CHAPTER IV

AROMATIC COMPOUNDS

AROMATIC HYDROCARBONS

Aromatic hydrocarbons may be prepared by the following methods :—

1. **Wurtz - Fittig reaction.** The interaction of an aryl halide, alkyl halide and sodium gives a reasonable yield of an alkyl aryl hydrocarbon, for example :

$$\underset{\text{Bromobenzene}}{C_6H_5Br} + 2Na + \underset{n\text{-Butyl bromide}}{BrCH_2CH_2CH_2CH_3} \longrightarrow \underset{n\text{-Butylbenzene (b.p. 182°)}}{C_6H_5CH_2CH_2CH_2CH_3}$$

The by-products are $C_4H_9^{\alpha}—C_4H_9^{\alpha} \equiv n\text{-}C_8H_{18}$, *n*-octane (b.p. 125°) and $C_6H_5—C_6H_5$, diphenyl (b.p. 254°), and can be readily separated by distillation.

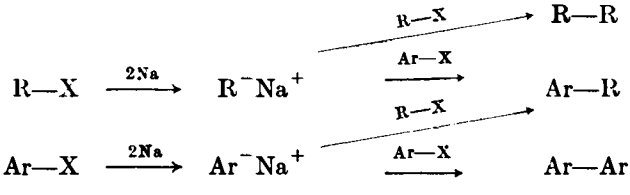
Two *mechanisms* have been proposed for the Wurtz reaction (compare Section **III,7**) and for the Wurtz - Fittig reaction. According to one, sodium reacts with the alkyl halide to produce a sodium halide and a free radical, which subsequently undergoes coupling, disproportionation, etc. :

$$C_4H_9^{\alpha}Br + Na \longrightarrow C_4H_9^{\alpha}. + NaBr$$
$$C_6H_5Br + Na \longrightarrow C_6H_5. + NaBr$$
$$C_6H_5. + C_4H_9^{\alpha}. \longrightarrow C_6H_5—C_4H_9^{\alpha}$$
$$C_6H_5. + C_6H_5. \longrightarrow C_6H_5—C_6H_5$$
$$C_4H_9^{\alpha}. + C_4H_9^{\alpha}. \longrightarrow C_4H_9^{\alpha}—C_4H_9^{\alpha}$$
$$2CH_3CH_2CH_2CH_2. \longrightarrow CH_3CH_2CH=CH_2 + CH_3CH_2CH_2CH_3$$

The other mechanism involves the intermediate formation of organosodium compounds :

$$R—X + 2Na \longrightarrow R^-Na^+ + NaX$$

The products from a mixture of alkyl and aryl halides may be represented by the following scheme :



The fact that *n*-butylbenzene can be prepared in reasonable yield by the action of sodium upon a mixture of bromobenzene and *n*-butyl bromide can be partly explained on the assumption that *n*-butyl bromide reacts with phenylsodium more rapidly than does bromobenzene. It is interesting to note that *n*-butylbenzene can be prepared either from benzylsodium and *n*-propyl bromide or from phenylsodium and *n*-butyl bromide (Section **VI,29**).

2. **Friedel and Crafts reaction.** An alkyl halide condenses with an aromatic hydrocarbon in the presence of anhydrous aluminium chloride to yield, in the first instance, a hydrocarbon in accordance with the following scheme :—

$$ArH + RX \xrightarrow{AlCl_3} ArR + HX$$

The reaction does not, however, stop at the stage of mono-substitution since the alkylbenzene ArR initially produced undergoes alkylation more easily than the original hydrocarbon ArH : mixtures of substances therefore result and extensive purification is required in order to isolate the mono-substituted compound. Furthermore, alkyl halides, which are capable of isomerisation, are generally isomerised during the condensation ; thus *n*-propyl halides and benzene give *iso*-propylbenzene, *n*-butyl halides yield *sec.*-butyl derivatives, etc. Some mono-alkylbenzenes may be prepared by using an excess of the hydrocarbon, which also acts as a diluent in moderating the violence of the reaction and prevents the undue formation of poly-alkylbenzenes, for example :

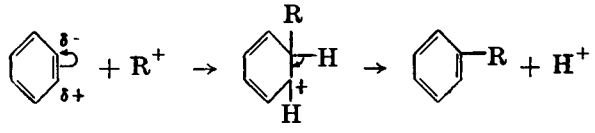
$$\underset{n\text{-Propyl chloride}}{CH_3CH_2CH_2Cl} + C_6H_6\ (\text{excess}) \xrightarrow{AlCl_3} \underset{iso\text{-Propylbenzene (cumene)}}{C_6H_5CH(CH_3)_2}$$

$$\underset{tert.\text{-Butyl chloride}}{(CH_3)_3CCl} + C_6H_6\ (\text{excess}) \xrightarrow{AlCl_3} \underset{tert.\text{-Butylbenzene}}{C_6H_5C(CH_3)_3}$$

Other catalysts which may be used in the Friedel - Crafts alkylation reaction include ferric chloride, antimony pentachloride, zirconium tetrachloride, boron trifluoride, zinc chloride and hydrogen fluoride but these are generally not so effective in academic laboratories. The alkylating agents include alkyl halides, alcohols and olefines.

The *mechanism* of the reaction is generally considered to proceed by way of carbonium ions (alkyl cations) which attack the aromatic nucleus :

$$R{-}X + AlCl_3 \longrightarrow R^+[AlCl_3X]^- \rightleftharpoons R^+ + [AlCl_3X]^-$$



$$H^+ + [AlCl_3X]^- \longrightarrow HX + AlCl_3$$

The formation of *iso*propylbenzene when *n*-propyl chloride is employed as the alkylating agent is readily accounted for by the isomerisation of the alkyl carbonium (or alkylium) ion :

$$CH_3CH_2CH_2^+ \rightleftharpoons (CH_3)_2CH^+$$

possibly by transfer of a hydride ion from secondary carbon to primary carbonium ion.

Two interesting applications of the Friedel and Crafts reaction to the preparation of aromatic hydrocarbons will be described, *viz.* :—

$$\underset{\text{Benzyl chloride}}{C_6H_5CH_2Cl} + C_6H_6\ (\text{excess}) \xrightarrow{AlCl_3} \underset{\text{Diphenylmethane}}{C_6H_5CH_2C_6H_5}$$

$$\underset{\text{Chloroform}}{CHCl_3} + 3C_6H_6\ (\text{excess}) \xrightarrow{AlCl_3} \underset{\text{Triphenylmethane}}{CH(C_6H_5)_3}$$

By-products are formed in both preparations : thus in the former, anthracene, and *o*- and *p*-dibenzylbenzenes are present in the fraction of high boiling point. Diphenylmethane is more conveniently obtained by the interaction of benzyl chloride and benzene in the presence of aluminium amalgam :

$$C_6H_5CH_2Cl + C_6H_6 \xrightarrow{Al{-}Hg} C_6H_5CH_2C_6H_5 + HCl$$

3. **Clemmensen reduction of aldehydes and ketones.** Upon reducing aldehydes or ketones with amalgamated zinc and concentrated hydrochloric acid, the main products are the hydrocarbons ($>C=O \longrightarrow >CH_2$), but variable quantities of the secondary alcohols (in the case of ketones) and unsaturated substances are also formed. Examples are :

$$C_6H_5CHO \xrightarrow[HCl]{Zn(Hg),} C_6H_5CH_3$$

$$\underset{\text{Acetophenone}}{C_6H_5COCH_3} \longrightarrow \underset{\text{Ethylbenzene}}{C_6H_5CH_2CH_3}$$

$$\underset{\text{Ethyl benzyl ketone}}{C_6H_5CH_2COCH_2CH_3} \longrightarrow \underset{n\text{-Butylbenzene}}{C_6H_5CH_2CH_2CH_2CH_3}$$

$$\underset{n\text{-Propyl-}\beta\text{-phenylethylketone}}{C_6H_5CH_2CH_2COCH_2CH_2CH_3} \longrightarrow \underset{n\text{-Hexylbenzene}}{C_6H_5(CH_2)_5CH_3}$$

The ketones are readily prepared, for example, acetophenone from benzene, acetyl chloride (or acetic anhydride) and aluminium chloride by the Friedel and Crafts reaction ; ethyl benzyl ketones by passing a mixture of phenylacetic acid and propionic acid over thoria at 450° ; and *n*-propyl-β-phenylethylketone by circulating a mixture of hydrocinnamic acid and *n*-butyric acid over thoria (for further details, see under *Aromatic Ketones*, Sections **IV,136**, **IV,137** and **IV,141**).

Purely aromatic ketones generally do not give satisfactory results : pinacols and resinous products often predominate. The reduction of ketonic compounds of high molecular weight and very slight solubility is facilitated by the addition of a solvent, such as ethanol, acetic acid or dioxan, which is miscible with aqueous hydrochloric acid. With some carbonyl compounds, notably keto acids, poor yields are obtained even in the presence of ethanol, etc., and the difficulty has been ascribed to the formation of insoluble polymolecular reduction products, which coat the surface of the zinc. The addition of a hydrocarbon solvent, such as toluene, is beneficial because it keeps most of the material out of contact with the zinc and the reduction occurs in the aqueous layer at such high dilution that polymolecular reactions are largely inhibited (see Section **IV,143**).

4. **Wolff-Kishner reduction of aldehydes and ketones.** Upon heating the hydrazone or semicarbazone of an aldehyde or ketone with potassium hydroxide or with sodium ethoxide solution (sealed tube), the corresponding hydrocarbon is obtained :

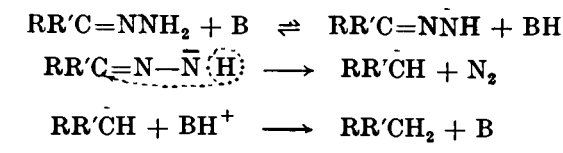
$$RR'CO \xrightarrow{N_2H_4} RR'C{=}NNH_2 \xrightarrow[NaOC_2H_5]{KOH\ or} RR'CH_2$$

The Huang-Minlon modification of the reaction has the following advantages: (i) the actual isolation of the hydrazone is unnecessary, (ii) the reaction time is considerably reduced, (iii) the reaction can be carried out at atmospheric pressure and on a large scale, and (iv) the yields are usually excellent. The hydrazone is first formed *in situ* by refluxing a solution of the carbonyl compound in a moderate amount of diethylene glycol or triethylene glycol with the commercial 85 or 90 per cent. hydrazine hydrate and about 3 equivalents of potassium hydroxide for 1 hour ; the water and excess of hydrazine are removed by distillation until a favourable temperature for the decomposition of the hydrazone is attained (170°–190°) and the solution is refluxed for 3-5 hours longer.

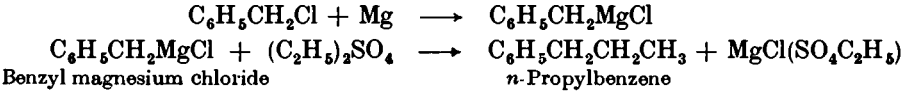
The reaction is illustrated by the preparation of ethylbenzene from acetophenone; the resulting hydrocarbon is quite pure and free from unsaturated compounds:

The disadvantages associated with the Clemmensen reduction of carbonyl compounds (see 3 above), *viz.*, (*a*) the production of small amounts of carbinols and unsaturated compounds as by-products, (*b*) the poor results obtained with many compounds of high molecular weight, (*c*) the non-applicability to furan and pyrrole compounds (owing to their sensitivity to acids), and (*d*) the sensitivity to steric hindrance, are absent in the modified Wolff-Kishner reduction.

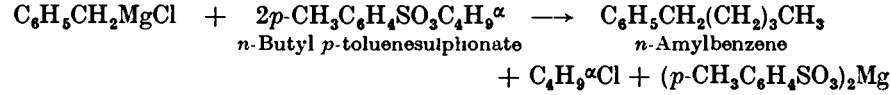
The *mechanism* of the reaction may involve the formation of an anion by the base B, followed by the shift of hydrogen on the hydrazone anion with simultaneous loss of nitrogen to yield a carbanion:



5. By the action of a dialkyl sulphate upon a Grignard reagent, for example:



6. By the interaction of a Grignard reagent and an alkyl *p*-toluenesulphonate for example:



For the preparation of alkyl *p*-toluenesulphonates, see Section **IV,210.**

IV,1. *n*-BUTYLBENZENE (*Wurtz - Fittig Reaction*)

Into a 1-litre round-bottomed flask, provided with a long (*e.g.*, a 30 cm.) double surface condenser, place 22·5 g. of clean sodium cut into small pieces (see Section **III,7**, *Note 1*, for experimental details concerning the handling of sodium) and mount the flask for heating on an asbestos-centred wire gauze. Prepare a mixture of 52 g. (35 ml.) of bromobenzene (Section **IV,18**) and 51 g. (40 ml.) of *n*-butyl bromide (Sections **III,35** and **III,37**). Add 5–7 ml. of the mixture through the condenser and warm the flask very gently with a small luminous flame. Immediately reaction commences (the sodium acquires a dark blue colour and much heat is evolved), remove the flame. Introduce the remainder of the mixture in small quantities during one hour; shake the mixture frequently and maintain a minute luminous flame beneath the flask. Reflux the reaction mixture for 1·1·5 hours using a *small luminous* flame; shake the fairly solid contents of the flask from time to time.

Allow to cool and add 50 ml. of rectified spirit during 30 minutes through a small separatory funnel fitted into the top of the condenser by means of a grooved cork ; introduce a mixture of 25 ml. of rectified spirit and 25 ml. of water during 30 minutes, followed by 50 ml. of water. This treatment will remove the excess of sodium. Reflux the resulting mixture for 2–3 hours. Add 500 ml. of water and filter at the pump from some sludge which is generally present ; it is advisable to wash the latter with a little ether. Transfer to a separatory funnel, remove the upper hydrocarbon layer, and wash it successively with 25 ml. of dilute sulphuric acid and 50 ml. of water ; dry over anhydrous magnesium or sodium sulphate and distil (50 ml. Claisen flask and air bath, Fig. *II*, *5*, 3).. Collect the *n*-butylbenzene at 178-188° (20 g.) ; an appreciable dark residue containing diphenyl remains in the flask. Upon redistillation, the *n*-butylbenzene boils at 178-184° (1).

Note.

(1) The *n*-butylbenzene contains some unsaturated hydrocarbons : these can be removed by repeated shaking with small quantities of concentrated sulphuric acid (see Section III,7,*Note* 2).

IV,2. *iso*-PROPYLBENZENE (CUMENE)

Fit a two-litre three-necked flask with a separatory funnel, a mechanical stirrer and a reflux condenser ; attach to the top of the condenser a tube leading to an inverted funnel or an adapter dipping just below the surface of a weighed quantity of water in a beaker or flask (compare Fig. *II*, *13*, 8). Place 700 g. (795 ml.) of dry benzene (1) and 20 g. of anhydrous aluminium chloride (2) in the flask, and set the stirrer in motion. Add a mixture of 300 g. (342 ml.) of dry benzene and 100 g. (112·5 ml.) of *n*-propyl chloride (compare Section **III,28**) or 157 g. (116 ml.) of *n*-propyl bromide (Section **III,35**) dropwise into the flask. Warm the flask to about 80° on a water bath ; the hydrogen halide evolved will be absorbed in the water. When this has increased in weight by 47 g. (104 g. for hydrogen bromide), pour the reaction mixture on to ice, remove the upper layer of hydrocarbon, wash it successively with dilute sodium hydroxide solution and water, and then dry with anhydrous magnesium sulphate. Distil through a well-lagged fractionating column (compare Fig. *II*, *15*, 5 and Fig. *II*, *16*, 1 ; see Sections **II,15–II,17**) ; the excess of benzene passes over first, followed by *iso*-propylbenzene at 151–153°. The yield is 118 g.

Notes.

(1) The moisture present in commercial benzene may be conveniently removed by distilling off about one-tenth of the liquid ; the first fraction contains all the moisture. It is generally unnecessary to distil the remaining liquid before use unless the technical benzene is suspected of being highly impure.

(2) The yield of *iso*-propylbenzene is influenced considerably by the quality of the anhydrous aluminium chloride employed. It is recommended that a good grade of technical material be purchased in small bottles containing not more than 100 g. each ; undue exposure to the atmosphere, which results in some hydrolysis, is thus avoided. Sealed bottles containing the reagent sometimes have a high internal pressure ; they should be wrapped in a dry cloth and opened with care.

IV,3. *tert.*-BUTYLBENZENE

Into a 1-litre three-necked flask, equipped as in Section IV,2, place 50 g. of anhydrous aluminium chloride (1) and 200 ml. of dry benzene; cool in a bath of crushed ice. Stir the mixture and add 50 g. (59 ml.) of *tert.*-butyl chloride (Section III,33) from the separatory funnel during 4–5 hours; the first addition should be 3–4 ml. in order to prevent the benzene from freezing. Maintain the mixture at a temperature of 0–5° by the addition of salt to the ice, if necessary. When all the *tert.*-butyl chloride has been run in, continue the stirring for 1 hour longer. Remove the separatory funnel and add 200 g. of finely-crushed ice in small portions with stirring; finally add 100 ml. of cold water to complete the decomposition of the intermediate addition compound. Arrange the flask for steam distillation (Fig. *II*, *41*, 1) and steam distil the resulting reaction mixture. Transfer the steam distillate to a separatory funnel, remove the upper hydrocarbon layer, extract the water layer with two 50 ml. portions of ether, and combine the extracts with the upper layer. Dry with anhydrous magnesium sulphate, distil off the ether on a water bath, and fractionally distil the residue twice, using a well-lagged column (compare Fig. *II*, *15*, 5 and Fig. *II*, *16*, 1). Collect the *tert.*-butylbenzene at 165–170°. The yield is 45 g. Pure *tert.*-butylbenzene boils at 168·5°.

Note.

(1) In an alternative procedure 25 g. of anhydrous ferric chloride replace the aluminium chloride, the mixture is cooled to 10°, and the 50 g. of *tert.*-butyl chloride is added. The mixture is slowly warmed to 25° and maintained at this temperature until no more hydrogen chloride is evolved. The reaction mixture is then washed with dilute hydrochloric acid and with water, dried and fractionally distilled. The yield of *tert.*-butyl benzene, b.p. 167-170°, is 60 g.

IV,4. DIPHENYLMETHANE

Method A (*Friedel and Crafts reaction*). Assemble an apparatus (1) consisting of a 500 ml. round-bottomed flask, a two-way addition tube (Fig. *II*, *1*, 8, *c*) and a reflux condenser (see Fig. *II*, *13*, 9 but with the separatory funnel replaced by a well-fitting cork); attach a water trap to the top of the condenser to absorb the hydrogen chloride produced in the reaction (compare Figs. *III*, *28*, 1 and *II*, *8*, 1). Place 38·5 g. (35 ml.) of redistilled benzyl chloride and 150 ml. of dry benzene (see Section IV,2, *Note* 1) in the flask. Weigh out 12 g. of anhydrous aluminium chloride (Section IV,2, *Note* 2) into a dry-stoppered test-tube with the minimum exposure to the atmosphere. Cool the flask in a bath of crushed ice and add about one-fifth of the aluminium chloride. Shake the mixture; a vigorous reaction will set in within a few minutes and hydrogen chloride will be evolved. When the reaction has subsided, add a further portion of the aluminium chloride and repeat the process until all has been introduced. The mixture should be kept well shaken and immersed in a freezing mixture during the addition. Finally reflux the mixture on a water bath for 30 minutes. Allow to cool. Cautiously add 100 g. of crushed ice, followed by 100 ml. of water in order to decompose the aluminium complex. Shake the mixture well, transfer to a separatory funnel, and run off the lower aqueous layer. Wash the upper layer

(benzene solution of diphenylmethane, etc.) successively with dilute hydrochloric acid and water; dry the benzene solution with anhydrous calcium chloride (warming on a water bath is advantageous). Remove the benzene with the aid of the apparatus shown in Fig. *II, 13,* 4 (50 or 100 ml. distilling flask). Distil the remaining liquid through an air condenser (Fig. *II, 13,* 2) either with a free flame or from an air bath (Fig. *II, 5,* 3). Collect the diphenylmethane at 250–275° (the pure substance boils at 262°) (2); there is an appreciable high boiling point residue. The distillate should solidify on cooling in ice and scratching with a glass rod, or by seeding with a crystal of the pure material. If it does not crystallise, redistil from a small flask and collect the fraction of b.p. 255–267°; this generally crystallises on cooling and melts at 24–25°. The yield is 30 g.

Notes.

(1) For preparations on a large scale a three-necked flask, provided with a reflux condenser, a mercury-sealed mechanical stirrer and the addition device shown in Fig. *II, 7,* 12, *c,* is recommended.

(2) Alternatively, the distillation may be conducted under diminished pressure; the fraction, b.p. 125–130°/10 mm., is collected. The removal of the benzene must then be conducted in a Claisen flask (compare Fig. *II, 13,* 4).

Method B (*with aluminium amalgam*). Assemble the apparatus shown in Fig. *II, 13,* 9, using a 1500 ml. round-bottomed flask. Place 500 g. (585 ml.) of dry benzene and 2·5 g. of aluminium amalgam (1) in the flask, and 125 g. (114 ml.) of redistilled benzyl chloride in the dropping funnel; insert a calcium chloride (or cotton wool) guard tube into the mouth of the latter. Heat the benzene to boiling on a water bath and remove the apparatus from the bath. Add the benzyl chloride slowly and at such a rate that the solution boils gently; hydrogen chloride is evolved and this may be absorbed by a trap (compare Figs. *III, 28,* 1 and *II, 8,* 1) fitted to the top of the condenser. If the reaction is slow in starting, do not add more than about 15 g. of benzyl chloride at first; warm on a water bath until hydrogen chloride is evolved indicating that reaction has set in. When all the benzyl chloride has been introduced (*ca.* 1 hour), heat the reaction mixture on a water bath for about 15 minutes or until the evolution of hydrogen chloride ceases. When cold, decant the benzene solution from the small quantity of tarry matter, wash it successively with 5 per cent. sodium hydroxide solution and water, and dry with anhydrous calcium chloride or magnesium sulphate. Remove the benzene at atmospheric pressure (Fig. *II, 13,* 4, but with distilling flask replaced by a Claisen flask) and distil the residue under reduced pressure. Collect the following fractions:—(i) up to 125°/10 mm.; (ii) 125–130°/10 mm. (this is the main fraction); and (iii) 130–150°/10 mm. Combine fractions (i) and (iii) and redistil; collect that boiling at 125–130°/10 mm. separately and add it to the fraction (ii). Upon cooling in ice, fraction (ii) (diphenylmethane) crystallises and melts at 24–25°. The yield is 85 g. The pure compound melts at 26–27°.

Note.

(1) The aluminium amalgam is prepared as described in Section **II,50,***12.* After washing with water, it should first be washed with methyl alcohol and finally with a little dry benzene.

