Ni(0) (equation 14)[65,66,68] (see also Section II.B). This approach was also successfully applied to the dibromides **136a** and **136b** which yield the electron-rich [6]radialenes **152a** and **152b** on treatment with $[Ni(PPh_3)_4]$/Zn–Cu in DMF (equation 15)[98].



(151) (93) (95) (14)



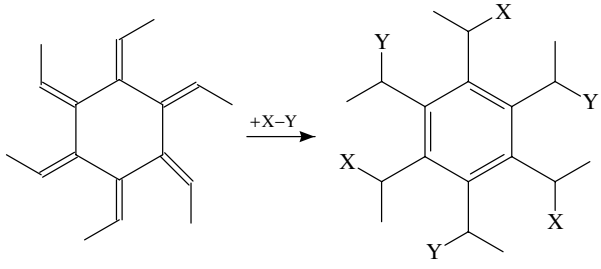
R = CO_2CH_3 **(136a)**
RR = —(CH=CH_2)$_2$ **(136b)**

(152a) 35%
(152b) 72% (15)

The parent [6]radialene has no stabilizing aromatic feature and is predicted to have a relatively low-lying HOMO as compared to the lower members of the series, **1–3**[99]. This may explain why it is so highly reactive that it is difficult to handle. As far as the chemical behavior of the [6]radialenes is concerned, it is the hexamethyl derivative **150**

which has been studied most thoroughly so far, undoubtedly due to its ready accessibility and its ease of handling.

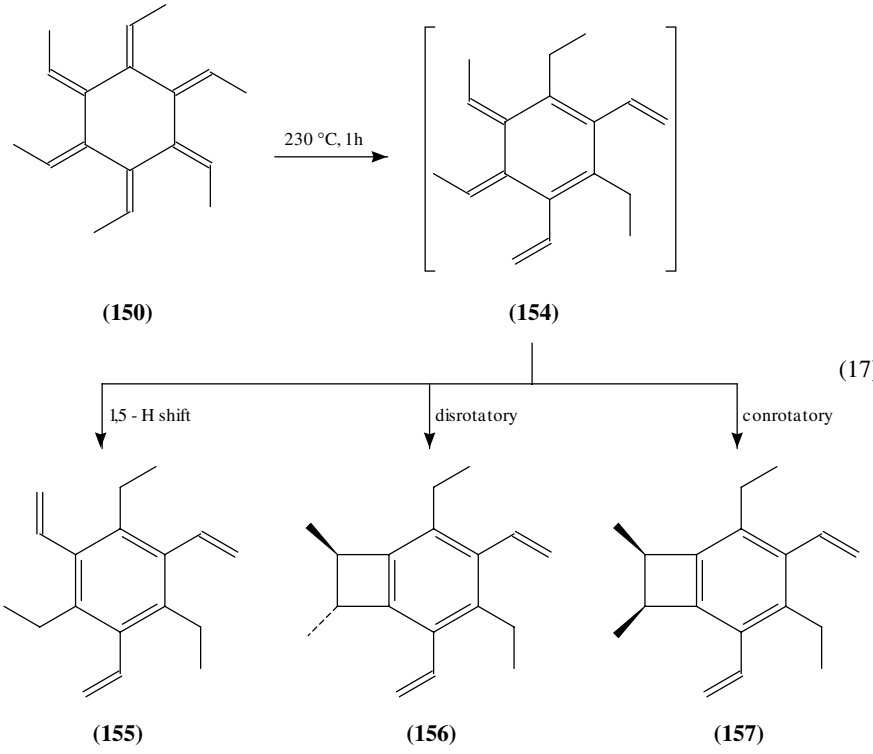
Not unexpectedly, **150** reacts with electrophilic reagents such as HCl, HBr and Br_2, and also with H_2 in a 1,4- fashion, to give the hexa-substituted benzene derivatives **153a** and **153b** (which are synthetic precursors of **150**), **153c** and **153d**, respectively (equation 16)[94,95].