IV,5. TRIPHENYLMETHANE

The apparatus required is similar to that described for *Diphenylmethane* (Section **IV,4**). Place a mixture of 200 g. (230 ml.) of dry benzene and 40 g. (26 ml.) of *dry* chloroform (1) in the flask, and add 35 g. of anhydrous aluminium chloride in portions of about 6 g. at intervals of 5 minutes with constant shaking. The reaction sets in upon the addition of the aluminium chloride and the liquid boils with the evolution of hydrogen chloride. Complete the reaction by refluxing for 30 minutes on a water bath. When cold, pour the contents of the flask very cautiously on to 250 g. of crushed ice and 10 ml. of concentrated hydrochloric acid. Separate the upper benzene layer, dry it with anhydrous calcium chloride or magnesium sulphate, and remove the benzene in a 100 ml. Claisen flask (see Fig. *II, 13,* 4) at atmospheric pressure. Distil the remaining oil under reduced pressure ; use the apparatus shown in Fig. *II, 19,* 1, and collect the fraction b.p. 190–215°/10 mm. separately. This is crude triphenylmethane and solidifies on cooling. Recrystallise it from about four times its weight of ethyl alcohol (2) ; the triphenylmethane separates in needles and melts at 92°. The yield is 30 g.

Notes.

(1) The chloroform is dried by leaving it over anhydrous calcium chloride or anhydrous calcium sulphate for about 12 hours.

(2) Triphenylmethane dissolves in about one-third of its weight of warm benzene ; it crystallises with one molecule of benzene of crystallisation which is lost on exposure to air or heating on a water bath or by recrystallisation from alcohol.

IV,6. ETHYLBENZENE

Method A (Clemmensen reduction)

Prepare 200 g. of amalgamated zinc in a 2-litre three-necked flask as detailed in Section **II,50,** *13.* Fit the flask with a reflux condenser, a mercury-sealed stirrer and a gas entry tube reaching to within 1 cm. of the bottom ; connect the last-named through an intermediate empty wash bottle to a Kipp's apparatus supplying hydrogen chloride gas (Section **II,48,** *1*). Place a mixture of 500 ml. of concentrated hydrochloric acid and 100 ml. of water in the flask and introduce 100 g. of acetophenone (Section **IV, 136**). Stir the mixture and pass in a slow stream of hydrogen chloride gas whilst warming the flask on an asbestos-centred wire gauze by means of a small flame. If the reaction becomes unduly vigorous, stop the supply of hydrogen chloride until it subsides somewhat. Most of the zinc dissolves after 6 hours, by which time the reaction is almost complete ; allow to stand overnight. Arrange the apparatus for steam distillation (Fig. *II, 41,* 1) and pass steam into the flask, heated by means of a small flame, until the distillate is clear. Separate the upper hydrocarbon layer, wash it with 5 per cent. sodium hydroxide solution, then with water, and dry over anhydrous magnesium sulphate. Distil from a 100 ml. Claisen flask and collect the ethylbenzene (1) at 134–135°. The yield is 50 g.

Note.

(1) The ethylbenzene contains some unsaturated compounds. These can be removed by repeated shaking with 5 per cent. of the volume of concentrated

sulphuric acid until the latter is colourless or, at most, very pale yellow. The hydrocarbon is then washed with 5 per cent. sodium carbonate solution, then with water, and dried over anhydrous magnesium sulphate. It is then distilled twice from sodium when pure ethylbenzene, b.p. 135°, is obtained.

Unsaturated hydrocarbons are present in nearly all products of the Clemmensen reduction of aromatic ketones and must be removed, if the hydrocarbon is required pure, by the above process. Secondary alcohols, often produced in small amount, are not appreciably steam-volatile.

COGNATE PREPARATIONS

Toluene. Use 200 g. of amalgamated zinc and 100 g. of freshly-distilled benzaldehyde. The yield of toluene, b.p. 109–110°, is 40 g.

***n*-Butylbenzene.** Use 225 g. of amalgamated zinc and 100 g. of ethyl benzyl ketone (Section **IV,141**). The yield of *n*-butylbenzene, b.p. 180–183°, is 75 g. With 200 g. of amalgamated zinc and 75 g. of butyrophenone, $C_6H_5COCH_2CH_2CH_3$ (Section **IV,137**), the yield of *n*-butylbenzene, b.p. 181-184°, is 40 g.

***n*-Hexylbenzene.** Use 200 g. of amalgamated zinc and 100 g. of *n*-propyl-β-phenylethylketone (Section **IV,141**); the yield of crude *n*-hexylbenzene, b.p. 218–230°, is 55 g. This, when purified by treatment with concentrated sulphuric acid and distillation from sodium, yields 40 g. of fairly pure *n*-hexylbenzene, b.p. 220–225° (mainly 222–224 °).

Method B (*Huang-Minlon modification of Wolff-Kishner reduction*)

Place 36·0 g. of redistilled acetophenone, b.p. 201° (Section **IV,136**), 300 ml. of diethylene glycol, 30 ml. of 90 per cent. hydrazine hydrate and 40 g. of potassium hydroxide pellets in a 500 ml. Claisen flask provided with a reflux condenser and a thermometer dipping into the liquid (compare Fig. *III*, *31*, 1). Warm the mixture on a boiling water bath until most of the potassium hydroxide has dissolved and then reflux (free flame) for one hour. Arrange the apparatus for distillation and distil until the temperature in the liquid rises to 175° (1); keep the distillate (*ca.* 50 ml.). Replace the reflux condenser in the flask and continue the refluxing for 3 hours.

Separate the upper hydrocarbon layer from the distillate and extract the aqueous layer twice with 20 ml. portions of ether; dry the combined upper layer and ethereal extracts with anhydrous magnesium sulphate, remove the ether on a water bath, and distil the residue from a 50 ml. Claisen flask. Collect the ethylbenzene at 135–136°; the yield is 20 g. By extracting the syrupy liquid in the reaction flask with three 30 ml. portions of ether, a further 2 g. of ethylbenzene, b.p. 136°, may be obtained.

Note.

(1) The reduction takes place at a comparatively low temperature and is fairly rapid for acetophenone. With higher ketones, the upper layer of the initial distillate should be returned to the contents of the flask and the refluxing continued for 3–5 hours. The reaction mixture and aqueous distillate are then combined, extracted with ether, etc.

IV,7. *n*-PROPYLBENZENE

Into a 1500 ml. three-necked flask, equipped with a dropping funnel, a mercury-sealed stirrer and a double surface condenser (the last-named provided at its upper end with a guard tube filled with a mixture of

anhydrous calcium chloride and soda lime in order to prevent the ingress of moisture and carbon dioxide into the apparatus), place 24·3 g. of clean, dry magnesium turnings, 100 ml. of anhydrous ether and a small crystal of iodine (1). Charge the dropping funnel with a solution of 126·5 g. (115 ml.) of freshly distilled benzyl chloride (b.p. 177–179°) in 500 ml. of sodium-dried ether. Allow about 12 ml. of this solution to run into the flask ; if the reaction does not commence within a minute or two, partially immerse the flask in a water bath at about 40°. Remove the flask from the bath immediately reaction sets in and commence stirring the mixture. Add the remainder of the benzyl chloride during 30 minutes ; control the vigorous reaction by immersing most of the flask in ice water. The reaction usually continues for about 15 minutes after all the benzyl chloride has been introduced, and is completed by refluxing for a further 15 minutes. Add to the vigorously stirred benzyl magnesium chloride solution 308 g. (261 ml.) of diethyl sulphate (see discussion before Section **III,49**) during 1 hour and cool the flask in ice water if the reaction becomes unduly vigorous ; after the addition, continue the stirring with gentle boiling for 15 minutes. Into a large beaker place 500 ml. of water, 500 g. of finely-crushed ice and 100 ml. of concentrated hydrochloric acid and stir mechanically ; add the cold reaction mixture from a separatory funnel. Separate the upper ethereal layer and remove the ether by distillation from a water bath through a fractionating column. Pour the residue into 500 ml. of 10 per cent. sodium hydroxide solution in about 50 per cent. ethyl alcohol, and reflux the mixture for one hour to decompose any unaltered diethyl sulphate. Dilute with a large volume of water in order to throw out the hydrocarbon, separate the *n*-propylbenzene and dry it by allowing it to stand over 10 g. of potassium hydroxide pellets overnight. Distil from a little sodium through a well-lagged fractionating column (compare Sections **II,15–II,17**) and collect the *n*-propylbenzene at 156–159° (2). The yield is 70 g.

Notes.

(1) For further general details on the preparation of the Grignard reagent, see Section **III,17**.

(2) This contains only a small proportion of unsaturated compounds ; these are easily removed by three washings with one tenth of the volume of concentrated sulphuric acid (compare Section **III,7**, *Note* 2). The resulting pure *n*-propylbenzene boils at 158–159°.

IV,8. *n*-AMYLBENZENE

Prepare a solution of benzyl magnesium chloride in a 2-litre three-necked flask from 24·3 g. of magnesium turnings, 600 ml. of sodium-dried ether and 126·5 g. (115 ml.) of redistilled benzyl chloride ; follow the experimental details given under n-*Propylbenzene* (Section **IV,7**). Cool the flask in running water or in ice water. Place a solution of 456 g. of *n*-butyl-*p*-toluenesulphonate (Section **IV,198**) in about twice its volume of anhydrous ether in the dropping funnel, and add it slowly with stirring, at such a rate that the ether just boils ; a white solid soon forms. The addition is complete after about 2 hours. Pour the reaction product

slowly into a mechanically-stirred mixture of 1 kilo of finely-crushed ice, 1 litre of water and 125 ml. of concentrated hydrochloric acid contained in a 4 or 5-litre beaker; the precipitated magnesium *p*-toluenesulphonate will ultimately pass into solution. Separate the ether layer, extract the aqueous layer with about 250 ml. of ether, and add the extract to the original ether layer. Wash the ethereal solution with about 100 ml. of water and dry it with about 10 g. of anhydrous potassium carbonate. Distil off the ether through a short fractionating column on a water bath; add 5–7 g. of sodium in small pieces to the residue and reflux for about 2 hours (in order to remove any benzyl alcohol formed by the atmospheric oxidation of the benzyl magnesium chloride). Decant the solution and distil from an air bath through a well-lagged and efficient fractionating column (compare Sections **II,15–II,17**) (1); collect the fraction of b.p. 190–210°. Redistil and collect the *n*-amylbenzene at 198-203°. The yield is 90 g.

Note.

(1) About 20 g. of *n*-butyl chloride, b.p. 76–80°, may be recovered by carefully refractionating the distillate that passes over below 85°.

IV,9. CHARACTERISATION OF AROMATIC HYDROCARBONS

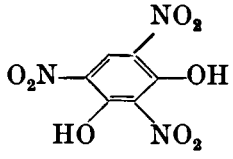
Unlike aliphatic hydrocarbons, aromatic hydrocarbons can be sulphonated and nitrated; they also form characteristic "molecular compounds" with picric acid, styphnic acid and 1 : 3 : 5-trinitrobenzene. Many of the reactions of aromatic hydrocarbons will be evident from the following discussion of crystalline derivatives suitable for their characterisation.

1. **Picrates.** Many aromatic hydrocarbons (and other classes of organic compounds) form molecular compounds with picric acid, for example, naphthalene picrate $C_{10}H_8.C_6H_2(NO_2)_3OH$. Some picrates, *e.g.*, anthracene picrate, are so unstable as to be decomposed by many, particularly hydroxylic, solvents; they therefore cannot be easily recrystallised. Their preparation may be accomplished in such non-hydroxylic solvents as chloroform, benzene or ether. The picrates of hydrocarbons can be readily separated into their constituents by warming with dilute ammonia solution and filtering (if the hydrocarbon is a solid) through a moist filter paper. The filtrate contains the picric acid as the ammonium salt, and the hydrocarbon is left on the filter paper.

Picrates are usually prepared by mixing solutions of equivalent quantities of the two components in the minimum volume of rectified spirit and allowing to cool; the derivative separates in a crystalline condition. It is filtered off, washed with a little ether, and pressed on a porous tile. If the picrate is stable, it is recrystallised from alcohol, ethyl acetate or ether.

The following are typical experimental details for the preparation of naphthalene picrate. Dissolve 0·1 g. of naphthalene and 0·2 g. of picric acid separately in the minimum volume of hot rectified spirit (about 2 ml.), mix the solutions and allow to cool. Filter and wash with 2 ml. of alcohol. Recrystallise from hot alcohol, ethyl acetate or ether.

2. **Styphnates.** Aromatic hydrocarbons (and also some amines and heterocyclic bases) form 1 : 1-addition products with styphnic acid (2 : 4 : 6-trinitroresorcinol),

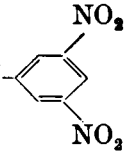


These derivatives do not crystallise quite so well as the corresponding picrates, but are frequently of great value. Benzene and its simple homologues do not give stable derivatives.

Dissolve equimolecular amounts of the hydrocarbon and styphnic acid in the minimum volume of hot acetic acid and allow to cool. Filter off the crystalline derivative which separates, wash it with a little acetic acid and dry in the air. Determine the m.p. Recrystallise from acetic acid and again determine the m.p.

Benzene must be employed as the solvent for anthracene styphnate since most other solvents lead to dissociation.

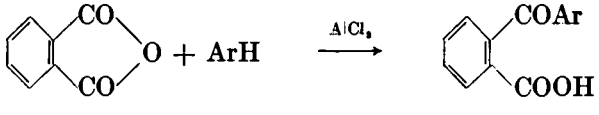
3. **Addition compounds with 1:3:5-trinitrobenzene**



This reagent affords compounds (1 : 1) with aromatic hydrocarbons and other classes of organic compounds (heterocyclic compounds, aromatic ethers, etc.).

Dissolve equimolecular quantities of the hydrocarbon and 1 : 3 : 5-trinitrobenzene in hot alcohol, benzene or glacial acetic acid, and allow to cool. Filter off the solid which separates and recrystallise it from one of these solvents.

4. **Aroylbenzoic acids.** Aromatic hydrocarbons condense with phthalic anhydride in the presence of anhydrous aluminium chloride producing aroylbenzoic acids in good yields :



Place a mixture of 1·0 g. of the hydrocarbon, 10 ml. of dry methylene chloride or ethylene dichloride or *sym.*-tetrachloroethane, 2·5 g. of powdered anhydrous aluminium chloride and 1·2 g. of pure phthalic anhydride in a 50 ml. round-bottomed flask fitted with a short reflux condenser. Heat on a water bath for 30 minutes (or until no more hydrogen chloride fumes are evolved), and then cool in ice. Add 10 ml. of concentrated hydrochloric acid cautiously and shake the flask gently for 5 minutes. Filter off the solid at the pump and wash it with 10–15 ml. of cold water. Boil the resulting crude aroylbenzoic acid with 10 ml. of 2·5*N* sodium carbonate solution and 0·2 g. of decolourising carbon for 5 minutes, and filter the hot solution. Cool, add about 10 g. of crushed ice and acidify

to Congo Red with dilute hydrochloric acid (1 : 1 ; 5–6 ml.). Collect the aroylbenzoic acid by suction filtration and recrystallise it from dilute alcohol or from acetic acid. The derivatives prepared from benzene and toluene crystallise with water of crystallisation ; this is removed by drying at 100°.

5. **Nitro derivatives.** No general experimental details for the preparation of nitro derivatives can be given, as the ease of nitration and the product formed frequently depend upon the exact experimental conditions. Moreover, some organic compounds react violently so that nitrations should always be conducted on a small scale. The derivatives already described are usually more satisfactory : for this reason the nitro derivatives have been omitted from Table **IV,9.**

Three typical nitrations will, however, be described in order to illustrate the results which may be obtained.

Benzene. Add 0·5 ml. of benzene slowly and with shaking and cooling to a mixture of 4 ml. each of concentrated sulphuric and nitric acids. Heat the mixture carefully until it just boils, cool and pour into excess of cold water. Filter off the precipitate, wash it free from acid and recrystallise it from dilute alcohol. *m*-Dinitrobenzene m.p. 90°, is formed.

Toluene. Proceed as for *Benzene* but use 0·5 ml. of toluene and a mixture of 3 ml. of concentrated sulphuric acid and 2 ml. of fuming nitric acid. Gently warm the mixture over a free flame for 1–2 minutes, cool, and pour into 20 ml. of ice water. Recrystallise the product from dilute alcohol. 2 : 4-Dinitrotoluene, m.p. 71°, is obtained.

Diphenyl. Reflux a mixture of 1 g. of diphenyl, 2 ml. of glacial acetic acid and 0·5 ml. of fuming nitric acid for 10 minutes. Pour into 20 ml. of cold water, filter off the precipitate, wash it with cold water until free from acid, and recrystallise from alcohol. The product is 4-nitrodiphenyl, m.p. 114°.

6. **Oxidation of a side chain by alkaline permanganate.** Aromatic hydrocarbons containing side chains may be oxidised to the corresponding acids : the results are generally satisfactory for compounds with one side chain (*e.g.*, toluene or ethylbenzene → benzoic acid ; nitrotoluene → nitrobenzoic acid) or with two side chains (*e.g.*, *o*-xylene → phthalic acid).

Suspend in a round-bottomed flask 1 g. of the substance in 75–80 ml. of boiling water to which about 0·5 g. of sodium carbonate crystals have been added, and introduce slowly 4 g. of finely-powdered potassium permanganate. Heat under reflux until the purple colour of the permanganate has disappeared (1–4 hours). Allow the mixture to cool and carefully acidify with dilute sulphuric acid. Heat the mixture under reflux for a further 30 minutes and then cool. Remove any excess of manganese dioxide by the addition of a little sodium bisulphite. Filter the precipitated acid and recrystallise it from a suitable solvent (*e.g.*, benzene, alcohol, dilute alcohol or water). If the acid does not separate from the solution, extract it with ether, benzene or carbon tetrachloride.

Data for a number of typical aromatic hydrocarbons are collected in Table **IV,9.**

TABLE IV,9. **AROMATIC HYDROCARBONS**

Hydrocarbon	B.P.	M.P.	$d_{4°}^{20°}$	$n_D^{20°}$	Picrate	Aroylbenzoic Acid	Compound with 1 : 3 : 5-Trinitrobenzene	Styphnate	Other Derivatives
Benzene	80°	6°	0·879	1·501	—	128°	—	—	*m*-Dinitro, 90°
Toluene	110	—	0·867	1·497	—	138	—	—	2 : 4-Dinitro, 71
o-Xylene	144	—	0·880	1·505	—	167	—	—	4 : 5-Dinitro, 71
m-Xylene	139	—	0·864	1·497	—	126	—	—	2 : 4 : 6-Trinitro, 182
p-Xylene	138	13	0·861	1·496	—	132	—	—	2 : 3 : 5-Trinitro, 139
Ethylbenzene	135	—	0·868	1·496	97°	128	—	—	2 : 4 : 6-Trinitro, 37
n-Propylbenzene	159	—	0·864	1·493	103	126	—	—	—
iso-Propylbenzene (1)	151	—	0·862	1·491	—	134	—	—	2 : 4 : 6-Trinitro, 109
Pseudo-cumene (2)	169	—	—	1·504	97	—	—	—	3 : 5 : 6-Trinitro, 185
n-Butylbenzene	182	—	0·860	1·490	—	98	—	—	—
sec.-Butylbenzene	172	—	0·861	1·490	—	—	—	—	$CrO_3 \rightarrow C_6H_5COCH_3$
tert.-Butylbenzene	169	—	0·867	1·493	—	—	—	—	2 : 4-Dinitro, 62
n-Amylbenzene	204	—	0·859	1·488	—	—	—	—	Dibromo, 64
Mesitylene (3)	164	—	0·865	1·499	97	212	—	—	—
p-Cymene (4)	177	—	0·857	1·490	—	124	—	—	2 : 6-Dinitro, 54
Durene (5)	193	79	—	—	—	264	—	—	3 : 6-Dinitro, 207
Prehnitene (6)	204	—	0·901	1·523	90	—	—	—	5 : 6-Dibromo, 208
iso-Durene (7)	197	—	0·891	1·513	—	—	—	—	4 : 6-Dinitro, 157
Pentamethylbenzene	231	54	—	—	131	—	121°	—	—
Hexamethylbenzene	264	164	—	—	170	—	174	—	—
*cyclo*Hexylbenzene	236	7	0·950	1·533	—	—	—	—	4-Nitro, 59
Naphthalene	218	80	—	—	150	173	156	168°	1-Nitro, 61
α-Methylnaphthalene	241	—	1·019	1·618	141	168	—	—	4-Nitro, 71
β-Methylnaphthalene	241	34	—	—	115	190	123	—	1-Nitro, 81
αα′-Dinaphthyl	—	160	—	—	145	--	—	—	—
ββ′-Dinaphthyl	—	188	—	—	184	—	—	—	—

TABLE IV,9. **AROMATIC HYDROCARBONS (*continued*)**

Hydrocarbon	B.P.	M.P.	$d_{4°}^{20°}$	$n_D^{20°}$	Picrate	Aroyl-benzoic Acid	Compound with 1 : 3 : 5-Trinitro-benzene	Styphnate	Other Derivatives
Diphenyl	255°	70°	—	—	—	226°	—	—	4 : 4′-Dinitro, 234° ; 4:4′-Dibromo, 164°
Dibenzyl	284	52	—	—	—	—	102°	—	4 : 4′- Dinitro, 180
Anthracene	340	216	—	—	138°	—	164	180°	Anthraquinone, 286
Phenanthrene	340	100	—	—	143	—	164	142	Phenanthraquinone, 202
Chrysene	—	254	—	—	273	214	186	—	—
Fluorene (8)	294	114	—	—	84	228	105	134	2 : 7-Dibromo, 165
Retene (9)	390	99	—	—	123	—	139	141	—
Acenaphthene	278	95	—	—	162	200	168	154	5-Nitro, 101
Pyrene	—	150	—	—	222	—	245	191	—
Tetralin (10)	207	—	0·971	1·540	—	154	—	—	5 : 7-Dinitro, 95
Indene	182	—	0·992	1·576	98	—	102	—	—
Hydrindene	177	—	0·965	1·538	—	—	—	—	—
Styrene (11)	146	—	0·909	1·546	—	—	—	—	—
Stilbene (12)	306	124	—	—	—	—	120	142	—
Diphenylmethane	262	25	—	—	—	—	—	—	2 : 4 : 2′ : 4′-Tetra-nitro, 172
Triphenylmethane	358	92	—	—	—	—	—	—	Triphenylcarbinol. 162

(1) Cumene.
(2) 1 : 2 : 4-Trimethylbenzene.
(3) 1 : 3 : 5-Trimethylbenzene.
(4) 4-*iso*Propyl-1-methylbenzene.
(5) 1 : 2 : 4 : 5-Tetramethylbenzene.
(6) 1 : 2 : 3 : 4-Tetramethylbenzene.
(7) 1 : 2 : 3 : 5-Tetramethylbenzene.
(8) Diphenylenemethane.
(9) 7-*iso*Propyl-1-methylphenanthrene.
(10) 1 : 2 : 3 : 4-Tetrahydronaphthalene.
(11) Phenylethylene.
(12) *trans* 1 : 2-Diphenylethylene.