(153)	X	Y
(a)	Cl	H
(b)	Br	H
(c)	Br	Br
(d)	H	H

(150) **(153)** (16)

When **150** is thermolyzed at 230 °C it rearranges to at least three isomers, **155–157**, which comprise approximately 75% of the product mixture[100]. Very likely this process is initiated by two 1,5-hydrogen shift reactions providing the isomer **154** first. Before this can undergo a third 1,5-hydrogen migration process to the most stable isomer **155** — formally

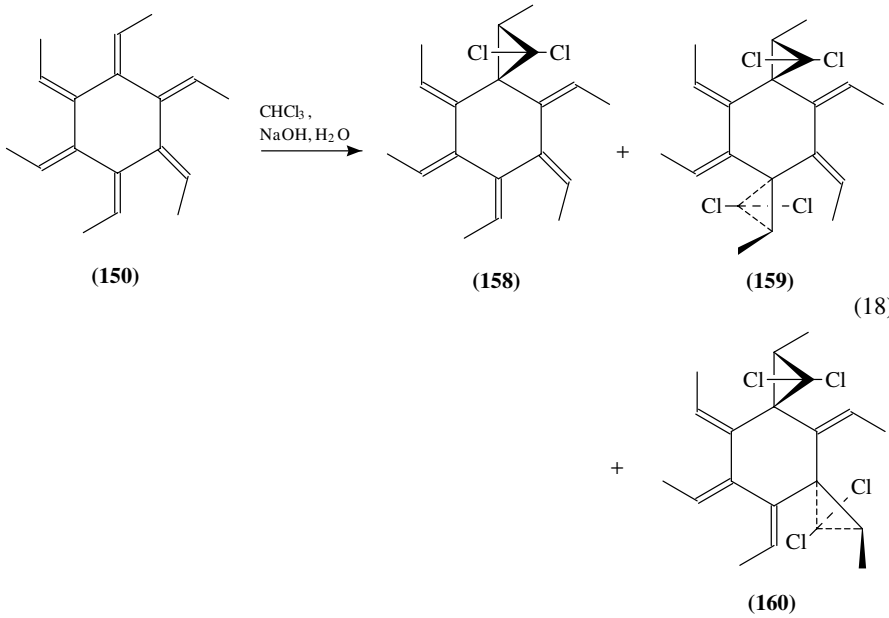


(150) **(154)** (17)

(155) **(156)** **(157)**

speaking, a threefold disproportionation product of **150** — it can also undergo electrocyclic ring-closure reactions at its remaining exocyclic butadiene system. This isomerization can take place either in a disrotatory or a conrotatory fashion leading to the benzocyclobutenes **156** and **157**, respectively (equation 17). Since the latter is the orbital symmetry-allowed process, it is not surprising that it is highly preferred (ratio **157**/**156** = 10 at 230 °C).

Dichlorocarbene adds to **150** to give the monoadduct **158** as well as the two bis-adducts **159** and **160** (equation 18)[101]. An 'ortho'-bis-adduct could not be detected among the cyclopropanation products — possibly because of steric hindrance in the immediate vicinity of **158**. The *anti*-arrangement of the two cylopropane rings in **159** and **160** was established by X-ray structural analysis[101]. Formally, the latter adducts represent hybrids of [6]radialenes and [6]rotanes ('rotaradialenes').



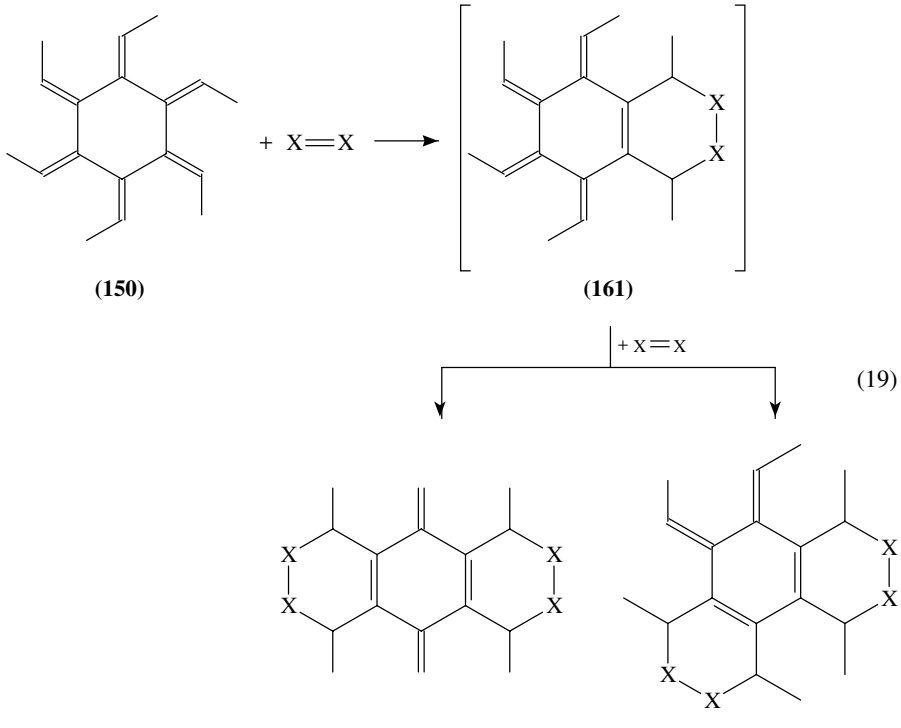
(150) **(158)** **(159)** (18)

(160)

Since the [6]radialenes are triple-diene systems, it comes as no surprise that they have been used in multiple Diels–Alder reactions. In fact, after a first 1:1 addition with **150**, leading to **161**, has taken place, the reaction could proceed in two fashions — a linear course of addition leading to a *para*-xylylene **162**, and an angular route which produces an *ortho*-xylylene intermediate **163** (equation 19)[102,103].

Whereas for the hexamethyl compound **150** only products formed by the linear route have been detected with a sizeable number of dienophiles (X=X *inter alia* TCNE, maleic anhydride, benzoquinone, 1,4-naphthoquinone, acrolein, methyl acrylate[102]), the parent system **4** undergoes threefold Diels–Alder addition in a star-shaped manner leading to **164** with dimethyl acetylenedicarboxylate and to **165** with fumaroyl chloride followed by methanolysis (equation 20)[92].

That this difference in (4+2)-cycloaddition behavior most likely has steric origins — the methyl groups in **150** or the derived monoadduct preventing an 'ortho'-addition of two equivalents of the dienophile — is supported by the observation that permethyl[6]radialene **95** is inert even towards the extremely reactive dienophile 4-phenyl-1,2,4-triazolinedione[68].



(150) **(161)** (19)