NITRATION OF AROMATIC HYDROCARBONS

Aromatic hydrocarbons may be **nitrated**, *i.e.*, the hydrogen atoms replaced by nitro (NO_2) groups, with concentrated nitric acid in the presence of concentrated sulphuric acid, for example :

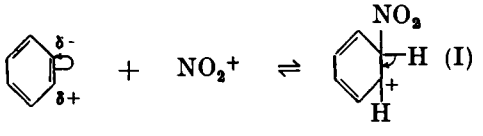
$$\underset{\text{Benzene}}{C_6H_5H} + HONO_2 \xrightarrow{H_2SO_4} \underset{\text{Nitrobenzene}}{C_6H_5NO_2} + H_2O$$

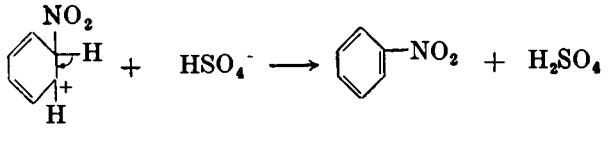
$$\underset{\text{Naphthalene}}{C_{10}H_7H} + HONO_2 \longrightarrow \underset{\alpha\text{-Nitronaphthalene}}{C_{10}H_7NO_2} + H_2O$$

The function of the sulphuric acid is to furnish a strongly acid medium and to convert the nitric acid into the highly reactive nitronium ion NO_2^+ , which is the real nitrating agent :

$$HNO_3 + 2H_2SO_4 \rightleftharpoons NO_2^+ + H_3O^+ + 2HSO_4^-$$

The *mechanism* of the aromatic substitution may involve the attack of the electrophilic NO_2^+ ion upon the nucleophilic aromatic nucleus to produce the carbonium ion (I) ; the latter transfers a proton to the bisulphate ion, the most basic substance in the reaction mixture

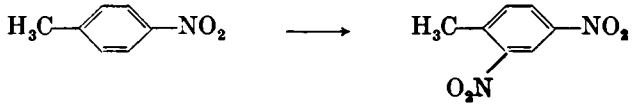




Nitrations are usually carried out at comparatively low temperatures; at higher temperatures there may be loss of material because of the oxidising action of the nitric acid. For substances which do not nitrate readily with a mixture of concentrated nitric and sulphuric acids (" mixed acid "), the intensity of the reaction may be increased *inter alia* by the use of fuming sulphuric acid (containing up to 60 per cent. of sulphur trioxide) or by fuming nitric acid. Thus nitrobenzene is converted by a mixture of fuming nitric acid and concentrated sulphuric acid into about 90 per cent. of *m*-dinitrobenzene and small amounts of the *o*- and *p*-isomers ; the latter are eliminated in the process of recrystallisation :

$$\underset{\text{Nitrobenzene}}{NO_2C_6H_4H} + HONO_2 \longrightarrow \underset{m\text{-Dinitrobenzene}}{m\text{-}NO_2C_6H_4NO_2} + H_2O$$

p-Nitrotoluene is similarly converted largely into 2 : 4-dinitrotoluene :



Nitration of bromobenzene with " mixed acid " yields largely *p*-bromo nitrobenzene accompanied by a little of the *o*-isomeride :

$$BrC_6H_4H + HONO_2 \longrightarrow p\text{-}BrC_6H_4NO_2 + H_2O$$

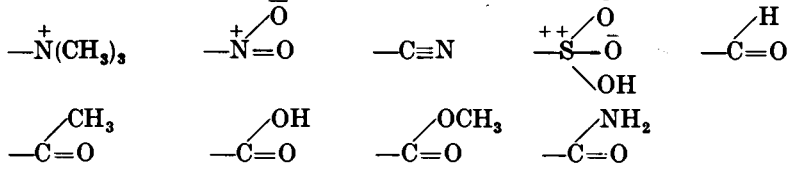
An interesting reaction, which is particularly valuable for the preparation of diphenyl derivatives, consists in heating copper powder or, better, copper bronze with an aryl halide (**Ullmann reaction**), for example:

o-Chloronitrobenzene — 2 : 2′-Dinitrodiphenyl

The use of dimethylformamide (b.p. 153°) as a solvent and diluent often increases the yield materially. The vigour of the exothermic reaction which occurs with a relatively reactive aryl halide is moderated and, furthermore, the dimethylformamide is easily removed from the reaction product since it is water soluble. Aryl halides which are inert under the usual Ullmann conditions do not react in the presence of dimethylformamide.

A brief account of **aromatic substitution** may be usefully given here as it will assist the student in predicting the orientation of disubstituted benzene derivatives produced in the different substitution reactions. For the nitration of nitrobenzene the substance must be heated with a mixture of fuming nitric acid and concentrated sulphuric acid : the product is largely *m*-dinitrobenzene (about 90 per cent.), accompanied by a little *o*-dinitrobenzene (about 5 per cent.) which is eliminated in the recrystallisation process. On the other hand phenol can be easily nitrated with dilute nitric acid to yield a mixture of *ortho* and *para* nitrophenols. It may be said, therefore, that orientation is *meta* with the nitro group and *ortho* - *para* with the hydroxyl group. The nitro group $-\overset{+}{N}\overset{O}{\overset{\diagup}{\underset{\diagdown}{=}}}\bar{O}$ is unsaturated and possesses a positively charged atom in the key position adjacent to the benzene ring, whereas the hydroxyl group is fully saturated. The *meta*-directing nitro group renders substitution more difficult, *i.e.*, exerts a deactivating effect on the aromatic nucleus : the *ortho* - *para* directive hydroxyl group, however, facilitates substitution, *i.e.*, exerts an activating influence on the aromatic nucleus. Most other substituent groups are sufficiently similar to the types exemplified by the nitro group or the hydroxyl group to justify an empirical classification into *meta* and *ortho* - *para* directing groups.

The ***meta* directing groups** include those in which the atom directly attached to the aromatic nucleus is either positively charged or strongly unsaturated. These are, in order of decreasing effectiveness :—



The ***ortho* - *para* directing groups** include those which are saturated or only weakly unsaturated at the point of the attachment of the ring. These are ($-N(CH_3)_2$, $-NH_2$ and $-OH$ are by far the most powerful) :—

$-N(CH_3)_2$ $-NH_2$ $-OH$ $-OCH_3$ $-NHCOCH_3$ $-OCOCH_3$
$-CH_3$ —Cl, Br, I $-C_6H_5$ $-CH_2COOH$ $-CH=CHCOOH$

The following rules, relating to the course of aromatic substitution (Hammick and Illingworth, 1930), will be found useful :

(i) If in a mono-substituted benzene derivative  —XY, Y is in a higher group of the periodic table than X, or if, being in the same group, Y is of lower atomic weight than X, then a second atom or group of atoms that enters the nucleus will do so in the *meta* position to the group XY. In all other cases, including that in which the group XY is a single atom, a second entering atom or group goes to the *ortho* and *para* positions.

(ii) The effect of ionic charges on XY is given by the statement that a positive charge directs *meta*, and a negative charge directs *ortho* and *para*.

To apply the above rules, only the following elements need be considered.

Group	I	II	III	IV	V	VI	VII
	H	Be	B	C	N	O	F
						S	Cl
							Br
							I

If Y consists solely of hydrogen atoms, (Group 1), rule (1) applies; if Y consists partly of hydrogen and partly of another element, both attached to X, then the effect of the hydrogen can usually be neglected and the rules applied to the remaining elements alone.

IV,10. NITROBENZENE

Place 50 g. (35 ml.) of concentrated nitric acid in a 500 ml. round-bottomed flask, and add, in portions with shaking, 74 g. (40 ml.) of concentrated sulphuric acid. Keep the mixture cool during the addition by immersing the flask in cold water. Place a thermometer (110° range) in the acid mixture. Introduce 26 g. (30 ml.) of benzene in portions of 2–3 ml.; shake the flask well, to ensure thorough mixing, after each addition of the benzene. Do not allow the temperature of the mixture to rise above 55°; immerse the flask, if necessary, in cold water or in ice water. When all the benzene has been added, fit a reflux condenser to the flask and heat it in a water bath maintained at 60° (but not appreciably higher) for 40–45 minutes; remove the flask from time to time from the bath and shake it vigorously to ensure good mixing of the immiscible layers. Pour the contents of the flask into about 500 ml. of cold water in a beaker, stir the mixture well in order to wash out as much acid as possible from the nitrobenzene, and allow to stand. When the nitrobenzene has settled to the bottom, pour off the acid liquor as completely as possible, and transfer the residual liquid to a separatory funnel. Run off the lower layer of nitrobenzene and reject the upper aqueous layer; return the nitrobenzene to the separatory funnel and shake it vigorously with about 50 ml. of water. Separate the nitrobenzene as completely as possible and run it into a small conical flask containing about 5 g. of anhydrous calcium chloride. If the nitrobenzene does not become clear on shaking because of the presence of emulsified water, warm the mixture, with shaking, for a short period on a water bath; the cloudiness will soon disappear. Filter the cold product through a small fluted filter paper into a small (50 or 100 ml.) distilling flask attached to an air condenser (Fig. *II*, *13*, 2). Heat the flask on an asbestos-centred wire gauze or preferably in an air bath (Fig. *II*, *5*, 3) and collect the fraction which boils at 206–211°. Do not distil quite to dryness nor allow the

temperature to rise above 214°, for there may be a residue of *m*-dinitrobenzene and higher nitro compounds and an explosion may result. The yield of nitrobenzene is 35 g. (1). Pure nitrobenzene is a clear, pale yellow liquid, b.p. 210°.

Note.

(1) Nitrobenzene (and many other liquid organic compounds containing nitrogen) is appreciably toxic and its vapour should not be allowed to escape into the atmosphere of the laboratory; the delivery tube of the condenser should pass well into the mouth of the receiver flask. The liquid is also a skin poison; if it is accidentally spilled on the skin, it should be removed by washing with a little methylated spirit, followed by soap and warm water.

IV,11. α-NITRONAPHTHALENE

Prepare a mixture of 40 ml. of concentrated nitric acid and 40 ml. of concentrated sulphuric acid as detailed in the previous Section. Introduce 50 g. of *finely-powdered* naphthalene in small quantities at a time and with vigorous shaking: maintain the temperature at 45–50° and cool in ice water if necessary. When all the naphthalene has been added, warm the mixture on a water bath at 55–60° for 30–40 minutes or until the smell of naphthalene has disappeared. Pour the mixture into 500 ml. of cold water; the nitronaphthalene will sink to the bottom. Decant the liquid. Boil the solid cake with 200 ml. of water for 20 minutes and pour the water away. Transfer the oil to a large flask and subject it to steam distillation (Fig. *II*, *40*, 1); any unattacked naphthalene will thus be removed. Pour the warm contents of the flask into a beaker containing a large volume of water which is vigorously stirred. Filter off the granulated α-nitronaphthalene at the pump, press it well, and recrystallise it from dilute alcohol. The yield of α-nitronaphthalene, m.p. 61°, is 60 g.

IV,12. *m*-DINITROBENZENE

Place 37·5 g. (21 ml.) of concentrated sulphuric acid and 22·5 g. (15 ml.) of fuming nitric acid, sp. gr. 1·5, in a 250 or 500 ml. round-bottomed flask; add a few fragments of unglazed porcelain or of broken glass. Attach a reflux condenser and place the apparatus in a fume chamber. Add slowly, in portions of about 3 ml., 15 g. (12·5 ml.) of nitrobenzene; after each addition, shake the flask to ensure thorough mixing. Heat the mixture, with frequent shaking, on a boiling water bath; securely clamp both the flask and condenser since the acid fumes usually attack the cork. Allow the mixture to cool somewhat and pour it cautiously with vigorous stirring into about 500 ml. of cold water; the dinitrobenzene soon solidifies. Filter with suction, wash thoroughly with cold water, and allow to drain as completely as possible.

Transfer the crude dinitrobenzene to a 250 ml. flask fitted with a reflux condenser, add 80–100 ml. of methylated (or rectified) spirit and heat on a water bath until all the crystalline solid dissolves. If the resulting solution is not quite clear, filter it through a fluted filter paper on a large funnel which has previously been warmed or through a warm Buchner funnel. Colourless crystals of *m*-dinitrobenzene (15 g.) are deposited on cooling. If the m.p. is below 89–90°, recrystallisation is necessary.

IV,13. 2 : 4-DINITROTOLUENE

Place 18 g. (12 ml.) of fuming nitric acid, sp. gr. 1·5, and 30 g. (16·5 ml.) of concentrated sulphuric acid and a few fragments of broken glass in a 250 or 500 ml. round-bottomed flask. Add gradually, in small portions, 14 g. of *p*-nitrotoluene ; do not allow the temperature to rise above 50° and cool the flask, if necessary, by immersion in cold water. Place a small funnel in the mouth of the flask and heat on a water bath at 90–95° for 30 minutes. Allow to cool almost to the laboratory temperature and pour the reaction mixture slowly into about 500 ml. of ice water containing a few small pieces of ice. Filter the crude dinitrotoluene through a Buchner funnel at the pump, wash it thoroughly with cold water, and drain as completely as possible. Recrystallise from the minimum volume of hot methyl alcohol (flask, reflux condenser, and water bath ; experimental details as in Section **IV,12**). The yield of pure 2 : 4-dinitrotoluene, m.p. 71°, is 12·5 g.

IV,14. *p*-BROMONITROBENZENE

Prepare a mixture of 28·5 g. (20 ml.) of concentrated nitric acid and 37 g. (20 ml.) of concentrated sulphuric acid in a 250 ml. round-bottomed flask (Section **IV,10**) and cool it to the laboratory temperature. Attach a reflux condenser to the flask. Add 16 g. (10·5 ml.) of bromobenzene (Section **IV,18**) in portions of 2–3 ml. during about 15 minutes : shake the flask vigorously during the whole process and do not allow the temperature to rise above 50–60° by cooling in running water, if necessary. When the temperature no longer tends to rise owing to the heat of reaction, heat the flask on a boiling water bath for 30 minutes ; clamp the flask and condenser securely. Allow to cool to room temperature and pour the reaction mixture with stirring into 200 ml. of cold water. Filter the bromonitrobenzene at the pump, wash well with cold water, and finally drain as far as possible. Recrystallise from 100 to 125 ml. of methylated spirit (flask, reflux condenser and water bath ; see Section **IV,12**). When cold, filter the almost pure *p*-bromonitrobenzene, m.p. 125°. The yield is 14 g. The mother liquor contains the *o*-bromonitrobenzene, contaminated with some of the *p*-isomeride.

IV,15. 2 : 2′-DINITRODIPHENYL

Place 50 g. of *o*-chloronitrobenzene and 75 g. of clean dry sand in a 250 ml. flask equipped with a mechanical stirrer. Heat the mixture in an oil or fusible metal bath to 215–225° and add, during 40 minutes, 50 g. of copper bronze or, better, of activated copper bronze (Section **II,50, *4***) (1). Maintain the temperature at 215–225° for a further 90 minutes and stir continuously. Pour the hot mixture into a Pyrex beaker containing 125 g. of sand and stir until small lumps are formed ; if the reaction mixture is allowed to cool in the flask, it will set to a hard mass, which can only be removed by breaking the flask. Break up the small lumps by powdering in a mortar, and boil them for 10 minutes with two 400 ml.

portions of alcohol; filter after each extraction. Cool the filtered extracts in ice, and collect the crude product on a Buchner funnel. Concentrate the filtrate to about half the original volume and thus obtain a second crop of crystals. The total yield of crude solid should be about 24 g.; if it is less than this, a third extraction of the reaction product should be made. Dissolve the crude solid in about 400 ml. of hot alcohol, add a little decolourising charcoal, boil for a few minutes, filter and cool in ice. Recrystallise again from hot alcohol. The yield of pure 2 : 2′-dinitrodiphenyl, m.p. 123–124°, is 20–22 g. (2).

The experimental conditions for conducting the above reaction in the presence of dimethylformamide as a solvent are as follows. In a 250 ml. three-necked flask, equipped with a reflux condenser and a tantalum wire Hershberg-type stirrer, place 20 g. of *o*-chloronitrobenzene and 100 ml. of dimethylformamide (dried over anhydrous calcium sulphate). Heat the solution to reflux and add 20 g. of activated copper bronze in one portion. Heat under reflux for 4 hours, add another 20 g. portion of copper powder, and continue refluxing for a second 4-hour period. Allow to cool, pour the reaction mixture into 2 litres of water, and filter with suction. Extract the solids with three 200 ml. portions of boiling ethanol: alternatively, use 300 ml. of ethanol in a Soxhlet apparatus. Isolate the 2 : 2′-dinitrodiphenyl from the alcoholic extracts as described above: the yield of product, m.p. 124–125°, is 11·5 g.

Notes.

(1) If the temperature is allowed to rise above 240°, reduction of the nitro groups will occur and carbazole will be formed.

(2) The filtrates should be evaporated to small bulk and the separated solid recrystallised twice from alcohol.

IV,16A. REACTIONS AND CHARACTERISATION OF AROMATIC NITRO COMPOUNDS

Nitro compounds, when liquid, have characteristic odours, are insoluble in water, highly refractive and with a density greater than unity. Many are crystalline solids. Most nitro compounds are slightly coloured, generally yellow; the intensity of the colour increases with the number of nitro groups. The following reactions will assist in their detection.

(i) **Action of alkali.** Provided acidic groups are absent, simple aromatic nitro compounds are practically unaffected by caustic alkalis, but a yellow or orange colour may develop. Aromatic compounds that contain two or more nitro groups in *meta* positions to each other, when treated in alcohol or acetone solution with aqueous alkali, give a red colouration.

(ii) **Reduction to the hydroxylamine.** This is a general test for a nitro group. With a neutral reducing agent, nitro compounds yield the corresponding hydroxylamines (compare Section **IV,83**), which can be detected by their action upon Tollen's reagent {see Section **III,70**, (i)}:

$$RNO_2 + 4H \longrightarrow RNHOH + H_2O$$

It must be noted, however, that nitroso, azoxy and azo compounds when subjected to the same treatment yield respectively hydroxylamines, hydrazo and hydrazine compounds, all of which reduce ammoniacal silver nitrate solution in the cold.

Dissolve 0·5 g. of the substance in 10 ml. of 50 per cent. alcohol, add 0·5 g. of solid ammonium chloride and about 0·5 g. of zinc powder. Heat the mixture to boiling, and allow the ensuing chemical reaction to proceed for 5 minutes. Filter from the excess of zinc powder, and test the filtrate with Tollen's reagent {Section **III,70,** (i)}. An immediate black or grey precipitate or a silver mirror indicates the presence of a hydroxylamine formed by reduction of the nitro compound. Alternatively, the filtrate may be warmed with Fehling's solution, when cuprous oxide will be precipitated if a hydroxylamine is present. Make certain that the original compound does not affect the reagent used.

Crystalline Derivatives

1. **Reduction with tin and hydrochloric acid and characterisation of the resulting primary amine.** Add 10 ml. of concentrated hydrochloric acid in small portions to a mixture of 1 g. of the compound and 3 g. of granulated tin contained in a small (say, 50 ml.) flask fitted with a reflux condenser. Shake the flask well to ensure thorough mixing during the addition of the acid. After 10 minutes warm under reflux at 100° with vigorous shaking until the nitro compound has dissolved and its odour is no longer apparent. (If the nitro compound dissolves slowly, add a few ml. of alcohol.) Cool the reaction mixture, and cautiously make it alkaline with 20-40 per cent. sodium hydroxide solution. Isolate the liberated amine by steam distillation or by ether extraction. Test a small portion qualitatively for an amine and then identify it as detailed under *Aromatic Amines,* Section **IV,100.**

2. **Oxidation of side chains.** Aromatic nitro compounds that contain a side chain (*e.g.*, nitro derivatives of alkyl benzenes) may be oxidised to the corresponding acids either by alkaline potassium permanganate (Section **IV,9,** *6*) or, preferably, with a sodium dichromate - sulphuric acid mixture in which medium the nitro compound is more soluble.

Mix 1 g. of the nitro compound with 4 g. of sodium dichromate and 10 ml. of water in a 50 ml. flask, then attach a reflux condenser to the flask. Add slowly and with shaking 7 ml. of concentrated sulphuric acid. The reaction usually starts at once ; if it does not, heat the flask gently to initiate the reaction. When the heat of reaction subsides, boil the mixture, cautiously at first, under reflux for 20–30 minutes. Allow to cool, dilute with 30 ml. of water, and filter off the precipitated acid. Purify the crude acid by extraction with sodium carbonate solution, precipitation with dilute mineral acid, and recrystallisation from hot water, benzene, etc.

A number of selected aromatic nitro compounds are collected in Table **IV,16A.** It will be noted that a few nitro aromatic esters have been included in the Table. These are given here because the nitro group may be the first functional group to be identified ; aromatic nitro esters should be treated as other esters and hydrolysed for final identification.

TABLE IV,16A. AROMATIC NITRO COMPOUNDS

Nitro Compound	B.P.	M.P.	Nitro Compound	B.P.	M.P.
Nitrobenzene (1)	211°	5°	*m*-Nitrobenzyl cyanide	—	62°
o-Nitrotoluene (2)	222	—	*p*-Nitrobenzyl cyanide	—	117
m-Nitrotoluene (3)	229	16	*o*-Nitrobenzyl alcohol	270°	74
p-Nitrotoluene	238	54	*m*-Nitrobenzyl alcohol	—	27
3-Nitro-*o*-xylene	240	15	*p*-Nitrobenzyl alcohol	—	93
4-Nitro-*o*-xylene	254	30	2 : 4-Dinitrochlorobenzene	315	51
2-Nitro-*m*-xylene	226	—	2 : 4-Dinitrobromobenzene	—	75
4-Nitro-*m*-xylene	244	—	2 : 4-Dinitroiodobenzene	—	88
5-Nitro-*m*-xylene	273	74			
2-Nitro-*p*-xylene	237	—	*o*-Nitroanisole	265	10
2-Nitro-*p*-cymene (4)	264	—	*m*-Nitroanisole	258	39
Nitromesitylene	255	44	*p*-Nitroanisole	259	54
			o-Nitrophenetole	267	2
α-Nitronaphthalene	304	61	*m*-Nitrophenetole	284	34
β-Nitronaphthalene	—	79	*p*-Nitrophenetole	283	60
2-Nitrodiphenyl	320	37			
4-Nitrodiphenyl	—	114	2 : 4-Dinitroanisole	—	95
o-Dinitrobenzene	—	118	2 : 4-Dinitrophenetole	—	87
m-Dinitrobenzene	—	90	2 : 4 : 6-Trinitroanisole	—	68
p-Dinitrobenzene	—	173	2 : 4 : 6-Trinitrophenetole	—	79
2 : 4-Dinitrotoluene	—	71			
1 : 8-Dinitronaphthalene	—	173	Methyl *o*-nitrobenzoate	275	—
1 : 5-Dinitronaphthalene	—	217	Methyl *m*-nitrobenzoate	—	78
2 : 2′-Dinitrodiphenyl	—	124	Methyl *p*-nitrobenzoate	—	96
4 : 4′-Dinitrodiphenyl	—	236	Ethyl *o*-nitrobenzoate	—	30
1 : 3 : 5-Trinitrobenzene	—	122	Ethyl *m*-nitrobenzoate	297	47
2 : 4 : 6-Trinitrotoluene	—	82	Ethyl *p*-nitrobenzoate	—	57
o-Nitrochlorobenzene	245	33	Methyl *o*-nitrocinnamate	—	73
m-Nitrochlorobenzene	236	46	Methyl *m*-nitrocinnamate	—	124
p-Nitrochlorobenzene	242	83	Methyl *p*-nitrocinnamate	—	161
o-Nitrobromobenzene	261	42	Ethyl *o*-nitrocinnamate	—	44
m-Nitrobromobenzene	256	56	Ethyl *m*-nitrocinnamate	—	79
p-Nitrobromobenzene	256	127	Ethyl *p*-nitrocinnamate	—	142
o-Nitroiodobenzene	—	54	Methyl 3-nitrosalicylate	—	132
m-Nitroiodobenzene	—	38	Ethyl 3-nitrosalicylate	—	118
p-Nitroiodobenzene	—	174	Methyl 5-nitrosalicylate	—	119
2 : 5-Dichloronitrobenzene	267	56	Ethyl 5-nitrosalicylate	—	102
3 : 4-Dichloronitrobenzene	255	43	Dimethyl 3-nitrophthalate	—	69
o-Nitrobenzyl chloride	—	49	Diethyl 3-nitrophthalate	—	46
m-Nitrobenzyl chloride	—	46	Dimethyl 4-nitrophthalate	—	66
p-Nitrobenzyl chloride	—	71	Diethyl 4-nitrophthalate	—	34
o-Nitrobenzyl bromide	—	47	Methyl 3 : 5-dinitrobenzoate	—	112
m-Nitrobenzyl bromide	—	59	Ethyl 3 : 5-dinitrobenzoate	—	94
p-Nitrobenzyl bromide	—	100	Methyl 3 : 5-dinitrosalicylate	—	127
o-Nitrobenzyl iodide	—	75	Ethyl 3 : 5-dinitrosalicylate	—	99
m-Nitrobenzyl iodide	—	86			
p-Nitrobenzyl iodide	—	127	Phenylnitromethane	227	—
o-Nitrobenzyl cyanide	—	84			

(1) $d_{4^\circ}^{20^\circ}$ 1·204 ; $n_D^{20^\circ}$ 1·553.

(2) $d_{4^\circ}^{20^\circ}$ 1·168 ; $n_D^{20^\circ}$ 1·546.

(3) $d_{4^\circ}^{20^\circ}$ 1·157 ; $n_D^{20^\circ}$ 1·547.

(4) $d_{4^\circ}^{20^\circ}$ 1·074 ; $n_D^{20^\circ}$ 1·531.

IV,16B. REACTIONS AND CHARACTERISATION OF ALIPHATIC NITRO COMPOUNDS

The following reactions will assist in the detection of aliphatic nitro compounds.

(i) **Action of alkali.** Add a few drops of the nitro compound to 1 ml. of 10 per cent. sodium hydroxide solution; it dissolves to produce, in general, a yellow solution. Acidify with dilute hydrochloric acid; the nitro compound is regenerated.

(ii) **Reduction to the hydroxylamine.** This test gives a positive result {see *Aromatic Nitro Compounds*, Section **IV,16A**, (ii)}.

(iii) **Sodium salt of the *aci*-form.** Dissolve 0·2 g. of sodium in 5 ml. of anhydrous methanol, and cool to room temperature. Add 0·5 ml. of the nitro compound, shake and cool. Both primary and secondary nitro compounds yield sodium derivatives

$$(RCH{=}\overset{O}{\overset{\nearrow}{N}}{-}ONa \quad \text{and} \quad R'R''C{=}\overset{O}{\overset{\nearrow}{N}}{-}ONa)$$

which may be filtered off and washed with methanol to remove traces of sodium methoxide. It should be kept moist with methanol; the sodium derivative, if allowed to dry, may become very explosive. Also, upon contact with a trace of water, it is liable to decompose with explosive violence. The sodium derivative may be dissolved by successively adding small quantities to cold water with continual stirring.

Add a little of the sodium derivative to about 5 ml. of water in a test-tube, followed by a drop of ferric chloride solution. A deep red colouration is produced but rapidly disappears as the iron is precipitated as ferric hydroxide.

The colouration is due to the production of an acid by partial hydrolysis:

$$RCH{=}\overset{O}{\overset{\nearrow}{N}}{-}ONa + HOH \rightleftharpoons RCH{=}\overset{O}{\overset{\nearrow}{N}}{-}OH + NaOH;$$

the acid, like many hydroxy compounds (compare *Phenols*, Section **IV,114**), gives a marked colouration with ferric chloride solution.

(iv) **Distinction between primary, secondary and tertiary aliphatic nitro compounds.** Dissolve a few drops of the nitro compound in concentrated sodium hydroxide solution, and add excess of sodium nitrite solution. Upon cautiously acidifying with dilute sulphuric acid, added a drop at a time, the following effects may be observed:—

(*a*) Primary nitro compound: intense red colour, disappearing upon acidification. The colouration is that of the alkali salt of the nitrolic acid (nitro oxime)-

$$RCH{=}\overset{O}{\overset{\nearrow}{N}}{-}ONa + NaNO_2 + H_2SO_4 \longrightarrow RC(\overset{NOH}{\diagup})-NO_2 + Na_2SO_4 + H_2O$$

(*b*) Secondary nitro compound: dark blue or blue green colour due to nitro-nitroso derivatives. The coloured compound is soluble in chloroform.

$$R'R''C{=}\overset{O}{\overset{\nearrow}{N}}{-}ONa + NaNO_2 + H_2SO_4 \longrightarrow R'R''C(\overset{NO}{\diagup})-NO_2 + Na_2SO_4 + H_2O$$

(*c*) Tertiary compound: no colouration.

CHARACTERISATION

Reduction with tin and hydrochloric acid and characterisation

of the primary amine. Experimental details are given in Section **IV,16A,** *1.* The amine is fairly volatile and cannot be diazotised (see Section **III,123**).

Most aliphatic nitro compounds are liquids: the physical properties (boiling point, density and refractive index) therefore provide valuable information for purposes of identification.

The physical properties of a number of aliphatic nitro compounds are listed in Table **IV,16B.**

TABLE IV,16B. ALIPHATIC NITRO COMPOUNDS

Nitro Compound	B.P.	$d_{4^\circ}^{20^\circ}$	$n_D^{20^\circ}$
Nitromethane	101°	1·137	1·381
Nitroethane	114	1·050	1·392
1-Nitropropane	131	1·001	1·401
2-Nitropropane	120	0·988	1·394
1-Nitro-*n*-butane	152	0·971	1·410
1-Nitro-*n*-pentane	66°/16 mm.	0·953	1·418
1-Nitro-*n*-hexane	82°/15	0·940	1·423
Phenylnitromethane	227	1·160	1·532

HALOGENATION OF AROMATIC HYDROCARBONS

Benzene and substituted benzenes do not react appreciably with chlorine and bromine in the cold, but in the presence of " halogen carriers," such as aluminium amalgam, pyridine, iodine and iron, reaction takes place readily, affording in the first instance the mono-halogen derivative as the main product. Di-substituted products (largely the *p*-isomeride) are obtained if the proportion of the halogen is increased. The following examples are given :

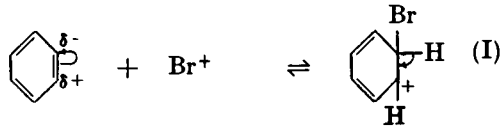
$$C_6H_6 + Cl_2 \xrightarrow{Al—Hg} C_6H_5Cl + HCl$$

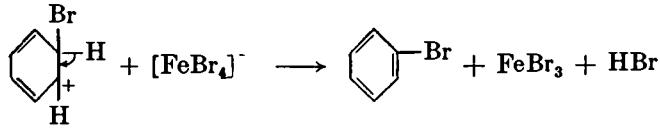
$$C_6H_6 + Br_2 \xrightarrow{C_5H_5N} C_6H_5Br + HBr$$

$$\underset{\text{Nitrobenzene}}{C_6H_5NO_2} + Br_2 \xrightarrow{Fe} \underset{m\text{-Bromonitrobenzene}}{BrC_6H_4NO_2\ (1:3)} + HBr$$

The **halogen carriers** or aromatic halogenation catalysts are usually all electrophilic reagents (ferric and aluminium halides, etc.) and their function appears to be to increase the electrophilic activity of the halogen. Thus the mechanism for the bromination of benzene in the presence of iron can be represented by the following scheme :

$$Br_2 + FeBr_3 \rightleftharpoons Br^+ + [FeBr_4]^-$$





The base $[FeBr_4]^-$ facilitates the elimination of a proton from the carbonium ion (I).

The reaction must be carried out in the absence of direct sunlight, since sunlight causes direct addition of the halogen to the hydrocarbon, particularly if the latter is warm ; benzene, for example, yields the hexahalide :

$$C_6H_6 + 3Br_2 \longrightarrow C_6H_6Br_6$$

Comparable results are not obtained with the less reactive iodine, because the hydrogen iodide formed tends to reduce the iodo compound and a condition of equilibrium is produced :

$$ArH + I_2 \rightleftharpoons ArI + HI$$

However, if an oxidising agent (fuming nitric acid or sodium persulphate) is present to destroy the hydrogen iodide as it is formed, the equilibrium is displaced and the iodo compound may be conveniently prepared, for example :

$$2C_6H_6 + I_2 \xrightarrow[(HNO_3,\ sp.\ gr.\ 1\cdot5)]{[O]} 2C_6H_5I + H_2O$$

Condensed aromatic hydrocarbons may be brominated directly with bromine in the presence of a solvent, such as carbon tetrachloride :

$$\underset{\text{Naphthalene}}{C_{10}H_8} + Br_2 \xrightarrow{(CCl_4)} \underset{\alpha\text{-Bromonaphthalene}}{\alpha\text{-}C_{10}H_7Br} + HBr$$

In the absence of catalysts, toluene when treated with chlorine (or bromine) at the boiling point, preferably with exposure to sunlight or other bright light source, undergoes halogenation in the side chain. The entrance of the first chlorine atom, for example, proceeds at a much faster rate than the entrance of the second chlorine atom so that in practice the major portion of the toluene is converted into benzyl chloride before appreciable chlorination of benzyl chloride occurs :

$$C_6H_5CH_3 + Cl_2 \xrightarrow[\text{(No catalyst)}]{\text{Sunlight, heat.}} \underset{\text{Benzyl chloride}}{C_6H_5CH_2Cl} \longrightarrow \underset{\text{Benzal chloride}}{C_6H_5CHCl_2} \longrightarrow \underset{\text{Benzotrichloride}}{C_6H_5CCl_3}$$

Rapid side-chain chlorination of toluene proceeds in the dark with sulphuryl chloride in the presence of dibenzoyl peroxide (0·001–0·005 mol per mol of SO_2Cl_2) as catalyst :

$$C_6H_5CH_3 + SO_2Cl_2 \xrightarrow{(C_6H_5CO)_2O_2} C_6H_5CH_2Cl + SO_2 + HCl$$

With excess of sulphuryl chloride, benzal chloride is formed, but chlorination does not proceed beyond this stage.

The replacement of a hydrogen atom in an aromatic compound by a chloromethyl (—CH_2Cl) group in a single operation is termed **chloromethylation.** The reaction consists essentially in the interaction with formaldehyde and hydrogen chloride in the presence of a catalyst such as zinc chloride or aluminium chloride (**Blanc chloromethylation reaction**). Thus benzyl chloride, accompanied by a little *p*-xylylene dichloride, m.p. 100°, may be obtained in good yield by passing hydrogen chloride gas into a suspension of paraformaldehyde and anhydrous zinc chloride in benzene. The paraformaldehyde depolymerises under the influence of the hydrogen chloride and the formaldehyde probably condenses as the addition product with hydrogen chloride $HOCH_2Cl$:

$$C_6H_6 + HCHO + HCl \xrightarrow{ZnCl_2} C_6H_5CH_2Cl + H_2O$$

The formaldehyde may be replaced by methylal $CH_2(OCH_3)_2$ or by chloromethyl ether CH_3OCH_2Cl, produced from paraformaldehyde, hydrogen chloride and methyl alcohol :

$$(CH_2O)_3 + 3CH_3OH + 3HCl \longrightarrow 3CH_3OCH_2Cl + 3H_2O$$

Monoalkyl benzene derivatives yield *para* chloromethyl compounds, frequently accompanied by small amounts of the *ortho* isomeride. The reaction is similar in some respects to that of Friedel and Crafts. Chloromethylation is of great value in synthetic work as the —CH_2Cl group can be converted into other groups such as —CH_2OH, —CHO, —CH_2OR, —CH_2CN, —$CH_2CH(COOC_2H_5)_2$ and —CH_3.

It is convenient to describe here certain polyvalent iodine compounds, formed by such substances as iodobenzene and *p*-iodotoluene. Iodobenzene in chloroform solution reacts readily with chlorine to form **iodobenzene dichloride** (*phenyl iododichloride*) (I) :

$$C_6H_5I + Cl_2 \longrightarrow C_6H_5ICl_2 \quad (I)$$

This is converted by aqueous sodium hydroxide into **iodosobenzene** (II) :

$$C_6H_5ICl_2 + 2NaOH \longrightarrow C_6H_5I{\rightarrow}O \ (II) + 2NaCl + H_2O$$

Iodosobenzene undergoes a slow change on keeping ; this change can be accelerated by heat and consists in a disproportionation to **iodoxybenzene** (III) and iodobenzene :

$$2C_6H_5I{\rightarrow}O \xrightarrow[\text{distillation}]{\text{Steam}} C_6H_5\overset{\nearrow O}{I}{=}O \ (III) + C_6H_5I$$

In practice, the iodosobenzene is steam distilled; pure iodobenzene is thus removed as formed.

The interaction of iodosobenzene and iodoxybenzene in the presence of aqueous sodium hydroxide yields the soluble **diphenyliodonium iodate** (IV); upon adding potassium iodide solution, the sparingly soluble **diphenyliodonium iodide** (V), analogous to ammonium iodide is precipitated:

$$C_6H_5IO + C_6H_5IO_2 \xrightarrow[aq.]{NaOH} [(C_6H_5)_2I]IO_3 \text{ (IV)}$$

$$[(C_6H_5)_2I]IO_3 + KI \longrightarrow [(C_6H_5)_2I]I \text{ (V)} + KIO_3$$

IV,17. CHLOROBENZENE

Into a 500 ml. bolt-head flask,* provided with an inlet tube (1) extending to within 1 cm. of the bottom and a reflux (double surface) condenser connected with a device (Fig. *II,8*, 1) for absorbing the hydrogen chloride gas subsequently evolved, place 220 g. (250 ml.) of sodium-dried A.R. benzene and 0·5 g. of aluminium amalgam (2). Weigh the flask and contents. Immediately pass in dry chlorine from a cylinder, preferably through an intermediate empty wash bottle. An exothermic reaction occurs and much hydrogen chloride is evolved. Cool the flask by immersion in a bath of cold water and allow the chlorination to proceed until the liquid has increased in weight by 85 g. Pour the liquid into about 250 ml. of cold water, separate the lower layer of chlorobenzene, and wash it successively with dilute sodium hydroxide solution and water; dry with anhydrous calcium chloride or anhydrous magnesium sulphate. Distil, using a well-lagged fractionating column (*e.g.*, Fig. *II*, *16*, 1), and collect the fraction b.p. 127–135° (3). Redistil and collect the pure chlorobenzene at 131–132°. The yield is about 155 g.

Notes.

(1) A gas distribution tube, provided with a sintered glass plate at its lower end is to be preferred.

(2) Prepared as described in Section IV,4, *Method B, Note* 1.

(3) The high boiling point residue contains *p*- (b.p. 173°, m.p. 53°) and *o*-dichlorobenzene (b.p. 179°), which may be separated, upon cooling in ice, the moderately pure solid *para* isomer separates out.

IV,18. BROMOBENZENE

Place 50 g. (57 ml.) of dry A.R. benzene and 0·5 ml. of dry pyridine (1) (dried over potassium hydroxide pellets) in a 500 ml. round-bottomed flask. Attach a reflux condenser to the flask and an inverted funnel (just dipping into some water in a beaker) to the top of the condenser (Fig. *II*, *13*, 8, *b*). Partially immerse the flask in a bath of cold water, supported upon a tripod and gauze. Carefully pour 125 g. (40 ml.) of bromine (for precautions to be taken with bromine, see Section **III,35**, *Note 1*) through a condenser and immediately insert the absorption device into the upper end of the condenser. A vigorous reaction soon occurs and hydrogen bromide is evolved which is absorbed by the water in the beaker; when the reaction slackens, warm the bath to 25–30° for

* Also termed a wide-necked flask or round-bottomed flask with short ring neck (Pyrex). A three-necked flask may also be used and the obvious modifications made.

1 hour. Finally raise the temperature of the bath to 65–70° for a further 45 minutes or until all the bromine has disappeared (no red vapours visible) and the evolution of hydrogen bromide has almost ceased. Keep the solution of hydrogen bromide in the beaker (2).

Two methods are available for isolating the pure bromobenzene.

Method 1. Arrange the flask containing the reaction mixture for steam distillation as in Fig. *II*, *40*, 1. Proceed with the steam distillation until crystals of *p*-dibromobenzene appear in the condenser. Change the receiver and continue with the distillation until all the *p*-dibromobenzene has passed over; from time to time run out the water from the condenser so that the crystals melt and run down into the receiver. Reject the residue in the flask. Transfer the first distillate to a separatory funnel, wash it with a little water, and dry the lower layer with a little anhydrous magnesium sulphate or anhydrous calcium chloride: filter. Distil slowly from a small distilling flask; use a wire gauze or an air bath (Fig. *II*, *5*, 3). Collect the fraction which passes over at 150–170°; pour the residue (R), while it is still hot, into a small beaker or porcelain basin for the isolation of *p*-dibromobenzene. Redistil the fraction of b.p. 150–170° and collect the bromobenzene at 154–157° (3). The yield is 60 g.

To isolate pure **p-dibromobenzene**, filter the second portion of the steam distillate through a small Buchner funnel with suction; press the crystals as dry as possible. Combine these crystals with the residue (R) and recrystallise from hot ethyl alcohol (for experimental details, see Section IV,12) with the addition of 1–2 g. of decolourising charcoal; use about 4 ml. of alcohol (methylated spirit) for each gram of material. Filter the hot solution through a fluted filter paper, cool in ice, and filter the crystals at the pump. The yield of *p*-dibromobenzene, m.p. 89°, is about 12 g.

Method 2. Transfer the dark-coloured reaction product to a separatory funnel and shake successively with water, with sufficient 5–10 per cent. sodium hydroxide solution to ensure that the washings are alkaline to litmus, and finally with water. Dry with anhydrous magnesium sulphate or calcium chloride. Filter through a fluted filter paper into a small distilling flask and distil slowly. Collect the crude bromobenzene at 150–170°; pour the residue whilst still hot into a small porcelain basin. Redistil the liquid of b.p. 150–170° (3) and collect the bromobenzene at 154–157°; the yield is about 60 g.

Isolate the pure *p*-dibromobenzene from the residue in the basin by the procedure described in *Method 1*. The yield is about 10 g.

Notes.

(1) Other halogen carriers may be used, *e.g.*, 1-2 g. of iron filings, or 1 g. of aluminium amalgam. The bromine must then be added slowly from a dropping funnel to the benzene warmed on a water bath; the apparatus shown in Fig. *II*, *13*, 9 is suitable and a trap for the hydrogen bromide must, however, be inserted into the top of the condenser. After all the bromine has been introduced, the mixture is heated on a water bath until no red vapours are visible above the liquid. The subsequent procedure is as above.

(2) This solution should be returned to the storeroom for subsequent recovery as constant boiling point hydrobromic acid. If time, permits the students should carry out this operation. Distil slowly from a distilling flask and when the tem-

perature rises to 126°, collect the constant boiling point acid. This contains 48 per cent of HBr and is a useful reagent in the laboratory.

(3) The best results are obtained by distillation from a small flask through a short fractionating column : a Hempel column filled with glass rings (Fig. *II*, *16*, 1) and lagged with asbestos cloth or several thicknesses of linen cloth is quite satisfactory.

IV,19. *m*-BROMONITROBENZENE

Equip a 1-litre three-necked flask with a separatory funnel, a mercury-sealed mechanical stirrer (1) and a double surface reflux condenser arrying an outlet tube connected to a gas trap (Fig. *II*, *8*, 1). Make all joints with asbestos paper–sodium silicate stoppers (Section **III,161**,*Note 2*) ; moderately satisfactory results may be obtained by employing " old " rubber stoppers. Support the flask in an oil bath. Place 90 g. (75 ml.) of dry, freshly-distilled nitrobenzene in the flask. Weigh out 10 g. of iron powder, " reduced by hydrogen " (" ferrum reductum "). Heat the oil bath to 135–145° and introduce 3 g. of the iron powder by temporarily removing the separatory funnel. Into the latter place 62·5 g. (20 ml.) of dry bromine (Section **II,49**, *8*) and run it into the flask at such a rate that bromine vapours do not rise appreciably in the condenser (*ca.* 20 minutes). Continue stirring and heating for 1 hour before adding a further 3 g. of iron powder and 20 ml. of dry bromine in a similar manner. Stir for a further hour, add another 3 g. of iron powder and 20 ml. of bromine. When there is no more bromine vapour in the condenser, make a final addition of 1 g. of iron powder and heat for 1 hour longer.

Pour the resulting dark reddish-brown liquid into 500 ml. of water to which 17 ml. of saturated sodium bisulphite solution has been added (the latter to remove the excess of bromine). Steam distil the resulting mixture (Fig. *II*, *41*, 1) ; collect the first portion of the distillate, which contains a little unchanged nitrobenzene, separately. Collect about 4 litres of distillate. Filter the yellow crystalline solid at the pump, and press well to remove the adhering liquid. The resulting crude *m*-bromonitrobenzene, m.p. 51–52°, weighs 110 g. If required pure, distil under reduced pressure (Fig. *II*, *19*, 1) and collect the fraction of b.p. 117–118°/9 mm. ; it then melts at 56° and the recovery is about 85 per cent.