(162) **(163)**

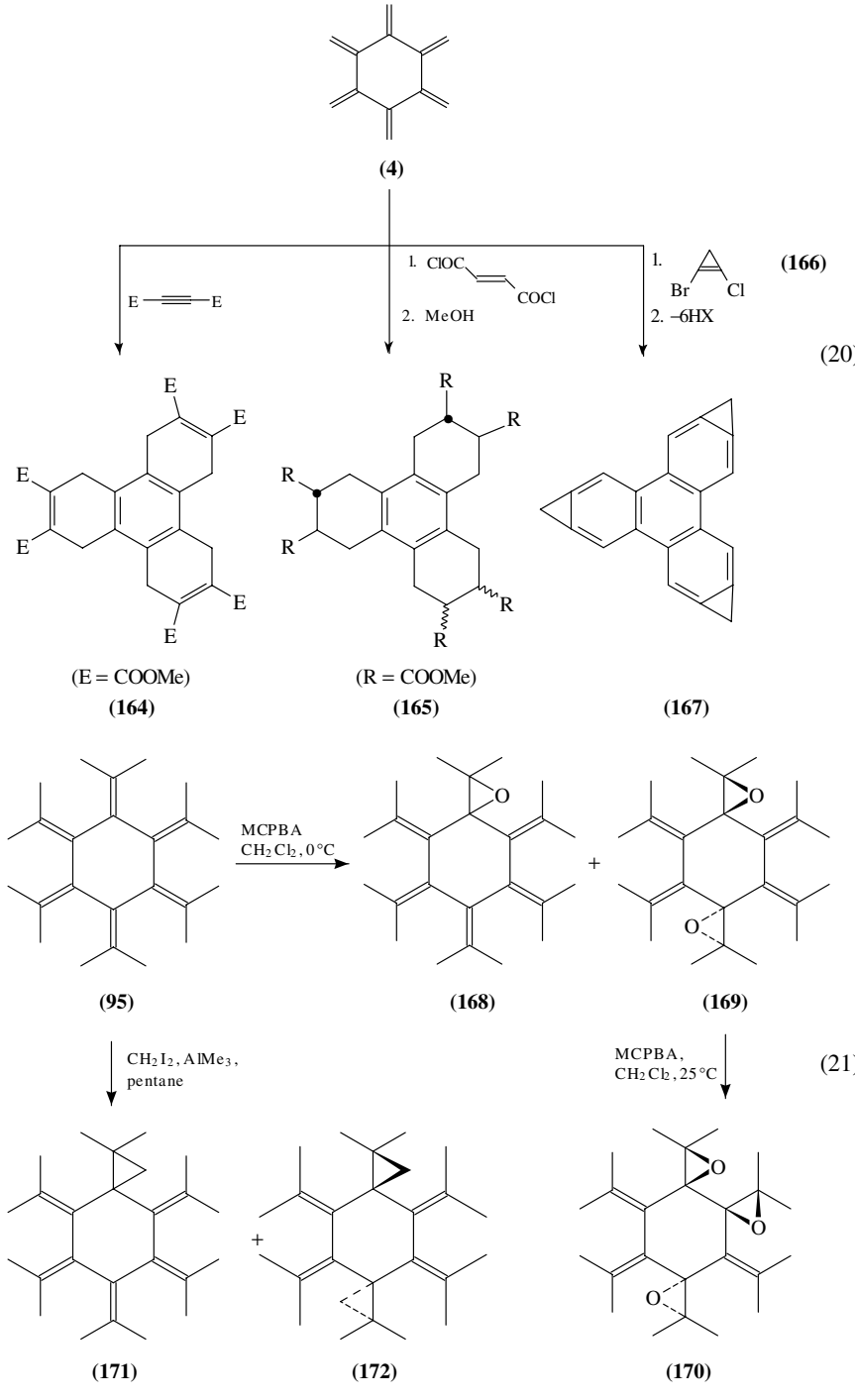
In a recent interesting application the 'tris-diene' **4** was first reacted with 1-bromo-2-chlorocyclopropene **166**, and the resulting *tris*-adduct was subsequently dehydrohalogenated to the tricycloproparene **167** (equation 20)[104].

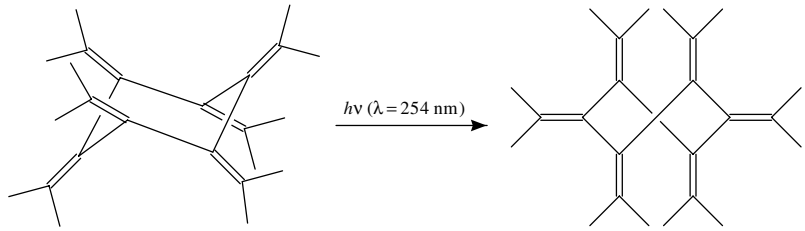
In very recent work the [6]radialene **95** has been epoxidized with *m*-chloroperbenzoic acid (MCPBA) to the mono- and the *bis*-epoxide **168** and **169**, respectively, at 0 °C, and to the *tris*-epoxide **170** at room temperature[100]. Methylenation with $CH_2I_2/AlMe_3$ provides the 'rotaradialenes' **171** and **172** (equation 21)[101]. Again, the relative orientation of the three-membered rings in these adducts follows from X-ray and NMR data[100,101].