Note.

(1) Mechanical stirring, although not essential and replaceable by occasional shaking by hand, is advantageous.

IV,20. α-BROMONAPHTHALENE

Use a 500 ml. three-necked flask equipped as in Section **IV,19**, but mounted on a water bath. Place 128 g. of naphthalene and 45 ml. of dry carbon tetrachloride in the flask, and 177 g. (55 ml.) of bromine in the separatory funnel. Heat the mixture to gentle boiling and run in the bromine at such a rate that little, if any, of it is carried over with the hydrogen bromide into the trap ; this requires about 3 hours. Warm gently, with stirring, for a further 2 hours or until the evolution of hydrogen bromide ceases. Replace the reflux condenser by a condenser set for downward distillation, stir, and distil off the carbon tetrachloride as completely as possible. Mix the residue with 8 g. of sodium

hydroxide pellets and stir at 90–100° for 3 hours; this treatment will remove impurities which gradually evolve hydrogen bromide. Transfer the liquid to a Claisen flask with fractionating side arm (Figs. *II,24*, 2–5) and distil under diminished pressure. Collect the following fractions:— (i) up to 131°/12 mm. (or 144°/20 mm.); (ii) 132–135°/12 mm. (or 145–148°/20 mm.); and (iii) above 135°/12 mm. (or 148°/20 mm.). Fraction (ii) is almost pure α-bromonaphthalene. Fraction (i) contains unchanged naphthalene, whilst (iii) contains dibromonaphthalene. Cool fraction (i) in ice when most of the naphthalene will crystallise out; filter this off on a sintered glass funnel, combine the filtrate with fraction (iii), redistil and collect the α-bromonaphthalene fraction separately. The total yield of colourless product is 150 g.

IV,21. IODOBENZENE

Equip a 500 ml. three-necked flask with a reflux condenser, a mercury-sealed mechanical stirrer and separatory funnel, and support it on a water bath. Attach an absorption device (Fig. *II*, *8*, 1, *c*) to the top of the condenser (1). Place 134 g. (152 ml.) of A.R. benzene and 127 g. of iodine in the flask, and heat the water bath to about 50°; add 92 ml. of fuming nitric acid, sp. gr. 1·50, slowly from the separatory funnel during 30 minutes. Oxides of nitrogen are evolved in quantity. The temperature rises slowly without the application of heat until the mixture boils gently. When all the nitric acid has been introduced, reflux the mixture gently for 15 minutes. If iodine is still present, add more nitric acid to the warm solution until the purple colour (due to iodine) changes to brownish-red.

Separate the lower oily layer, mix with it an equal volume of 10 per cent. sodium hydroxide solution, and steam distil from a 1-litre flask until no more oil passes over. A yellow solid, consisting of nitro compounds, may collect towards the end of the distillation; remove this by mechanical stirring of the oil for about 3 hours with 7 ml. of concentrated hydrochloric acid, 100 ml. of water and 70 g. of iron filings in a 1-litre three-necked flask connected with a reflux condenser. Allow the mixture to cool and filter. Render the filtrate distinctly acid to Congo red with hydrochloric acid and again steam distil. Separate the oil, dry it with anhydrous calcium chloride or magnesium sulphate, and distil with the aid of a suitably lagged fractionating column or from a Claisen flask with fractionating side arm (Figs. *II*, *24*, 2–5); collect the fraction of b.p. 180–190°. Upon redistillation, pure iodobenzene, b.p. 184–186°, is obtained. The yield is 180 g.

Note.

(1) "Old" rubber stoppers may be used, but are slightly attacked. Asbestos-sodium silicate stoppers (for preparation, see Section III,161,*Note* 2) or ground glass joints are, of course, to be preferred.

IV,22 BENZYL CHLORIDE (*Chlorination of Toluene*)

Method 1. Fit a 500-ml. three-necked flask with a thermometer (the bulb of which is within 2 cm. of the bottom), and inlet tube extending to the bottom of the flask, and a double surface condenser. Use "old"

rubber stoppers throughout (1). Connect the top of the condenser through a calcium chloride (or cotton wool) guard tube to two wash bottles containing 10 per cent. sodium hydroxide solution: the long lead-in tubes in the wash bottles should be just above the surface of the alkali solution in order to avoid "sucking back." Place 100 g. (115·5 ml.) of dry toluene and a few chips of porous plate in the flask. Boil the toluene gently and pass in a stream of chlorine from a cylinder—interpose an empty wash bottle between the flask and the cylinder—until the thermometer registers 157–158° (2). The reaction time may be considerably shortened by exposing the mixture to bright sunlight or to a small mercury-vapour lamp; if neither of these is practicable, support a 200-watt lamp a few inches from the flask.

Transfer the reaction mixture to a Claisen flask and distil under atmospheric pressure until the temperature reaches 135–140° (3). Distil the residue under diminished pressure and collect the benzyl chloride at 64–69°/12 mm. The latter upon redistillation boils largely at 63–65°/12 mm. The yield of benzyl chloride is about 100 g.

Notes.

(1) Ideal connections for chlorine are ground glass joints, but previously used and well-fitting rubber stoppers give satisfactory results. Owing to the poisonous character of chlorine, the apparatus should be fitted up in the fume cupboard.

(2) An alternative method of determining the completion of the reaction is to weigh the flask and toluene, and to stop the passage of chlorine when the increase in weight is 37 g.

(3) The benzyl chloride may also be isolated by distillation under atmospheric pressure. The material boiling between 165° and 185° is collected and redistilled; the final product is collected at 178–182° (pure benzyl chloride has b.p. 179°). The resulting benzyl chloride is, however, of lower purity unless an efficient fractionating column is used.

Method 2. In a 500-ml. round-bottomed flask, fitted with an efficient reflux condenser, place 92 g. (106 ml.) of toluene, 68 g. (41 ml.) of redistilled sulphuryl chloride and 1 g. of dibenzoyl peroxide (Section **IV,196**). Reflux gently, when a vigorous reaction takes place: the reaction is complete in 30 minutes. Isolate the benzyl chloride as described in *Method 1.* The yield is 50 g.

Cognate Preparation

Benzal chloride (benzylidene chloride). Use 100 g. of toluene and continue the passage of chlorine until the increase in weight of the flask and contents is 74 g. or, alternatively, until the temperature rises to 187°. Collect the benzal chloride at 204–208° or at 104–105°/30 mm. Pure benzylidene chloride has b.p. 206°.

IV,23. BENZYL CHLORIDE (*Chloromethylation of Benzene*)

Into a 1-litre three-necked flask, equipped with a reflux (double surface) condenser, a mechanical stirrer (preferably of the Hershberg type, Fig. *II*, 7, 8) and a gas lead-in tube extending to near the bottom of the flask, place 200 g. (227 ml.) of dry benzene, 20 g. of paraformaldehyde (1) and 20 g. of finely-pulverised, anhydrous zinc chloride. Support the flask on a water bath so arranged that the level of the water in it is about

the same height as the reaction mixture. Heat the bath to 60° and pass in (through an intervening empty wash bottle) a rapid stream of hydrogen chloride (Section **II,48,***1*) until no more gas is absorbed (about 20 minutes): allow to cool. Transfer the reaction mixture to a separatory funnel, wash it successively with two 50 ml. portions of cold water, two 50 ml. portions of saturated sodium bicarbonate solution (2) and finally with 20 ml. of water. Dry with anhydrous calcium chloride or magnesium sulphate, and distil under normal pressure from a Claisen flask with fractionating side arm (Figs. *II, 24*, 2–5) until the temperature rises to 100–110°. After cooling somewhat, distil under reduced pressure and collect the benzyl chloride at 63–65°/12 mm. The yield is 70 g. Some (about 4 g.) *p*-xylylene dichloride, m.p. 100°, and a small amount of diphenylmethane are present in the residue in the flask.

Notes.

(1) Formalin (40 per cent.) may also be used ; the proportions are then 200 g. of benzene, 38 g. of 40 per cent. formalin and 50 g. of pulverised zinc chloride.

(2) It is essential to remove all the zinc salts in the washing process, otherwise the product largely resinifies during the distillation.

Cognate Preparations

p-Ethylbenzyl chloride. Use a mixture of 250 g. of dry ethylbenzene (Section **IV,6**), 30 g. of paraformaldehyde and 20 g. of anhydrous pulverised zinc chloride, and proceed exactly as detailed for benzyl chloride. Collect the *p*-ethylbenzyl chloride at 95–96°/15 mm. ; the yield is 100 g.

α-Chloromethylnaphthalene. *CAUTION :* Both α-chloromethylnaphthalene and the by-products are lachrymators and vesicants. The preparation should therefore be conducted in a fume cupboard (hood) and precautions should be taken in the handling of the substance and the apparatus.

In a 1-litre flask, fitted with a reflux condenser and Hershberg stirrer, place 64 g. of naphthalene, 27·5 g. of paraformaldehyde, 65 ml. of glacial acetic acid, 41 ml. of 85 per cent. orthophosphoric acid and 107 g. (90·5 ml.) of concentrated hydrochloric acid. Heat the mixture, with vigorous stirring, in a water bath at 85–90° for 6 hours : maintain the level of the water bath at the same height as that of the stirred reaction mixture. Cool the mixture to room temperature, transfer it to a 500 ml. separatory funnel, wash the crude product with two 250 ml. portions of cold water (5–10°), then with 125 ml. of cold 10 per cent. potassium carbonate solution, and finally with 125 ml. of cold water : the product is the lower layer in all the washings. Add 50 ml. of ether, dry the ethereal solution by standing over 2·5 g. of anhydrous potassium carbonate with frequent shaking for 1 hour, run off the lower aqueous layer, add a further 5·6 g. of anhydrous potassium carbonate, and leave for 8–10 hours. Distil off the ether at atmospheric pressure and the residue under reduced pressure : use a Claisen flask with short side tube and a distilling flask as receiver (compare Fig. *II, 19*, 1 ; alternatively, the flask shown in Fig. *II, 19*, 3 may be employed). A fore-run of unreacted naphthalene, amounting to about 9 g., passes over at 120–126°/9 mm. ; care should be taken that the naphthalene does not solidify in the side arm by gently warming, if necessary. This is followed (the receiver should be changed at this point) by 56 g.

of α-chloromethylnaphthalene at 147–152°/13 mm. An appreciable brown residue, containing bis-(chloromethyl)-naphthalene and di-α-naphthylmethane, remains in the flask.

IV,24. IODOBENZENE DICHLORIDE

Equip a 500-ml. three-necked flask with a mechanical stirrer, an inlet tube at least 10 mm. in diameter for the introduction of chlorine, and an outlet tube carrying a calcium chloride (or cotton wool) guard tube. Charge the flask with 75 ml. of chloroform (dried with anhydrous calcium chloride : see Section **II,47,***25*) and 51 g. of iodobenzene (Section **IV,21**) ; adjust the inlet tube so that it terminates about 5 mm. above the surface of the liquid. Set up the apparatus in the fume cupboard and protect it from the light. Cool the flask in an ice-salt mixture and pass in dry chlorine (1) as rapidly as the solution will absorb it until an excess is present (1·5–2 hours). Filter the yellow, crystalline iodobenzene dichloride at the pump, wash it sparingly with chloroform and dry it in the air upon filter paper. The yield is 65 g. The substance decomposes slowly upon standing ; it may be kept unchanged for a short period in a well-fitting, ground glass stoppered bottle.

Note.

(1) Chlorine from a cylinder is passed through two wash bottles containing concentrated sulphuric acid, then through an empty wash bottle filled with glass wool to remove spray.

IV,25. IODOSOBENZENE

Cool a large glass mortar in ice and then place in it 50 g. of anhydrous sodium carbonate, 55 g. of iodobenzene dichloride (Section **IV,24**) and 100 g. of finely crushed ice. Grind the mixture thoroughly until all the ice has melted and a thick paste results. Add 140 ml. of 5*N*-sodium hydroxide in 20 ml. portions and triturate vigorously after each addition ; finally add 120 ml. of water and allow to stand overnight. Filter with suction, press well with a large flat glass stopper on the filter, transfer to a beaker, and stir with 300 ml. of water (1). Filter again at the pump transfer again to a beaker containing 300 ml. of water, filter and wash with about 200 ml. of water on the filter. Dry in the air upon filter papers, stir with a little chloroform (to dissolve a little iodobenzene which is present), filter with suction, and dry on filter paper in the air. The yield is 27 g.

Iodosobenzene explodes violently at about 220°, so that determinations of the melting point should not be attempted. It may, however, be converted into **iodobenzene diacetate** in the following manner. Dissolve 2 g. of iodosobenzene in 6 ml. of glacial acetic acid ; boiling is usually necessary. Cool. The resulting diacetate is readily soluble in acetic acid but is insoluble in ether. Add about 50 ml. of ether in order to precipitate the iodobenzene diacetate. Filter and wash with ether. The yield is

2 g., m.p. 157°. It may be recrystallised from benzene, and will keep indefinitely (unlike the iodobenzene dichloride).

$$C_6H_5IO + 2CH_3COOH \longrightarrow C_6H_5I(OOCCH_3)_2 + H_2O$$

Note.

(1) The filtrate contains some diphenyliodonium salts; these may be recovered as the sparingly soluble diphenyliodonium iodide (about 8 g.) (Section **IV,27**) by the addition of potassium iodide.

IV,26. IODOXYBENZENE

Fit up a 1-litre round-bottomed flask for steam distillation (Fig. *II*, *40*, 1) and place in it 22 g. of iodosobenzene (Section **IV,25**) made into a thin paste with water (1). Steam distil until almost all the iodobenzene has been removed (about 9 g.); cool the residue in the flask at once, filter the white solid with suction and dry in the air. Wash it with a little chloroform, filter with suction, and dry in the air upon filter paper. The yield is 10·5 g. It may be recrystallised from 800–900 ml. of water. Iodoxybenzene melts with explosive decomposition at 237°.

Note.

(1) Iodosobenzene when heated directly may decompose with explosive violence, particularly when dry.

IV,27. DIPHENYLIODONIUM IODIDE

Grind together 12 g. of iodoxybenzene (Section **IV,26**), 11 g. of iodosobenzene (Section **IV,25**) with 25 ml. of water, add 100 ml. of *N* sodium hydroxide solution and stir for 24 hours in a 1-litre vessel. Dilute with 500 ml. of cold water, stir thoroughly, allow to settle, and decant the supernatant solution of diphenyliodonium iodate, through a fluted filter paper. Extract the solid residue with two 250 ml. portions of water, and decant the extract through a fluted filter paper: a small tarry residue remains. To the combined filtrates add an aqueous solution containing 10 g. of potassium iodide. Allow the bulky white precipitate of diphenyliodonium iodide to stand for 1·5 hours with occasional shaking, and then filter it with suction. Dry on a porous tile. The yield is 15 g. The product melts at 173-175° with vigorous decomposition.

IV,28. REACTIONS AND CHARACTERISATION OF HALOGENATED AROMATIC HYDROCARBONS

The following reactions will assist the student in the identification of halogenated aromatic hydrocarbons.

(i) **Alcoholic silver nitrate solution.** Chlorobenzene and similar nuclear substituted compounds do not react. Benzyl chloride and other aromatic compounds with the halogen in the side chain react rapidly.

For details of test, see under *Alkyl Halides*, Section **III,42,**(ii).

(ii) **Alcoholic potassium hydroxide solution.** This reagent gives similar results to alcoholic silver nitrate solution.

For details of test, see under *Alkyl Halides*, Section **III,42,**(iii).

Crystalline Derivatives

1. **Nitration products.** Although no general method of nitration can be given, the following procedure is widely applicable.

Add 1 g. of the compound to 4 ml. of concentrated sulphuric acid and cautiously introduce, drop by drop, 4 ml. of fuming nitric acid. Warm the mixture on a water bath for 10 minutes, then pour it on to 25 g. of crushed ice (or 25 ml. of ice water). Collect the precipitate by filtration at the pump, and recrystallise it from dilute alcohol.

Twenty per cent. oleum may be substituted for the concentrated sulphuric acid for compounds which are difficult to nitrate.

2. **Reaction with chlorosulphonic acid ("chlorosulphonylation"). Sulphonamides.** Many aryl halides, either alone or in chloroform solution, when treated with excess of chlorosulphonic acid afford the corresponding sulphonyl chlorides in good yield (compare Section **IV,106**): the latter may be readily converted into the aryl sulphonamides by reaction with concentrated ammonia solution or with solid ammonium carbonate.

The following give abnormal results when treated with chlorosulphonic acid alone, preferably at 50° for 30–60 minutes:—fluobenzene (4 : 4′-difluorodiphenylsulphone, m.p. 98°); iodobenzene (4 : 4′-di-iododiphenylsulphone, m.p. 202°); *o*-dichlorobenzene (3 : 4 : 3′ : 4′-tetrachlorodiphenylsulphone, m.p. 176°); and *o*-dibromobenzene (3 : 4 : 3′ : 4′-tetrabromodiphenylsulphone, m.p. 176–177°). The resulting sulphones may be crystallised from glacial acetic acid, benzene or alcohol, and are satisfactory for identification of the original aryl halide. In some cases sulphones accompany the sulphonyl chloride; they are readily separated from the final sulphonamide by their insolubility in cold 6*N* sodium hydroxide solution; the sulphonamides dissolve readily and are reprecipitated by 6*N* hydrochloric acid.

Procedure 1. Dissolve 1 g. of the compound in 5 ml. of chloroform in a test-tube and cool in ice. Add 5 ml. of chlorosulphonic acid (*CAUTION* in handling) dropwise and with shaking. When the initial evolution of hydrogen chloride subsides, remove the reaction mixture from the ice and, after 20 minutes, pour it into a 50 ml. beaker filled with crushed ice. Separate the chloroform layer, wash it well with water, and evaporate the solvent. Recrystallise the residual aryl sulphonyl chloride from light petroleum (b.p. 40–60°), chloroform or benzene; this is not essential for conversion into the sulphonamide.

Procedure 2. Follow Procedure 1 except that no solvent is employed. Pour the syrupy reaction mixture on to crushed ice, remove the resulting aryl sulphonyl chloride and/or sulphone, if a solid, by filtration with suction and, if a liquid, by means of a small separatory funnel or dropper, and wash with water.

To convert the aryl sulphonyl chloride into the sulphonamide, use either of the following methods:—

(i) Boil 0·5 g. with 5 ml. of concentrated ammonia solution, sp. gr. 0·88, for 10 minutes, cool to room temperature, add 10 ml. of cold water, filter with suction, wash well, and recrystallise to constant m.p. from dilute alcohol; dry at 100°.

(ii) Mix the product from the chlorosulphonylation (0·5 g.) with 2·0 g. of dry, powdered ammonium carbonate and heat at 100° for 30 minutes. Wash with several 10 ml. portions of cold water, filter, and recrystallise from dilute alcohol.

If the presence of a sulphone is suspected, treat the product with 6*N* sodium hydroxide solution (only the sulphonamide dissolves), filter and reprecipitate the sulphonamide by 6*N* hydrochloric acid.

3. **Oxidation of side chains.** The oxidation of halogenated toluenes and similar compounds and of compounds with side chains of the type $-CH_2Cl$ and $-CH_2OH$ proceeds comparatively smoothly with alkaline permanganate solution (for experimental details, see under *Aromatic Hydrocarbons*, Section **IV,9,6** or under *Aromatic Ethers*, Section **IV,106**). The resulting acid may be identified by a m.p. determination and by other tests (see Section **IV,175**).

4. **Picrates.** Some halogen derivatives of the higher aromatic hydrocarbons form picrates (for experimental details, see under *Aromatic Hydrocarbons*, Section **IV,9,** *1*), for example, α-chloronaphthalene (m.p. 137°), α-bromonaphthalene (m.p. 134°), and β-bromonaphthalene (m.p. 86°).