A series of remarkable transformations takes place when **95** is irradiated with 254-nm light. As has been shown by X-ray structure determination, this radialene adopts the chair configuration **c-95** in its ground state[68]. On irradiation **c-95** is first converted into the twist-isomer **t-95**, whose structure has been determined by X-ray analysis again[101]. In a second step, two photochemical 1,5-hydrogen shifts take place leading to the *para*-xylylenes **173** and **174** (equation 22). Normally, these all-carbon analogues of *p*-benzoquinone are very reactive and cannot be obtained in substance. In the present instance they can be handled easily under normal laboratory conditions[100]. Most likely this stability is caused by the complete substitution of the *para*-xylylene core of these hydrocarbons.

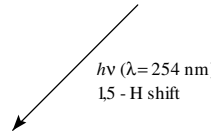
Whether [6]radialenes have a potential as novel ligands for metal complexes remains to be seen. A first example of a successful complexation is provided by **150**, which reacts with tris(acetonitrile)tricarbonylchromium in dioxane at room temperature to give the *ortho*-xylylene chromium complex **175** in excellent yield (83%) (equation 23)[105].

It should be noted that **175** is the chromium complex of **154**, the intermediate postulated in the thermal isomerization of hexamethyl[6]radialene **(150)**.

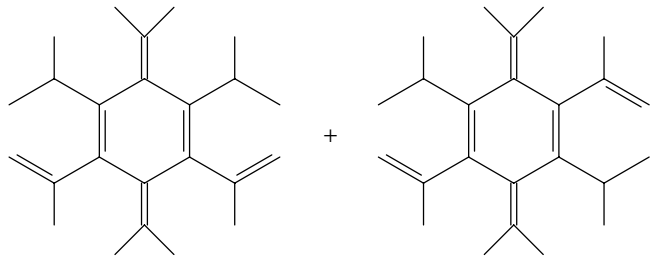

(4)
E—≡—E
1. ClOC—═—COCl
2. MeOH
1. Br Cl
2. –6HX
(166)
(20)
(E = COOMe)
(164)
(R = COOMe)
(165)
(167)
MCPBA
CH2Cl2, 0 °C
(95)
(168)
(169)
CH2I2, AlMe3,
pentane
MCPBA,
CH2Cl2, 25 °C
(21)
(171)
(172)
(170)



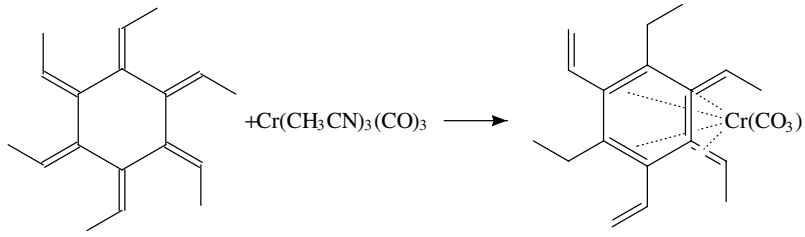
(c-95) **(t-95)**



(22)



(173) **(174)**

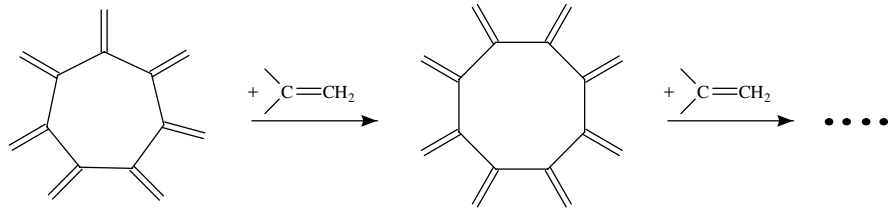


(150) **(175)** (23)

E. Higher Radialenes

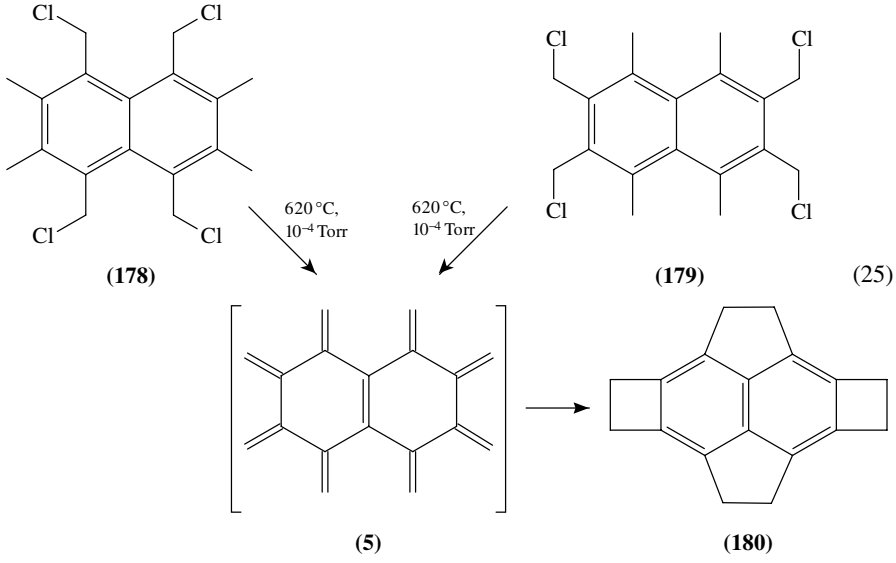
Higher radialenes may be generated in several different ways. The most obvious one consists in just inserting additional exocyclic double bonds into the monocyclic ring system, thus generating [7]- **(176)** and [8]radialene **(177)** as the next members of the homologous series (e.g. as in equation 24). These compounds — which are unknown at the present time — are not only of interest in their own right and as targets of novel preparative routes which very likely have to be developed to prepare them. Based on the predicted first vertical ionization potential of only about 7.0 eV[99], these higher radialenes are expected to be extremely reactive and hence quite unstable, but they could in principle also serve as core units for extended π-systems in the same way in which [5]radialene plays this role in, e.g., corannulene **(147)** or C_{60}. Undoubtedly these cores will generate

topologies in these larger π-systems which are different from those produced by five-membered rings.



(176) **(177)** (24)

Secondly, the carbon framework 'holding' the exocyclic double bonds could be extended. This is demonstrated by naphtharadialene **5**, a highly reactive intermediate which has been generated by thermal dehydrochlorination from either the tetrachloride **178** or its isomer **179**[106]. Radialene **5** has not been detected as such in these eliminations; rather, its temporary formation was inferred from the isolation of the thermolysis product **180** which was isolated in 15% yield (equation 25). Formally, **5** may also be regarded as an [8]radialene into whose center an ethylene unit has been inserted. In principle, other center units — cyclobutadiene, suitable aromatic systems — may be introduced in this manner, thus generating a plethora of novel radialene structures.

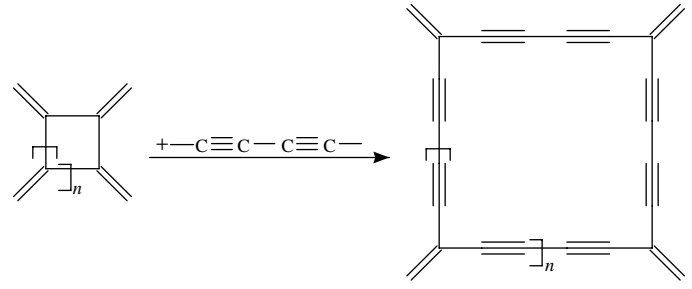


(178) **(179)** (25)

(5) **(180)**

A third route to higher or 'expanded' radialenes (see Introduction) also rests on an 'insertion principle'. It employs the rodlike butadiyne unit and inserts it between the neighboring double bonds of the basic radialene systems **181**, thus converting these into the boxlike molecules **12** (equation 26)[107,108].