The properties of a number of aromatic halogen compounds are collected in Table **IV,28.**

Compound	B.P.	M.P.	$d_{4°}^{20°}$	$n_D^{20°}$	Nitration Product		Sulphonamide ($-SO_2NH_2$, 1)		Other Derivatives
					Position	M.P.	Position	M.P.	
Fluorobenzene	85°	—	1·024	1·466	—	—	4, F	125°	Sulphone, 98°
Chlorobenzene	132	—	1·107	1·525	2 : 4	52°	4, Cl	143	—
Bromobenzene	156	—	1·494	1·560	2 : 4	75	4, Br	162	—
Iodobenzene	188	—	1·831	1·620	4	174	—	—	Sulphone, 202
o-Fluorotoluene	114	—	—	—	—	—	3, CH_3; 4, F	105	*o*-Fluobenzoic acid, 127
m-Fluorotoluene	116	—	—	—	—	—	2, CH_3; 4, F	173	*m*-Fluobenzoic acid, 124
p-Fluorotoluene	116	—	0·998	1·469	—	—	2, CH_3; 5, F	141	*p*-Fluobenzoic acid, 186
o-Chlorotoluene	159	—	1·082	1·527	3 : 5	64	3, CH_3; 4, Cl	126	*o*-Chlorobenzoic acid, 141
m-Chlorotoluene	162	—	1·072	1·522	4 : 6	91	2, CH_3; 4, Cl	185	*m*-Chlorobenzoic acid, 158
p-Chlorotoluene	162	7°	1·071	1·521	2	38	2, CH_3; 5, Cl	143	*p*-Chlorobenzoic acid, 242
o-Bromotoluene	181	—	1·425	—	3 : 5	82	3, CH_3; 4, Br	146	*o*-Bromobenzoic acid, 148
m-Bromotoluene	183	—	1·410	—	4 : 6	103	2, CH_3; 4, Br	168	*m*-Bromobenzoic acid, 155
p-Bromotoluene	185	26	1·390	—	2	47	2, CH_3; 5, Br	165	*p*-Bromobenzoic acid, 251
o-Iodotoluene	207	—	1·698	—	6	103	—	—	*o*-Iodobenzoic acid, 162
m-Iodotoluene	204	—	1·698	—	—	—	—	—	*m*-Iodobenzoic acid, 186
p-Iodotoluene	211	35	—	—	—	—	—	—	*p*-Iodobenzoic acid, 269
Benzyl chloride	179	—	1·100	1·539	—	—	—	—	S Benzyl-*iso*-thiuronium picrate, 188
Benzal chloride	205	—	1·250	1·550	—	—	—	—	Benzaldehyde phenylhydrazone, 156
Benzo-trichloride	220	—	1·173	—	—	—	—	—	Benzoic acid, 121
Benzyl bromide	198	—	1·438	—	—	—	—	—	—
Benzal bromide	156°/23	—	—	1·541	—	—	—	—	—
Benzyl iodide	93°/10	24	—	—	—	—	—	—	—
o-Difluorobenzene	—	92	—	—	—	—	—	—	—
m-Difluorobenzene	—	82	—	—	—	—	—	—	—
p-Difluorobenzene	—	88	—	—	—	—	—	—	—
o-Dichlorobenzene	180	—	1·305	1·551	4 : 5	110	3 : 4, diCl	135	Sulphone, 176

TABLE IV,28. **AROMATIC HALOGEN COMPOUNDS (*continued*)**

Compound	B.P.	M.P.	$d_{4°}^{20°}$	$n_D^{20°}$	Nitration Product		Sulphonamide ($-SO_2NH_2$: 1·)		Other Derivatives
					Position	M.P.	Position	M.P.	
m-Dichlorobenzene	173°	—	1·288	1·546	4 : 6	103°	2 : 4, diCl	180°	—
p-Dichlorobenzene	174	53°	—	—	2	54	2 : 5, diCl	180	—
o-Dibromobenzene	224	7	1·956	1·609	4 : 5	114	3 : 4, diBr	176	Sulphone, 177°
m-Dibromobenzene	219	—	1·952	1·606	4	62	2 : 4, diBr	189	—
p-Dibromobenzene	219	89	—	—	2 : 5	84	2 : 5, diBr	195	—
o-Di-iodobenzene	287	27	—	—	—	—	—	—	—
m-Di-iodobenzene	285	40	—	—	—	—	—	—	—
p-Di-iodobenzene	285	129	—	—	2 : 5	171	—	—	—
o-Bromochlorobenzene	195	—	1·646	1·580	—	—	—	—	—
p-Bromochlorobenzene	195	67	—	—	—	72	—	—	—
o-Bromoiodobenzene	257	—	2·262	1·665	—	—	—	—	—
p-Bromoiodobenzene	251	92	—	—	—	—	—	—	—
2 : 4-Dichlorotoluene	199	—	1·249	1·549	3 : 5	104	2 : 4, diCl, 5Me	176	2 : 4-Dichlorobenzoic acid, 164
2 : 6-Dichlorotoluene	199	—	1·269	1·551	3	53	2 : 4, diCl, 3Me	204	2 : 6-Dichlorobenzoic acid, 139
2 : 5-Dibromotoluene	236	—	1·811	—	—	—	—	—	2 : 5-Dibromobenzoic acid, 157
3 : 4-Dibromotoluene	240	—	1·811	—	—	—	—	—	3 : 4-Dibromobenzoic acid, 235
1 : 2 : 4-Trichlorobenzene	213	17	1·468	1·554	5	56	—	—	—
1 : 2 : 3-Trichlorobenzene	218	53	—	—	4	56	2 : 3 : 4, triCl	230	—
1 : 3 : 5-Tribromobenzene	271	120	—	—	—	—	2 : 4 : 6, triBr	222d	—
1 : 2 : 4 : 5-Tetrachlorobenzene	240	140	—	—	3	99	—	—	—
1 : 2 : 4 : 5-Tetrabromobenzene	—	181	—	—	3	168	—	—	—
Bromomesitylene	225	−1	—	—	—	—	—	—	—
2-Bromocymene	234	—	1·267	—	—	—	—	—	—

TABLE IV,28. **AROMATIC HALOGEN COMPOUNDS (*continued*)**

Compound	B.P	M.P.	$d_{4°}^{20°}$	$n_D^{20°}$	Nitration Product		Sulphonamide ($-SO_2NH_2$, 1)		Other Derivatives
					Position	M.P.	Position	M.P.	
Hexachlorobenzene	—	229°	—	—	—	—	—	—	—
α-Fluoronaphthalene	214°	—	1·134	1·594	—	—	—	—	Picrate, 113°
β-Fluoronaphthalene	—	60	—	—	—	—	—	—	Picrate, 101
α-Chloronaphthalene	259	—	1·191	1·633	4 : 5	180°	4, Cl	186°	Picrate, 137
β-Chloronaphthalene	256	61	—	—	1 : 8	175	7, Cl	232	Picrate, 81
α-Bromonaphthalene	281	—	1·484	1·658	4	85	4, Br	193	Picrate, 134
β-Bromonaphthalene	282	59	—	—	—	—	7, Br	208	Picrate, 86
α-Iodonaphthalene	302	—	—	—	—	—	—	—	Picrate, 127
β-Iodonaphthalene	309	54	—	—	—	—	—	—	Picrate, 95
2-Chlorodiphenyl	273	32	—	—	—	—	—	—	*o*-Chlorobenzoic acid, 141
4-Chlorodiphenyl	291	77	—	—	—	—	—	—	*p*-Chlorobenzoic acid, 242
2-Bromodiphenyl	297	—	—	—	—	—	—	—	*o*-Bromobenzoic acid, 148 (CrO_3)
4-Bromodiphenyl	310	89	—	—	—	—	—	—	*p*-Bromobenzoic acid, 251 (CrO_3)
2-Iododiphenyl	158°/6	—	—	—	—	—	—	—	—
4-Iododiphenyl	—	114	—	—	—	—	—	—	—
1 : 2-Dichloronaphthalene	296	35	—	—	—	—	—	—	—
1 : 2-Dibromonaphthalene	—	68	—	—	—	—	—	—	—
2 : 2′-Dichlorodiphenyl	—	60	—	—	—	—	—	—	—
4 : 4′-Dichlorodiphenyl	—	149	—	—	—	—	—	—	*p*-Chlorobenzoic acid, 242 (CrO_3)
2 : 2′-Dibromodiphenyl	—	81	—	—	—	—	—	—	—
4 : 4′-Dibromodiphenyl	—	164	—	—	—	—	—	—	*p*-Bromobenzoic acid, 251 (CrO_3)
Naphthalene tetrachloride (1 : 2 : 3 : 4)	—	183	—	—	—	—	—	—	—

SULPHONATION OF AROMATIC HYDROCARBONS

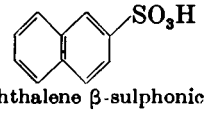
Aromatic hydrocarbons may be mono-sulphonated by heating with a slight excess of concentrated sulphuric acid ; for benzene, oleum (7-8 per cent. SO_3) gives somewhat better results. The reaction is usually complete when all the hydrocarbon has dissolved. Examples are :

$$C_6H_6 + HOSO_3H \longrightarrow \underset{\text{Benzenesulphonic acid}}{C_6H_5SO_3H} + H_2O$$

$$\underset{\text{Toluene}}{CH_3C_6H_5} + HOSO_3H \longrightarrow \underset{p\text{-Toluenesulphonic acid}}{CH_3C_6H_4SO_3H\ (1:4)} + H_2O$$


Naphthalene

$$+ HOSO_3H \longrightarrow$$



Naphthalene β-sulphonic acid

$$+ H_2O$$

Because of the great solubility of sulphonic acids in water and the consequent difficulty in crystallisation, the free sulphonic acids are not usually isolated but are converted directly into the sodium salts. The simplest procedure is partly to neutralise the reaction mixture (say, with solid sodium bicarbonate) and then to pour it into water and add excess of sodium chloride. An equilibrium is set up, for example :

$$C_6H_5SO_3H + NaCl \rightleftharpoons C_6H_5SO_3Na + HCl$$

The high sodium ion concentration results in facile crystallisation of the sodium salt. This process of salting out with common salt may be used for recrystallisation, but sodium benzenesulphonate (and salts of other acids of comparable molecular weight) is so very soluble in water that the solution must be almost saturated with sodium chloride and consequently the product is likely to be contaminated with it. In such a case a pure product may be obtained by crystallisation from, or Soxhlet extraction with, absolute alcohol ; the sulphonate is slightly soluble but the inorganic salts are almost insoluble. Very small amounts of sulphones are formed as by-products, but since these are insoluble in water, they separate when the reaction mixture is poured into water :

$$C_6H_5SO_3H + C_6H_6 \longrightarrow \underset{\text{Diphenyl sulphone}}{C_6H_5SO_2C_6H_5} + H_2O$$

The sulphonation of toluene at 100-120° results in the formation of *p*-toluenesulphonic acid as the chief product, accompanied by small amounts of the *ortho* and *meta* isomers ; these are easily removed by crystallisation in the presence of sodium chloride. Sulphonation of naphthalene at about 160° yields largely the β-sulphonic acid ; at lower temperatures (0-60°) the α-sulphonic acid is produced almost exclusively.

Sulphonation is a reversible reaction and, in general, an excess of sulphuric acid is employed, for example :

$$CH_3C_6H_5 + H_2SO_4 \rightleftharpoons CH_3C_6H_4SO_3H\ (1:4) + H_2O$$

If, however, the water formed is removed as formed (compare the preparation of di-*n*-butyl ether, Section **III,57**), the sulphuric acid may react completely and the method may be employed for the preparation of the free sulphonic acid.

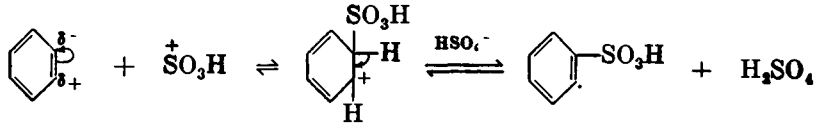
The *mechanism* of aromatic sulphonation may be similar to that previously described for nitration and halogenation, involving attack of the electrophilic $\overset{+}{S}O_3H$ ion. The latter may be formed thus :

$$2HO—SO_2—OH \rightleftharpoons H_2\overset{+}{O}—SO_2—OH + HSO_4^-$$

$$H_2\overset{+}{O}—SO_2—OH \rightleftharpoons H_2O + \overset{+}{S}O_2—OH$$

$$HO—SO_2—OH + H_2O \rightleftharpoons H_3O^+ + HSO_4^-$$

The $\overset{+}{S}O_2$—OH ion attacks the nucleophilic aromatic nucleus :



It has been suggested that SO_3 is the actual electrophilic reagent leading to $C_6H_5SO_3^-$*, the anion of $C_6H_5SO_3H$. However, in sulphuric acid, the following equilibrium probably exists :

$$SO_3 + H_2SO_4 \rightleftharpoons HSO_3^+ + HSO_4^-,$$

and it may well be that both SO_3 and HSO_3^+ are the active reagents. A further complication is the reversibility of the over-all sulphonation reaction.

IV,29. SODIUM BENZENESULPHONATE

Into a 200-ml. round-bottomed flask place 75 g. (40 ml.) of fuming sulphuric acid, sp. gr. 1·88, containing 7–8 per cent. of sulphur trioxide. Add, with frequent shaking, 20 g. (22·5 ml.) of thiophene-free benzene (1) in portions of about 3 ml. during about 15 minutes. Make sure that the first portion has dissolved before adding the next portion, etc.; maintain the temperature of the reaction mixture between 30° and 50°, and cool in a vessel of cold water if necessary. When all the benzene has completely reacted, cool and pour the reaction mixture slowly and with constant stirring into about 200 ml. of water. Cool to the laboratory temperature and, if necessary, filter from any diphenylsulphone $C_6H_5SO_2C_6H_5$ (a by-product) which may separate. Partially neutralise the acid solution by adding carefully and in small portions 24 g. of sodium bicarbonate : then add 40 g. of sodium chloride and heat until it dissolves. Filter the hot solution with suction through a Buchner funnel (previously warmed in the steam oven or by pouring boiling water through it), transfer the warm filtrate to a beaker, and cool rapidly (ice and cold water) with stirring. Filter the sodium benzenesulphonate which separates on a Buchner funnel and press well with a wide glass stopper; wash with about 30 ml. of a filtered saturated sodium chloride solution and press

* This anion may be formed according to the following scheme :

$$C_6H_5H + SO_3^- \rightleftharpoons \overset{+}{C}_6H_5\begin{matrix}H\\ \diagdown SO_3^-\end{matrix}$$

$$\overset{+}{C}_6H_5\begin{matrix}H\\ \diagdown SO_3^-\end{matrix} \rightleftharpoons C_6H_5SO_3^- + H^+$$

veniently done with the aid of the warm air blower shown in Fig. *II*, *2*, 1. It consists of an inexpensive commercial hair drier * mounted on a retort stand ; a cork carrying a wide glass tube (about 10 mm. in diameter) is fitted into the air orifice and securely wired into position. The air blast is controlled by a three-way combination switch : with one setting of the switch the apparatus blows air at the laboratory temperature, with another setting it blows hot air, and with a third setting the blower is switched off. The apparatus, moist with organic solvent, is held (or supported) over the glass tube and cold air is first passed through for a minute or two, and this is soon followed by hot air until the apparatus is thoroughly dry.

A less satisfactory method of drying after the washing with the organic solvent is to pass a stream of air from a blowpipe bellows (foot or electrically operated) into the vessel through a long wide glass tube. When most or all of the solvent has evaporated, a length of the glass tube may be heated in a flame, thus introducing warm air into the vessel to complete the drying.

II,3. USE OF CORK AND RUBBER STOPPERS

Two points must be borne in mind when selecting a cork stopper. In the first place, the cork should be examined for freedom from flaws ; unless corks of the highest quality are employed, they are liable to have deep holes, which render them useless. In the second place, the cork should originally fit as shown in Fig. *II*, *3*, 1, *a* and not as in *b*. It should then be softened by rolling in a cork press or by wrapping it in paper and rolling under the foot.

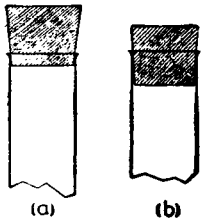


Fig. *II*, *3*, 1.

To bore a cork, a borer should be selected which gives a hole only very slightly smaller than that desired. The cork borer is moistened with water or alcohol or best with glycerine ; it is convenient to keep a small bottle (*ca.* 25 ml. capacity) containing glycerine, Fig. *II*, *3*, 2, for this purpose. The borer is held in the right hand and the cork in the left hand. The hole is started at the narrow end with a continuous rotary motion. Beginners should bear in mind that the borer is a cutting instrument and not a punch, and on no account should it be allowed to burst its way through the cork because the borer, upon emerging, will almost invariably tear the surface of the cork. It is a good plan to examine the borer from time to time as it advances through the cork to see that it is cutting a straight hole. Boring should be stopped when it is half through the cork † and the tool removed from the hole. The cork plug is pushed out with the aid of the solid metal rod supplied with the set of borers, and the remainder of the hole is bored from

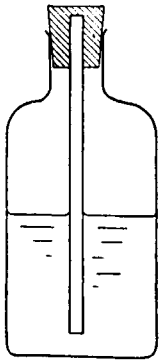


Fig. *II*, *3*, 2.

* An excellent and inexpensive hot air drier (" A.M. Industrial Type Blower ") is manufactured by Bylock Electric Ltd., Ponders End, Enfield, Middlesex.

† With a little experience this can usually be accomplished in one operation without the necessity of stopping to see whether a straight hole is being cut.

the crystals as dry as possible. Finally wash with a little alcohol. Dry in the air upon filter paper, powder, and dry in the oven at 100–110°. The yield of the dry sodium benzenesulphonate is about 20 g. The product contains traces of sodium chloride and other salts, but is pure enough for most purposes. The impurities may be completely removed by recrystallisation from rectified spirit; about 18 ml. are required for each gram of solid. The volume of alcohol required for recrystallisation may be considerably reduced by the use of a Soxhlet extractor (Figs. *II*, *44*, 4–6).

Note.

(1) Commercial benzene may be purified by shaking repeatedly with 10 per cent. of its volume of concentrated sulphuric acid until the acid layer is almost colourless, then washing successively with cold water, 10 per cent. sodium carbonate solution and water, and drying with anhydrous calcium chloride or magnesium sulphate. Distillation then yields pure benzene.

COGNATE PREPARATION

Sodium *p*-bromobenzenesulphonate. Equip a 500-ml. bolt-head or three-necked flask with a separatory funnel, a mechanical stirrer (*not* mercury-sealed) and a thermometer. Place 75 g. (40 ml.) of fuming sulphuric acid, sp. gr. 1·88 (7·8 per cent. SO_3) in the flask and 40 g. (27 ml.) of bromobenzene (Section **IV,18**) in the separatory funnel. Add the bromobenzene in small portions so that the temperature does not rise above 100°. If any bromobenzene remains unattacked, warm the mixture on a water bath until all of it has passed into solution. Allow to cool, and pour the reaction mixture in a thin stream with stirring into 140 ml. of cold water. If a precipitate separates (dibromodiphenylsulphone $BrC_6H_4SO_2C_6H_4Br$, a by-product), filter the warm solution at the pump. Add 55 g. of sodium chloride to the filtrate and heat (with stirring) until the salt dissolves. Cool the solution rapidly with stirring, filter the separated crude sulphonate at the pump, and press the crystals as dry as possible. Upon drying in the air, the yield is 47 g. To purify the crude sodium *p*-bromobenzenesulphonate, powder the crystals in a mortar, transfer to a beaker, add 75 ml. of a filtered, saturated solution of sodium chloride, stir, heat on a water bath for 30 minutes, allow to cool, filter and press the crystals as dry as possible; finally wash with a little alcohol. Dry in the air by spreading upon filter papers. The yield of purified sodium *p*-bromobenzenesulphonate is 45 g. The product, although pure enough for most practical purposes, contains traces of sodium chloride and other salts: these can be removed either by recrystallisation from hot rectified spirit (1 g. of salt requires *ca.* 25 ml. of alcohol) or, more economically, by extraction with alcohol in a Soxhlet apparatus (Figs. *II*, *44*, 4–6).

IV,30. SODIUM *p*-TOLUENESULPHONATE

Into a 500-ml. bolt-head or three-necked flask, provided with a mechanical stirrer and a reflux condenser, place 60 g. (69 ml.) of thiophene-free toluene (Section **II,47,*16***) and 60 g. (33 ml.) of concentrated sulphuric acid. Heat the mixture, with stirring, in an oil bath maintained at

110-120°. When the toluene layer has disappeared (*ca.* 1 hour), allow the reaction mixture to cool to room temperature. Pour it with stirring into 250 ml. of cold water; filter from any solid substance which may separate. Partly neutralise the acid solution by adding cautiously and in small portions 30 g. of sodium bicarbonate. Heat the solution to boiling and saturate it with sodium chloride (about 100 g. of salt are required), filter hot through a hot water funnel (Fig. *II*, *1*, 6) or through a Buchner funnel previously warmed to about 100°. Transfer the hot filtrate to a beaker and cool the solution, with stirring, in ice. Filter the crystals at the pump (rinse any residual crystals out of the beaker with a little of the filtered mother liquor), press well with a large glass stopper, and wash with 30 ml. of saturated salt solution. To recrystallise the crude sodium *p*-toluenesulphonate, dissolve it in 200–250 ml. of water, heat to boiling, saturate with salt, allow to cool somewhat, stir with 2–3 g. of decolourising charcoal (if the solution is coloured), and filter the hot solution with suction through a previously warmed Buchner funnel. Transfer the warm filtrate to a beaker and cool in ice: filter the sulphonate with suction through a Buchner funnel, wash it with 20 ml. of saturated sodium chloride solution, press well, and finally wash with a little alcohol. Dry the hydrated crystals in air upon filter papers, powder in a mortar, and then dry in a steam oven or in an air oven at 100-110°. The yield of anhydrous sodium *p*-toluenesulphonate is 50 g. It still contains traces of sodium chloride and other salts; these can be removed by recrystallisation from rectified spirit (1 g. of solid to about 40 ml. of alcohol) or by extraction in a Soxhlet apparatus with boiling alcohol (Figs. *II*, *44*, 4–6).

IV,31. SODIUM β-NAPHTHALENESULPHONATE

Equip a 500-ml. bolt-head or three-necked flask with a separatory funnel, a thermometer with its bulb about 2 cm. from the bottom, and a mechanical stirrer; the bearing for the stirrer consists of a glass tube lubricated with a little glycerine. Place 100 g. of naphthalene in the flask and heat it either in an air bath (Fig. *II*, *5*, 3) or by means of a free flame. When the naphthalene melts, start the stirrer and adjust the heating so that the temperature is 160 ± 5°. Run in 166 g. (90 ml.) of concentrated sulphuric acid from the funnel during 5–6 minutes: take care to maintain the temperature at 160° and remove the flame if necessary. Stir for 5 minutes and pour the solution into 750 ml. of cold water. If the sulphonation has been properly conducted, there will be no precipitate of naphthalene but about 4 g. of insoluble di-β-naphthyl sulphone $C_{10}H_7SO_2C_{10}H_7$ may separate. Boil with 3–4 g. of decolourising carbon and filter with suction through a Buchner funnel. Partly neutralise the clear solution by carefully adding 40 g. of sodium bicarbonate in small portions. Heat the solution to the boiling point, saturate with sodium chloride (about 70 g. are required) and then set aside to crystallise. Filter the crude sodium β-naphthalenesulphonate at the pump and recrystallise from hot 10 per cent. sodium chloride solution; dry by heating on a water bath or in a steam oven. The yield is 140 g.

IV,32. *p*-TOLUENESULPHONIC ACID

Use the apparatus employed for *Di*-n-*butyl Ether* (Fig. *III*, *57*, 2); it is advantageous to have the " water separator tube " calibrated (as in the Dean and Stark apparatus), otherwise place sufficient water in *A* so that with a further 9 ml. the water level is at *B*. Place 87 g. (100 ml.) of thiophene-free toluene (Section **II,47,***16*) and 37 g. (20 ml.) of concentrated sulphuric acid (92 per cent. H_2SO_4 by weight) in the 250 or 300-ml. bolt-head flask and heat to gentle boiling. When 9 ml. of water have been collected in the " water separator tube " (4–5 hours), extinguish the flame. The water is derived partly from the reaction (6·25 ml.) and partly from the sulphuric acid. Add 6·3 ml. of water to the cold contents of the flask; crystallisation then occurs. Spread the resulting solid on a porous tile and press well with a glass stopper; toluene and *o*-toluenesulphonic acid are thus removed. Dissolve the residual solid (47 g.) in about 22 ml. of water and saturate the solution with hydrogen chloride gas; use any convenient device (*e.g.*, a small funnel) to prevent " sucking back." After several hours the acid crystallises out as colourless prisms. Filter rapidly through a sintered glass funnel, wash with a little concentrated hydrochloric acid, and dry in a vacuum desiccator charged with stick potassium hydroxide and anhydrous calcium chloride. The yield is 35 g., m.p. 105–106° (sealed tube).

IV,33. REACTIONS AND CHARACTERISATIONS OF AROMATIC SULPHONIC ACIDS

Sulphonic acids are frequently crystalline solids, readily soluble in water and often hygroscopic. Because of the difficulty of isolation of the free acids, they are usually encountered as the alkali metal salts.

(i) **Fusion with caustic alkali.** When the preliminary tests for elements indicate the presence of sulphur (and frequently also of a metal), it is advisable to carry out a fusion with caustic alkali. In a nickel crucible of about 20 ml. capacity mix thoroughly 0·5–1 g. of the substance with 3 g. of potassium hydroxide pellets and 4–5 drops of water. Support the crucible in a circular hole in a sheet of asbestos or uralite board of such size that it fits tightly and only about one-third is below the board; this will ensure that the contents of the crucible are not contaminated by sulphur compounds from the gas flame. (Alternatively, place the nickel crucible in a larger iron crucible fitted with an asbestos ring so arranged that the nickel crucible is held about 5 mm. from the bottom of the iron crucible). Heat the crucible so that the mixture *just* melts and continue the fusion with occasional stirring with a small nickel spatula for 5–10 minutes. Allow to cool, add about 5 ml. of water and dissolve the mass by warming with a small flame. Pour the solution into a small test-tube; acidify by the cautious addition of 50 per cent. sulphuric acid. Note whether there is any odour of sulphur dioxide: test for this gas either with filter paper moistened with acidified potassium dichromate solution, or better, by the highly sensitive **sulphur dioxide test reagent**. In the

latter case it is best to use the semimicro technique for the identification of evolved gases.*

$$ArSO_3K + 2KOH \longrightarrow ArOK + K_2SO_3 + H_2O.$$

The sulphur dioxide test reagent is prepared by mixing 50 ml. of 0·1*N* hydrochloric acid, 15 ml. of *N* barium chloride solution and 5 ml. of 0·1*N* potassium permanganate solution. Its use is based upon the transient formation of barium sulphite which is immediately oxidised by the permanganate to give a white precipitate of insoluble barium sulphate ; the permanganate solution is simultaneously decolourised. The method is inapplicable in the presence of hydrogen sulphide, which gives the same visible result.

Extract the acidified solution with ether, remove the ether and identify the phenol in the usual manner (see Section **IV,114**).† Add a few drops of bromine water or nitric acid to the aqueous layer and test for sulphate with barium chloride solution.

Once the presence of a sulphonate group has been established (and, if possible, the phenol isolated), the compound may be characterised by the preparation of a derivative. It must be remembered that both *sulphoxides* RSOR′ and *sulphones* RSO_2R' yield sulphur dioxide on fusion with caustic alkali and acidification.

Crystalline Derivatives

1. **Sulphonamides.** Mix together 1·0 g. of the dry acid or 1·2 g. of the anhydrous salt with 2·5 g. of phosphorus pentachloride ‡ and heat under a reflux condenser in an oil bath at 150° for 30 minutes. Cool the mixture, add 20 ml. of dry benzene, warm on a steam bath and stir the solid mass well to extract the sulphonyl chloride : filter. Add the benzene solution slowly and with stirring to 10 ml. of concentrated ammonia solution. If the sulphonamide precipitates, separate it by filtration ; if no solid is obtained, evaporate the benzene on a steam bath. Wash the sulphonamide with a little cold water, and recrystallise from water, aqueous ethanol or ethanol to constant m.p.

The procedure is not usually applicable to aminosulphonic acids owing to the interaction between the amino group and the phosphorus pentachloride. If, however, the chlorosulphonic acid is prepared by diazotisation and treatment with a solution of cuprous chloride in hydrochloric acid, the crystalline chlorosulphonamide and chlorosulphonanilide may be obtained in the usual way. With some compounds, the amino group may be protected by acetylation. Sulphonic acids derived from a phenol or naphthol cannot be converted into the sulphonyl chlorides by the phosphorus pentachloride method.

The **sulphonanilides** may be prepared by either of the following methods :—(i) Reflux the solution of the sulphonyl chloride in benzene obtained as above, with 2·5 g. of aniline for 1 hour. Concentrate the benzene solution to half its volume and cool in ice. Collect the solid which separates on a filter, wash with hot water, and recrystallise from ethanol or dilute ethanol.

(ii) Treat the crude sulphonyl chloride {isolated by evaporating the solvent after extraction with benzene (or ether or chloroform) as above} with 1 g. of *p*-toluidine and 30 ml. of *ca.* 2*N* sodium hydroxide solution.

* See, for example, Vogel, *A Text-Book of Macro and Semimicro Qualitative Inorganic Analysis*, Fourth Edition, 1954, p. 181 (Longmans, Green and Co. Ltd.).

† The phenol cannot always be isolated in good yield, particularly if it contains substituent groups, owing to the destructive action of the alkali fusion upon the radical R.

‡ If preferred, the PCl_5 may be replaced by 4–5 ml. of $POCl_3$ and the mixture refluxed for 4 hours. The subsequent procedure is identical with that given in the text.

Shake for 10–15 minutes. Extract the alkaline solution with ether to remove excess of *p*-toluidine, acidify, filter, and recrystallise the residue as in (i).

$$RSO_2ONa + PCl_5 \longrightarrow RSO_2Cl + POCl_3 + NaCl$$

$$RSO_2Cl + 2NH_3 \longrightarrow RSO_2NH_2 + NH_4Cl$$

$$RSO_2Cl + 2C_6H_5NH_2 \longrightarrow RSO_2NHC_6H_5 + C_6H_5NH_3^+Cl^-$$

2. **S-Benzyl-*iso*-thiuronium salts (S-Benzyl-*iso*-thiourea salts)*** (for a discussion of this reagent, see under *Carboxylic Acids*, Section **III, 85,*4***). If the substance is the free sulphonic acid, dissolve 0·5 g. of it in 5–10 ml. of water, add a drop or two of phenolphthalein indicator, and neutralise with *ca. N* sodium hydroxide solution. Then add 2–3 drops of 0·1*N* hydrochloric acid to ensure that the solution is almost neutral (*pale* pink colour); under alkaline conditions the reagent tends to decompose to produce the evil-smelling benzyl mercaptan.

To a solution of 0·5 g. of the salt in 5 ml. of water and 2–3 drops of 0·1*N* hydrochloric acid (or to a solution of the acid treated as above), add a slight excess of a cold, 15 per cent. aqueous solution of benzyl-*iso*-thiourea hydrochloride (if the molecular weight of the compound is not known, use a solution of 1 g. of the reagent in 5 ml. of water), and cool in ice. Filter off the crystalline derivative and recrystallise it from 50 per cent. alcohol.

$$\left\{C_6H_5CH_2—S—C(=NH_2)—NH_2\right\}^+ Cl^- + RSO_3Na \longrightarrow \left\{C_6H_5CH_2—S—C(=NH_2)—NH_2\right\}^+ SO_3R^- + NaCl$$

3. **Sulphonacetamides.** Sulphonacetamides are derivatives of sulphonamides (Section **IV,33A**), but since the latter are readily prepared from the sulphonic acids or their salts, sulphonacetamides may be employed for the characterisation of sulphonic acids; for this reason they are included in this Section.

Sulphonamides upon heating with acetyl chloride are converted into the *N*-acetyl derivatives or sulphonacetamides:

$$ArSO_2NHR + CH_3COCl \longrightarrow ArSO_2NRCOCH_3 + HCl \ (R = H \text{ or alkyl})$$

The sulphonacetamides (R = H) are freely soluble in sodium bicarbonate solution thus rendering purification facile. Sulphonacetamides are moderately strong acids, and can generally be titrated in aqueous or aqueous-alcoholic solution with phenolphthalein as indicator. The acidic properties of sulphonacetamides may be used to effect a **separation of a sulphonamide from a *N*-alkylsulphonamide.** Acetylation of such a mixture gives a sulphonacetamide and a *N*-alkylsulphonacetamide, of which only the former is soluble in sodium bicarbonate solution. Both sulphonacetamides and *N*-alkylsulphonacetamides are readily hydrolysed by boiling with excess of 5 per cent. potassium hydroxide solution for about 1 hour, followed by acidification with dilute hydrochloric acid, giving the corresponding sulphonamides and *N*-alkylsulphonamides respectively.

* Also known as S-benzylthiuronium salts and as S-benzyl-ψ-thiuronium salts.

Reflux 1 g. of the sulphonamide with 2·5 ml. of acetyl chloride for 30 minutes; if solution is not complete within 5 minutes, add up to 2·5 ml. of glacial acetic acid. Remove the excess of acetyl chloride by distillation on a water bath, and pour the cold reaction mixture into water. Collect the product, wash with water and dissolve it in warm sodium bicarbonate solution. Acidify the filtered solution with glacial acetic acid; filter off the precipitated sulphonacetamide and recrystallise it from aqueous alcohol.

The melting points of a number of sulphonacetamides are :—benzenesulphonic acid, 125°; *p*-toluenesulphonic acid, 137°; *p*-bromobenzenesulphonic acid, 203°; *m*-nitrobenzenesulphonic acid, 189°; *p*-nitrobenzenesulphonic acid, 192°; naphthalene-α-sulphonic acid, 185°; and naphthalene-β-sulphonic acid, 146°.

4. ***p*-Toluidine salts of sulphonic acids.** These are prepared by the interaction of the sulphonic acid or its sodium salt with *p*-toluidine hydrochloride in aqueous solution :

$$RSO_3^-Na^+ + H^+Cl^- + p\text{-}CH_3—C_6H_4—NH_2$$
$$\longrightarrow (p\text{-}CH_3—C_6H_4—NH_3)^+(RSO_3)^- + Na^+Cl^-$$

Dissolve 1 g. of the sulphonic acid or its sodium salt in the *minimum* volume of boiling water and add a saturated aqueous solution of 1 g. of *p*-toluidine hydrochloride. Cool, filter off the precipitate of the *p*-toluidine salt, and recrystallise it from hot water or from dilute ethanol.

The melting points of the derivatives of a number of selected sulphonic acids are collected in Table **IV,33**; the melting points of the corresponding sulphonyl chlorides are included for purposes of reference.

TABLE IV,33. SULPHONIC ACIDS

Acid	Sulphonamide, $ArSO_2NH_2$	S-Benzyl-*iso*-thiuronium Salt	Sulphonanilide $ArSO_2NHPh$	*p*-Toluidine Salt	Sulphonyl Chloride, $ArSO_2Cl$
Benzenesulphonic	153°	150°	110°	205°	—
o-Toluenesulphonic	156	170	136	204	68°
m-Toluenesulphonic	108	—	96	—	12
p-Toluenesulphonic	137	182	103	198	71
o-Chlorobenzenesulphonic	188	—	—	—	28
m-Chlorobenzenesulphonic	148	—	—	—	—
p-Chlorobenzenesulphonic	144	175	104	209	53
o-Bromobenzenesulphonic	186	—	—	—	51
m-Bromobenzenesulphonic	154	—	—	—	—
p-Bromobenzenesulphonic	166	170	119	216	75
o-Nitrobenzenesulphonic	193	—	115	—	69
m-Nitrobenzenesulphonic	168	146	126	222	64
p-Nitrobenzenesulphonic	179	—	136	—	80
Sulphanilic	164	187	200	—	—
Orthanilic	153	132	—	—	—
Metanilic	142	148	—	—	—
o-Sulphobenzoic (salt)	—	206	—	200	79
m-Sulphobenzoic	170	163	—	—	20
p-Sulphobenzoic	236	213	—	—	57
Phenol-*p*-sulphonic	177	169	—	202	—
Thymolsulphonic	—	213	—	—	—
o-Xylenesulphonic	144	208	—	—	52
m-Xylenesulphonic	138	146	110	—	34
p-Xylenesulphonic	148	184	—	—	25
Naphthalene-α-sulphonic	150	137	112	181	68
Naphthalene-β-sulphonic	217	191	132	221	79
Anthraquinone-α-sulphonic	—	191	216	—	217
Anthraquinone-β-sulphonic	261	211	193	—	197
1-Naphthylamine-4-sulphonic	206	195	—	—	—
1-Naphthylamine-5-sulphonic	260	180	—	—	—
1-Naphthylamine-6-sulphonic	219	191	—	—	—
1-Naphthylamine-7-sulphonic	181	—	—	—	—
1-Naphthylamine-8-sulphonic	—	300	140	—	—
2-Naphthylamine-1-sulphonic	—	139	—	—	—
2-Naphthylamine-6-sulphonic	—	184	—	—	—
1-Naphthol-2-sulphonic	—	170	—	—	—
1-Naphthol-4-sulphonic	—	104	200	196	—
1-Naphthol-5-sulphonic	—	—	201	—	—
2-Naphthol-1-sulphonic	—	136	—	162	124
2-Naphthol-6-sulphonic	238	217	—	248	—
2-Naphthol-8-sulphonic	—	218	195	232	—
Benzene-*o*-disulphonic	254	206	241	—	143
Benzene-*m*-disulphonic	229	214	144	—	63
Benzene-*p*-disulphonic	288	—	—	—	131
Naphthalene-1 : 4-disulphonic	273	—	179	—	—
Naphthalene-1 : 5-disulphonic	310	257	249	332	183
Naphthalene-1 : 6-disulphonic	298	235	—	315	129
Naphthalene-2 : 6-disulphonic	305	256	—	360	225
Naphthalene-2 : 7-disulphonic	243	211	—	300	159
2-Naphthylamine-4 : 8-disulphonic	—	210	—	—	—
2-Naphthylamine-5 : 8-disulphonic	—	276	—	—	—
2-Naphthylamine-6 : 7-disulphonic	—	—	—	—	—

TABLE IV,33. SULPHONIC ACIDS (*continued*)

Acid	Sulphonamide $ArSO_2NH_2$	S-Benzyl-*iso*-thiuronium Salt	Sulphonanilide $ArSO_2NHPh$	*p*-Toluidine Salt	Sulphonyl Chloride, $ArSO_2Cl$
1-Naphthylamine-3 : 6-disulphonic	—	—	—	—	—
1-Naphthylamine-3 : 8-disulphonic	—	—	—	—	—
1-Naphthol-3 : 6-disulphonic .	—	217°	—	—	—
1-Naphthol-4 : 8-disulphonic .	—	205	—	—	—
2-Naphthol-3 : 6-disulphonic .	—	233	202°	—	—
2-Naphthol-6 : 8-disulphonic .	—	228	195	—	162°
d-Camphorsulphonic . . .	132°	210	—	—	88

ALIPHATIC SULPHONIC ACIDS

Sulphonic Acid	B.P.	Sulphonyl chloride, b.p.	Sulphonamide, m.p.	*S*-Benzyl-*iso*-thiuronium salt, m.p.	Sulphonanilide, m.p.
Methane . .	167°/10	163°	90°	—	99°
Ethane . .	—	177	59	115°	58
2-Propane . .	—	79°/18	60	—	84
1-Propane . .	—	78°/13	52	—	—
1-Butane . .	—	75°/10	45	—	—

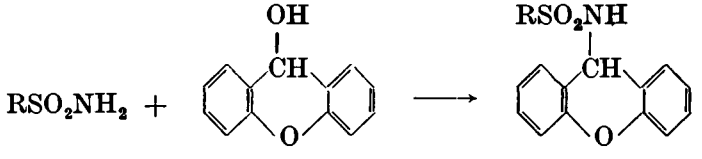
IV,33A. REACTIONS AND CHARACTERISATION OF AROMATIC SULPHONAMIDES

Sulphonamides are most readily identified by hydrolysis with concentrated hydrochloric acid or with 80 per cent. sulphuric acid (for experimental details, see Section **X,7,*12***) :

$$RSO_2NHR' + HCl + H_2O \longrightarrow RSO_3H + R'NH_2,HCl$$
$$RSO_2NR'R'' + HCl + H_2O \longrightarrow RSO_3H + R'R''NH,HCl$$

The amine is removed by the addition of alkali and characterised by a suitable derivative ; the sulphonic acid may then be recovered as the sodium salt and converted into a crystalline derivative, ***e.g.***, the S-benzyl-*iso*-thiuronium salt.

Primary sulphonamides RSO_2NH_2 may be most simply characterised by condensation with xanthhydrol to yield the corresponding ***N*-xanthylsulphonamides** :



The best results are obtained with freshly prepared xanthhydrol (reduction of xanthone with sodium amalgam, Section **VII,16**). Dissolve 0·25 g. of xanthhydrol and 0·25 g. of the primary sulphonamide in 10 ml. of glacial acetic acid. Shake for 2–3 minutes at the laboratory temperature and allow to stand for 60–90 minutes. Filter off the derivative, recrystallise it from dioxan-water (3 : 1), and dry at room temperature under water pump suction for 30 minutes.

The melting points of a number of *N*-xanthylsulphonamides are collected in Table **IV,33A.**

TABLE IV,33A. AROMATIC SULPHONAMIDES

Sulphonamide	M.P.	*N*-Xanthylsulphonamide
Benzene-	153°	200°
Toluene-*o*-	156	183
Toluene-*p*-	137	197
Benzene-1 : 3-di-	229	170
p-Ethylbenzene-	110	196
2 : 4-Dimethylbenzene-	137	188
2 : 5-Dimethylbenzene-	147	176
2 : 4 : 6-Trimethylbenzene-(mesityl-)	142	203
p-Aminobenzene- (sulphanilamide)	165	208
Saccharin	224	198

Sulphonamides may also be characterised as **sulphonacetamides** : for experimental details, see Section **IV,33,*3***.

AROMATIC AMINES AND THEIR SIMPLE DERIVATIVES

AROMATIC AMINES

Aromatic amines may be divided into three classes :—

(i) **Primary amines** : (*a*) purely aromatic with the amino group directly attached to the aromatic ring, *e.g.*, aniline $C_6H_5NH_2$, and (*b*) with the NH_2 group in the side chain, *e.g.*, benzylamine $C_6H_5CH_2NH_2$. The latter possesses properties similar to those of aliphatic amines (Section III,123).

(ii) **Secondary amines** : (*a*) purely aromatic amines, *e.g.*, diphenylamine $(C_6H_5)_2NH$, and (*b*) aromatic - aliphatic amines, *e.g.*, monomethylaniline $C_6H_5NHCH_3$.

(iii) **Tertiary amines** : (*a*) purely aromatic amines, *e.g.*, triphenylamine $(C_6H_5)_3N$, and (*b*) aromatic - aliphatic amines, *e.g.*, dimethylaniline $C_6H_5N(CH_3)_2$.

Arylamines are generally prepared by the reduction of nitro compounds. When only small quantities are to be reduced and the time element is important and cost is a secondary consideration, tin and hydrochloric acid may be employed, for example :

$$C_6H_5NO_2 + 6H \longrightarrow C_6H_5NH_2 + 2H_2O$$

The various stages in the reduction may be represented as follows :

$$Sn + 2HCl \longrightarrow SnCl_2 + 2H;$$

stannous chloride is itself an excellent reducing agent :

$$SnCl_2 + 2HCl \longrightarrow SnCl_4 + 2H$$

i.e., $Sn \equiv 4H$; this must be borne in mind when calculating the quantities required for the reaction. The stannic chloride forms the complex chlorostannic acid with hydrochloric acid, which combines with the aniline produced in the reaction :

$$SnCl_4 + 2HCl \longrightarrow H_2[SnCl_6] \xrightarrow{2C_6H_5NH_2} (C_6H_5NH_3)_2[SnCl_6]$$

With a large excess of sodium hydroxide solution, the salt complex is decomposed and the free amine is liberated :

$$(C_6H_5NH_3)_2[SnCl_6] + 8NaOH \longrightarrow 2C_6H_5NH_2 + Na_2SnO_3 + 6NaCl + 5H_2O$$

On the technical scale, the cheaper iron and hydrochloric acid is employed as the reducing agent :

$$C_6H_5NO_2 + 2Fe + 6HCl \longrightarrow C_6H_5NH_2 + 2FeCl_3 + 2H_2O$$

or

$$C_6H_5NO_2 + 3Fe + 6HCl \longrightarrow C_6H_5NH_2 + 3FeCl_2 + 2H_2O$$

In practice, however, the amount of hydrochloric acid employed is less than 5 per cent. of the amounts indicated by either of the above equations. Various explanations have been advanced to account for this ; one is that the following reaction is catalysed by acid or by hydroxonium ions :

$$C_6H_5NO_2 + 2Fe + 4H_2O \xrightarrow{H_3O^+} C_6H_5NH_2 + 2Fe(OH)_3$$

Benzylamine may be obtained by the **Gabriel synthesis,** which depends upon the use of potassium phthalimide. The latter upon heating with benzyl

the other end. If the holes are carefully aligned, a clean cut hole is obtained. Experienced laboratory workers frequently complete the whole boring operation from one side, but beginners usually tear the edges of the cork by this method, which is therefore not recommended. A well-fitting cork should slide over the tube (side arm of distilling flask, thermometer, lower end of condenser, etc.) which is to pass through it with only very moderate pressure. The bored cork should be tested for size; if it is too small, the hole should be enlarged to the desired diameter with a small round file. When the correct size is obtained, the tube is held near the end and inserted into the cork. The tube is then grasped *near* the cork and cautiously worked in by gentle twisting. Under no circumstances should the tube be held too far from the cork nor should one attempt to force a tube through too small an opening in a cork; neglect of these apparently obvious precautions may result in a severe cut in the hand from the breaking of the glass tube.

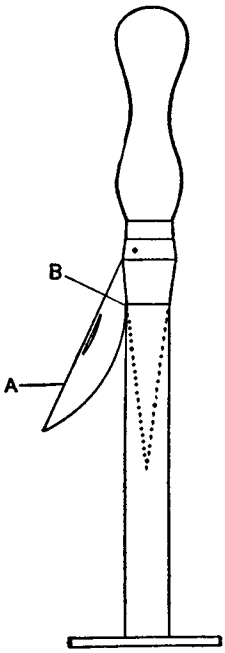


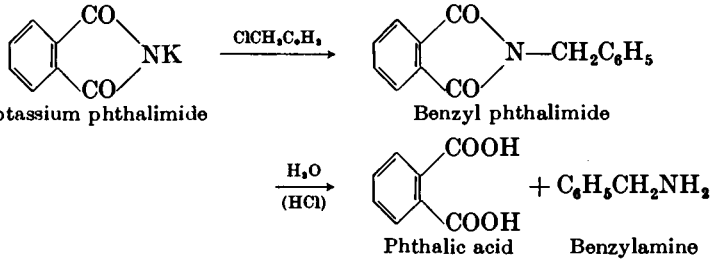
Fig. *II*, *3*, 3.

For consistently successful results in cork boring, a sharp cork borer must be used. The sharpening operation will be obvious from Fig. *II*, *3*, 3. The borer is pressed gently against the metal cone, whilst slight pressure is applied with the "cutter" *A* at *B*; upon slowly rotating the borer a good cutting edge will be obtained. If too great pressure is applied either to the borer or to the "cutter," the result will be unsatisfactory and the cutting circle of the borer may be damaged. To maintain a cork borer in good condition, it should be sharpened every second or third time it is used.