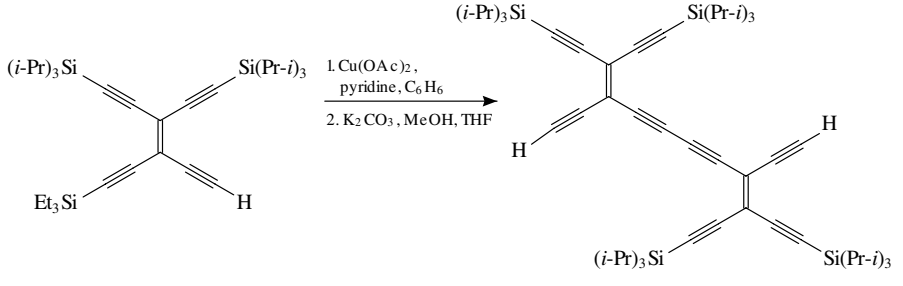
The first representatives of these interesting π-systems have recently been described. In the even series (**12**, $n = 1,3,\ldots$) the synthesis of the square molecule **184** and the hexagonal one **185** starts from the building block **182**. This is first oxidatively dimerized



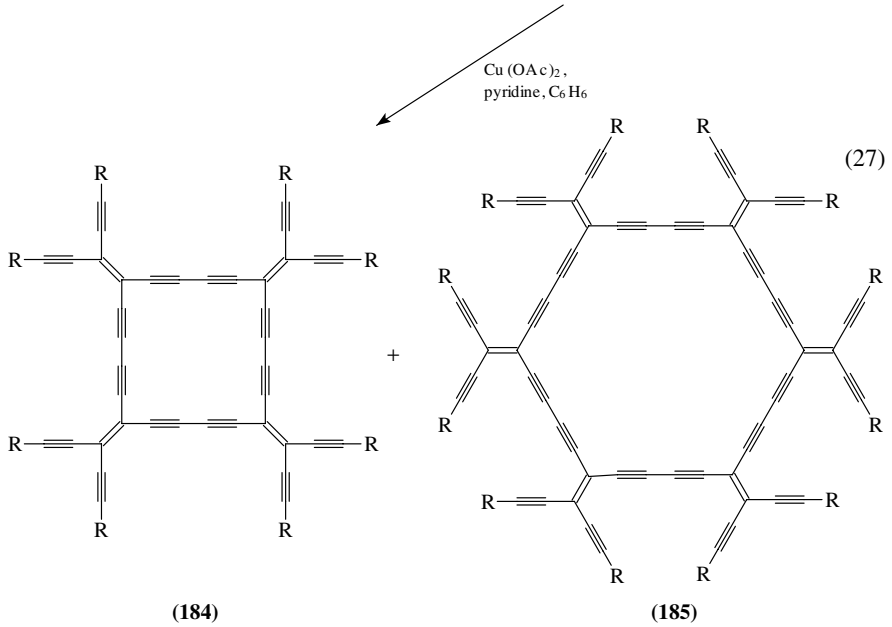
(26)

$n = 0, 1, 2, ...$ $n = 0, 1, 2, ...$

(181) **(12)**



(182) **(183)**



(27)

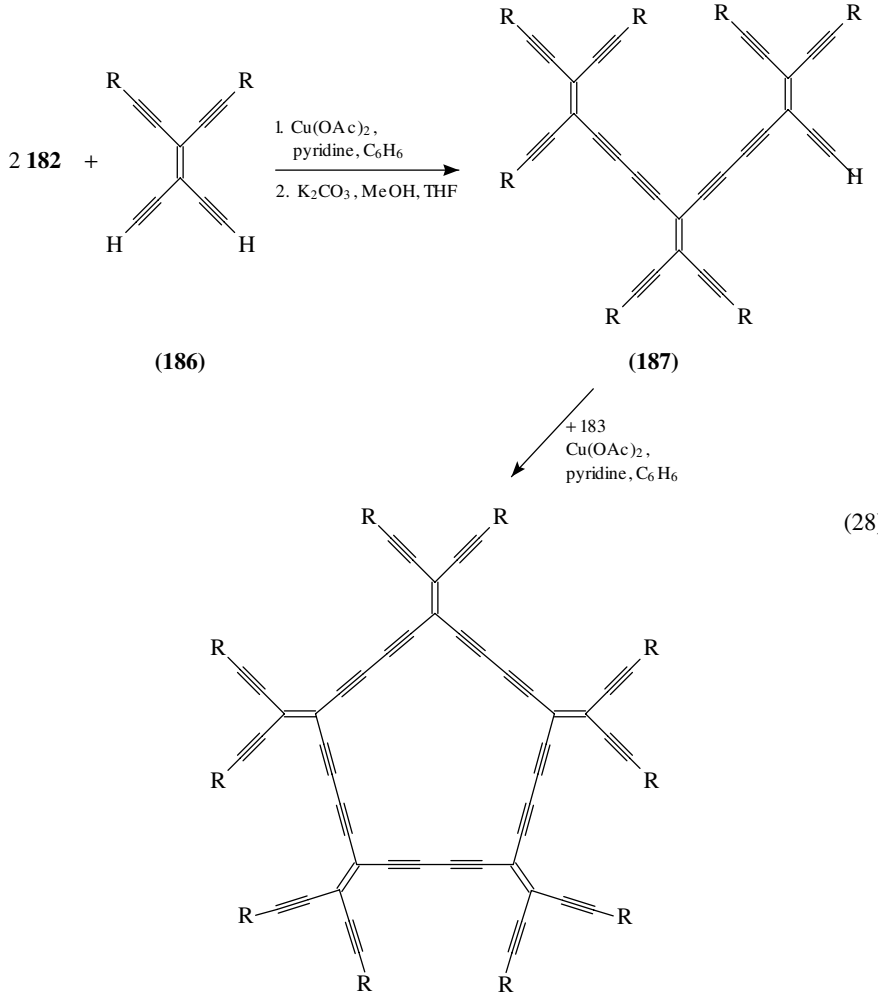
(184) **(185)**

R = Si(Pr-i)$_3$

and the product formed is deprotected to give **183**, which possesses two 'free' triple bonds. Cyclization by oxidative coupling is hence possible, and it results in the formation of **184** and **185** which are produced in remarkably good yields (15 and 20%, respectively) (equation 27)[107,108].

To generate the pentagonal structure **188**, two equivalents of **182** were first coupled with the tetraethynylethene **186**. After deprotection of the appropriate ethynyl groups the resulting intermediate **187** could be 'roofed' with **183** to yield the desired product **188** (yield of last step: 15%) (equation 28)[107,108].

Clearly, this is a rich playground for chemists interested in novel π-structures and topologies, and it is likely that many novel radialene-derived compounds will be prepared in the not too distant future.



III. CONCLUDING REMARKS

We have already pointed out in the Introduction (see above) that the first review article on radialenes is only a few years old[1]. In this first summary we have enclosed a comprehensive survey and discussion of the structural and spectroscopic properties of the radialenes. Since progress in this latter area has not been very rapid in the last few years, we do not address here again these aspects of the radialenes. Furthermore, nothing new can be added to the statement that all radialenes are nonaromatic and that they have localized endocyclic single bonds and exocyclic double bonds[1] (for recent discussions of $\pi-\pi$ interaction in [5]- and [3]radialene, see elsewhere[90a,109]).

However, the present chapter clearly shows that preparative radialene chemistry is an active and quickly evolving area of synthetic organic chemistry. Many different radialenes are now accessible by various, often surprisingly simple synthetic routes. New substitution patterns and π-system topologies, often emerging in a conceptual approach to new organic materials[1,110], continue to be a challenge for synthetic chemists. If this development remains alive the need will certainly arise in a few years time to present all of radialene chemistry in a (first) monograph on this interesting class of compounds.

IV. ACKNOWLEDGMENTS

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