Rubber stoppers are frequently employed in the laboratory in "vacuum distillation" assemblies (compare Section **II,19**); for distillations under atmospheric pressure bark corks are generally used. Many organic liquids and vapours dissolve new rubber stoppers slightly and cause them to swell. In practice, it is found that rubber stoppers which have been previously used on one or two occasions are not appreciably attacked by most organic solvents, owing presumably to the formation of a resistant surface coating. **To bore a rubber stopper,** it is essential to employ a very sharp cork borer of the same size as the tube to be inserted into the hole. The borer is lubricated with a little glycerine (Fig. *II*, *3*, 2) and steadily rotated under only very slight pressure. The operation requires a good deal of patience and time and frequent lubrication may be necessary; if too much pressure be exerted on the borer, a hole of irregular shape and diminishing size will result.

The insertion of a glass tube into a rubber stopper or into rubber tubing is greatly facilitated by moistening the rubber with a little glycerine. After some use rubber may stick to glass and great care must be taken not to break the glass tube when removing it. Frequently the exertion of gentle pressure on the rubber stopper by means of the two thumbs whilst the end of the tube (or thermometer) rests vertically on

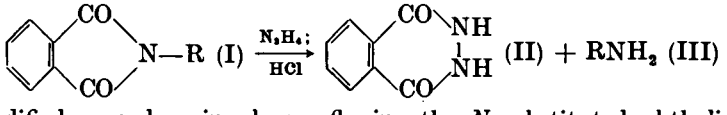
chloride at 180–190° yields benzyl phthalimide, which may be hydrolysed by fuming hydrochloric acid at 200° to phthalic acid and benzylamine:



Potassium phthalimide — Benzyl phthalimide

Phthalic acid — Benzylamine

The independent preparation of potassium phthalimide (from a solution of phthalimide in absolute ethanol and potassium hydroxide in 75 per cent. ethanol) may be avoided in many cases by boiling phthalimide with the halide in the presence of anhydrous potassium carbonate. The *N*-substituted phthalimide (I) is frequently cleaved with difficulty: this is often facilitated by reaction with hydrazine hydrate to give an intermediate product, which is easily decomposed by hydrochloric acid to yield the insoluble hydrazide of phthalic acid (II) and the primary amine (III):



The modified procedure involves refluxing the *N*-substituted phthalimide in alcohol with an equivalent quantity of hydrazine hydrate, followed by removal of the alcohol and heating the residue with hydrochloric acid on a steam bath; the phthalyl hydrazide produced is filtered off, leaving the amine hydrochloride in solution. The Gabriel synthesis has been employed in the preparation of a wide variety of amino compounds, including aliphatic amines and amino acids: it provides an unequivocal synthesis of a pure primary amine.

β-Phenylethylamine is conveniently prepared by the hydrogenation under pressure of benzyl cyanide with Raney nickel catalyst (see Section **VI,5**) in the presence of either a saturated solution of dry ammonia in anhydrous methyl alcohol or of liquid ammonia; the latter are added to suppress the formation of the secondary amine, di-β-phenylethylamine:

$$\underset{\text{Benzyl cyanide}}{C_6H_5CH_2CN} \xrightarrow[120°]{H_2,\ \text{Raney Ni}} \underset{\beta\text{-Phenylethylamine}}{C_6H_5CH_2CH_2NH_2} + \underset{\text{Di-}\beta\text{-phenylethylamine}}{(C_6H_5CH_2CH_2)_2NH}$$

α-Phenylethylamine may be obtained by a general method applicable to the synthesis of compounds having an amino group in the alkyl side chain from acyl derivatives of aromatic hydrocarbons. Acetophenone is heated with excess of ammonium formate to form α-phenylethylformamide; this upon hydrolysis with hydrochloric acid yields α-phenylethylamine hydrochloride, from which the free base can be obtained by the action of aqueous sodium hydroxide:

$$\underset{\text{Acetophenone}}{C_6H_5COCH_3} + 2HCOONH_4 \longrightarrow \underset{\alpha\text{-Phenylethylformamide}}{C_6H_5CH(NHCHO)CH_3} + NH_3 + CO_2 + 2H_2O$$

$$C_6H_5CH(NHCHO)CH_3 + HCl + H_2O \longrightarrow \underset{\alpha\text{-Phenylethylamine hydrochloride}}{C_6H_5CH(NH_3Cl)CH_3} + HCOOH$$

$$C_6H_5CH(NH_3Cl)CH_3 + NaOH \longrightarrow \underset{\alpha\text{-Phenylethylamine}}{C_6H_5CH(NH_2)CH_3} + NaCl + H_2O$$

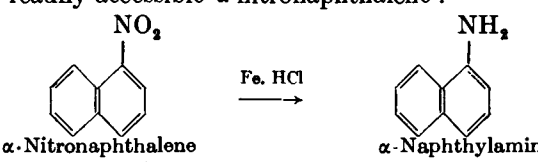
The conversion of an aldehyde or ketone into the corresponding amine by heating with ammonium formate or with formamide and formic acid at about

165-190° is generally termed the **Leuckart reaction.** The procedure has been satisfactorily applied to many aliphatic-aromatic, alicyclic and aliphatic-heterocyclic ketones, some aromatic ketones and aldehydes, and to some aliphatic aldehydes and ketones boiling at about 100° or higher. The method is superior to that involving the formation and reduction of aldoximes and ketoximes (compare Section **III,121**), particularly with compounds in which functional groups are present that are readily attacked by reducing agents, *e.g.*, in the preparation of amines from *p*-chloro-, *p*-bromo- and *p*-nitro-acetophenone. The reaction is an example of *reductive aminolysis* of aldehydes and ketones : an equivalent result is obtained by reduction of a mixture of an aldehyde or ketone and ammonia in ethanol in the presence of Raney nickel under pressure.

$$RCHO + NH_3 \rightleftharpoons RCH(OH)NH_2 \xrightarrow[(Ni)]{H_2} RCH_2NH_2 + H_2O$$

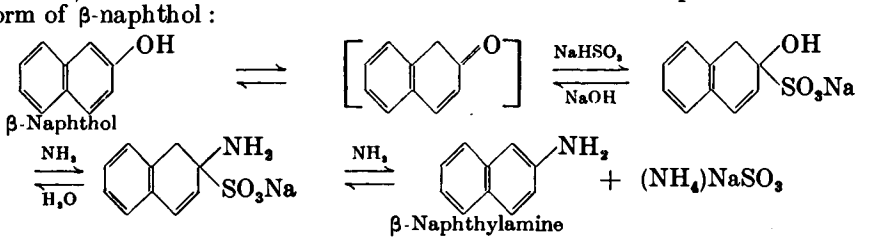
$$RCH(OH)NH_2 \xrightleftharpoons{-H_2O} RCH{=}NH \xrightarrow[(Ni)]{H_2} RCH_2NH_2$$

In the naphthalene series, **α-naphthylamine** is easily obtained by the reduction of the readily accessible α-nitronaphthalene :



α-Nitronaphthalene α-Naphthylamine

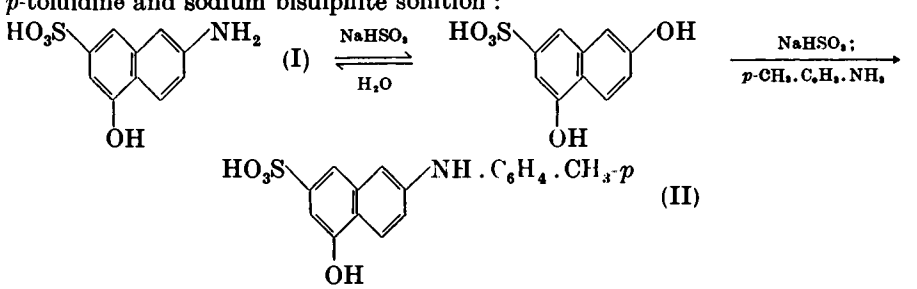
β-Nitronaphthalene is not formed by direct nitration. For the preparation of β-naphthylamine, the **Bucherer reaction** may be applied to β-naphthol, *i.e.*, by heating with ammoniacal ammonium sulphite solution at 150° (under pressure). The reaction involves the addition of the bisulphite to the keto form of β-naphthol :



β-Naphthylamine

The amination reaction is reversible ; thus β-naphthylamine can be reconverted into β-naphthol by heating with aqueous sodium bisulphite solution, then adding alkali and boiling until all the ammonia is expelled.

The reversibility of the Bucherer reaction is utilised in the preparation of 2-*p*-tolylamino-5-hydroxynaphthalene-7-sulphonic acid (II) from 2-amino-5-hydroxynaphthalene-7-sulphonic acid or " J " acid (I) by heating with *p*-toluidine and sodium bisulphite solution :



CAUTION : Attention is drawn to the carcinogenic properties (leading to papilloma of the bladder) of β-naphthylamine and to a much smaller degree of α-naphthylamine and of benzidine. In consequence, the manufacture of β-naphthylamine has ceased altogether in Great Britain. Great care should therefore be taken in the preparation and handling of β-naphthylamine, by the use of rubber gloves and by conducting all operations in a fume cupboard provided with a powerful exhaust system.

Secondary and tertiary amines are not generally prepared in the laboratory. On the technical scale **methylaniline** is prepared by heating a mixture of aniline hydrochloride (55 parts) and methyl alcohol (16 parts) at 120° in an autoclave. For **dimethylaniline**, aniline and methyl alcohol are mixed in the proportion of 80 : 78, 8 parts of concentrated sulphuric acid are added and the mixture heated in an autoclave at 230–235° and a pressure of 25-30 atmospheres. Ethyl- and diethyl-aniline are prepared similarly. One method of isolating pure methyl- or ethyl-aniline from the commercial product consists in converting it into the *N*-nitroso derivative with nitrous acid, followed by reduction of the nitroso compound with tin and hydrochloric acid :

$$\underset{\text{Methylaniline}}{C_6H_5NHCH_3} + NaNO_2 + HCl \longrightarrow \underset{N\text{-nitroso-methylaniline}}{C_6H_5N(NO)CH_3} + NaCl + H_2O$$

$$C_6H_5N(NO)CH_3 + 6H \xrightarrow[HCl]{Sn,} C_6H_5NHCH_3 + NH_3 + H_2O$$

Commercial dialkyl-anilines may be purified by refluxing with an excess of acetic anhydride : any unchanged aniline and monoalkyl-aniline are converted into the difficultly-volatile acetyl derivatives :

$$\underset{\text{Aniline}}{C_6H_5NH_2} + (CH_3CO)_2O \longrightarrow \underset{\text{Acetanilide}}{C_6H_5NHCOCH_3} + CH_3COOH$$

$$\underset{\text{Methylaniline}}{C_6H_5NHCH_3} + (CH_3CO)_2O \longrightarrow \underset{\text{Acetyl-methylaniline}}{C_6H_5N(COCH_3)CH_3} + CH_3COOH$$

Upon fractionation, the acetic acid and acetic anhydride pass over first, followed by the pure dialkyl-aniline.

A convenient method for preparing pure ***NN*-dialkyl anilines and substituted anilines** directly from the corresponding amines consists in heating the latter with trialkyl orthophosphates :

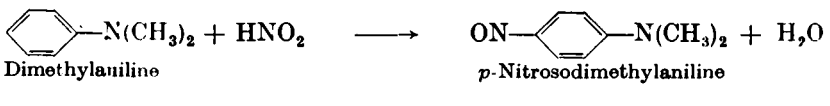
$$3ArNH_2 + 2(RO)_3PO \longrightarrow 3ArNR_2 + 2H_3PO_4$$

Thus good yields (> 60 per cent) are obtained with aniline and methyl, ethyl, *n*-propyl and *n*-butyl phosphates ; with α- and β-naphthylamine and methyl or ethyl phosphate ; nuclear substituted anilines and methyl or ethyl phosphate.

The nitroso compound (**diphenylnitrosamine**) of the purely aromatic secondary amine diphenylamine is a crystalline solid, and therefore provides an interesting preparation eminently suitable for students :

$$\underset{\text{Diphenylamine}}{(C_6H_5)_2NH} + HNO_2 \longrightarrow \underset{\text{Diphenylnitrosamine}}{(C_6H_5)_2N(NO)} + H_2O$$

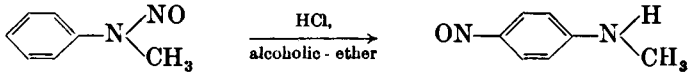
Tertiary aliphatic - aromatic amines, unlike those of the aliphatic series, react with nitrous acid with the formation of *C*-nitroso compounds; the nitroso group enters almost exclusively in the *para* position if available, otherwise in the *ortho* position. Thus dimethylaniline yields ***p*-nitrosodimethylaniline** :



Dimethylaniline — *p*-Nitrosodimethylaniline

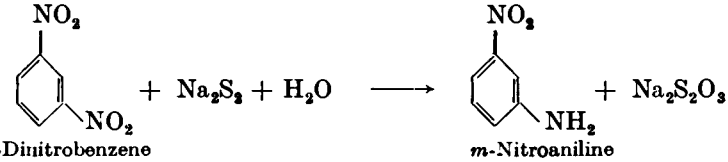
It is interesting to observe that the hydrochloride is yellow, whereas the free base is a green crystalline compound.

***N*-Nitrosomethylaniline** undergoes an interesting molecular rearrangement in ether-alcoholic solution under the catalytic influence of hydrogen chloride. The substance rearranges to ***p*-nitroso-*N*-methylaniline** which separates as the hydrochloride; this involves the migration of the nitroso group from the side chain to the *p*-position (compare *Sulphanilic Acid*, Section **IV,55**):



N-Nitroso-*N*-methylaniline — *p*-Nitroso-*N*-methylaniline

It is convenient to include under *Aromatic Amines* the preparation of ***m*-nitroaniline** as an example of the selective reduction of one group in a polynitro compound. When *m*-dinitrobenzene is allowed to react with sodium polysulphide (or ammonium sulphide) solution, only one of the nitro groups is reduced and *m*-nitroaniline results. Some sulphur separates, but the main reaction is represented by:



m-Dinitrobenzene — *m*-Nitroaniline

IV,34. ANILINE

Method A. **Reduction with tin and hydrochloric acid.** Into a 500-ml. round-bottomed flask equipped with a reflux condenser, place 25 g. (21 ml.) of nitrobenzene and 45 g. of granulated tin. Measure out 100 ml. of concentrated hydrochloric acid. Pour about 15 ml. of this acid down the condenser and shake the contents of the flask steadily. The mixture becomes warm and before long the reaction should be quite vigorous; if it boils very vigorously, moderate the reduction somewhat by temporarily immersing the flask in cold water. When the initial reaction slackens of its own accord, pour another 15 ml. of hydrochloric acid down the condenser, shake the flask steadily to ensure thorough mixing, and cool again if the reduction becomes too violent. Do not cool more than is necessary to keep the reaction under control; keep the mixture well shaken. Proceed in this way until all the 100 ml. of acid has been added. Finally heat the mixture on a boiling water bath for 30–60 minutes, *i.e.*, until the odour of nitrobenzene is no longer perceptible and a few drops of the reaction mixture when diluted with water yield a perfectly clear solution. During the course of the reduction, particularly during the cooling, the complex of aniline hydrochloride and stannic chloride may separate as a white or yellow crystalline solid.

Cool the reaction mixture to room temperature and add gradually a solution of 75 g. of sodium hydroxide in 125 ml. of water; if the mixture boils during the addition of the alkali, cool again. The hydroxide of tin which is first precipitated should all dissolve and the solution should be strongly alkaline: the aniline separates as an oil. Equip the flask for steam distillation as in Fig. *II*, *40*, 1, and pass steam into the warm

mixture until, after the distillate has ceased to pass over as a turbid liquid, a *further* 120 ml. of clear liquid are collected. Since aniline is appreciably soluble (*ca.* 3 per cent.) in water, it must be " salted out " by saturating the distillate with salt. Use about 20 g. of commercial salt for each 100 ml. of liquid. Transfer the distillate, saturated with salt, to a separatory funnel, add about 40 ml. of ether, and shake to ensure intimate mixing of the solution and the ether ; relieve the pressure within the funnel by momentarily lifting the stopper. [All flames in the vicinity must be extinguished during the extraction.] Allow the two layers to separate ; run off the lower aqueous layer into a beaker, and pour the remaining ethereal layer through the mouth of the funnel into a 200 ml. flask. Return the aqueous solution to the funnel and extract with a further 40 ml. of ether. Proceed as before, and pour the ethereal extract into the flask. Dry the combined ethereal solutions with a few grams of anhydrous potassium carbonate (1) : shake the well-stoppered flask for several minutes. Alternatively, conduct the drying operation in a separatory funnel ; stand a beaker beneath the funnel to collect the solution should the stopcock accidentally fall out or leak.

Remove the ether with the aid of the apparatus shown in Fig. *II, 13,* 4 ; the distilling flask should have a capacity of 50–75 ml. and the solution should first be filtered through a small fluted filter paper. Remember to place 2–3 fragments of porous porcelain in the flask. Since ether is extremely volatile and also highly inflammable, the flask must be heated in a beaker or bath of warm water ; the water should be warmed in another part of the laboratory. Before commencing the distillation, read Section **II,13** (on the method of using the apparatus of Fig. *II, 13,* 4) and also Section **II,14** (fire hazards attending the distillation of inflammable solvents). When all the ethereal solution has been introduced into the flask and no more ether distils on a boiling water bath, detach the Buchner flask receiver and pour the ether into the ETHER RESIDUES bottle. Run out the water from the condenser, have two small conical flasks available as receivers, and distil the aniline either by direct heating over a wire gauze or, preferably, using an air bath (Fig. *II, 5,* 3). A small quantity of ether may pass over during the early part of the distillation ; it is therefore advisable to interpose an asbestos or uralite board between the receiver and the flame. Collect the fraction b.p. 180–184° in a weighed conical flask. The yield of aniline is 18 g.

Pure aniline has a b.p. of 184°. When freshly distilled it is a colourless liquid, but becomes discoloured on standing, particularly when exposed to light owing to atmospheric oxidation. The colour may usually be removed by distillation from a little zinc dust.

Note.

(1) Calcium chloride cannot be used to dry the ethereal solution because it combines with aniline (and other amines) to form molecular compounds. The best drying agent is sodium or potassium hydroxide (pellet form).

Method B. **Reduction with iron and hydrochloric acid.** Place 40 ml. of water and 30 g. of grease-free iron filings (1) in a 750- or 1,000-ml. round-bottomed flask, and 25 g. (21 ml.) of nitrobenzene in a small beaker or conical flask. Warm the former on a water bath at about 60°. Add

1 ml. of nitrobenzene and 2·5 ml. of concentrated hydrochloric acid, and shake well; the temperature will rise appreciably. In the subsequent reduction maintain the temperature inside the flask at 80–90° by alternate heating on a water bath or cooling the flask in running water as may be found necessary. Add the nitrobenzene 1–2 ml. at a time over a period of 20–30 minutes. Test for completeness of the reaction (when the smell of nitrobenzene can no longer be detected at the mouth of the flask) by removing a small portion and diluting with dilute hydrochloric acid; the odour of nitrobenzene should be absent and a clear solution should be formed. (If nitrobenzene is present, warm on a water bath under reflux and with frequent shaking until the reduction is complete.) Render the reaction mixture alkaline by the cautious addition of 5 g. of anhydrous sodium carbonate, and steam distil (Fig. *II*, *40*, 1) until the steam distillate is no longer turbid and a further 100 ml. of clear liquid passes over. Measure the total volume of the distillate, transfer it to a separatory funnel, add 20 g. of commercial salt for each 100 ml. of liquid present and shake vigorously until the salt dissolves. The aniline may be isolated, if desired, by ether extraction as in *Method 1*. An alternative procedure is to carefully separate the upper layer and pour it into a 50 or 75 ml, distillation flask. Use the assembly shown in Fig. *II*, *12*, 1 and heat the flask either on a wire gauze or in an air bath (Fig. *II*, *5*, 3). A little water passes over first; collect this separately. When aniline commences to distil, stop the distillation. Run out the water from the condenser, dry out the inner tube, and continue the distillation. Collect the aniline at 180–184° (2). The yield is 18 g.

Notes.

(1) Commercial "Iron filings, grease free" are quite satisfactory. If fine iron filings are used, they should be washed with ether and dried in the air.

(2) If the presence of unreduced nitrobenzene is suspected (odour and/or high b.p. residue), treat all the product with excess of dilute hydrochloric acid and remove the nitrobenzene either by steam distillation or by ether extraction; render the residue alkaline with sodium hydroxide solution and isolate the aniline as before.

Cognate Preparations

***p*-Toluidine** ($NH_2C_6H_4CH_3$ 1 : 4). Reduce *p*-nitrotoluene with tin and hydrochloric acid and isolate the amine by ether extraction. Since *p*-toluidine is a solid (m.p. 45°; b.p. 200°), it may crystallise in the condenser used for steam distillation: it is easily melted by stopping the current of cooling water in the condenser for a moment or two.

o-Chloroaniline. The vapours of *o*-chloroaniline are toxic and produce serious after-effects: the preparation must therefore be conducted in a fume cupboard. In a 2-litre three-necked flask, equipped with a mechanical stirrer, a reflux condenser and a glass funnel, the hole of which is plugged by means of a glass rod covered with a rubber tube, place 480 g. of iron filings and 360 ml. of water. Heat the mixture on a boiling water bath and, when hot, remove the water bath. While stirring vigorously, add 40 g. of *o*-chloronitrobenzene through the funnel and at the same time introduce 10 ml. of concentrated hydrochloric acid by means of a separatory funnel fitted into the top of the condenser with a grooved

cork. A vigorous reaction commences as soon as the acid has been added. Then introduce 200 g. of melted *o*-chloronitrobenzene through the funnel all at once. After about 10 minutes, add 50 ml. of concentrated hydrochloric acid, as before, at such a rate (about 15-20 minutes) that vapours of *o*-chloroaniline do not escape from the top of the condenser. Heat on a water bath, with stirring, for 1 hour in order to complete the reaction. Then add a solution of 20 g. of sodium hydroxide in 40 ml. of water to decompose any chloroaniline hydrochloride that might have formed. Filter the reaction mixture whilst still hot ; separate the lower layer of the filtrate (*o*-chloroaniline) from the water layer. Return the iron residues to the flask and boil with 200 ml. of benzene : filter the hot benzene solution through the same funnel and wash the iron residues with a second 200 ml. of hot benzene. Combine the benzene extracts with the *o*-chloroaniline originally separated from the water, dry with anhydrous magnesium sulphate, and remove most of the benzene under normal pressure. Transfer the residue (*CAUTION :* the vapours are toxic) to a 400 ml. Claisen flask and distil under reduced pressure Fig. *II*, *20*, 1) : some benzene passes over first, followed by *o*-chloroaniline at 113-117°/20 mm. The yield is 185 g. The *o*-chloroaniline may also be distilled under ordinary pressure without decomposition : b.p. 206-209°.

$$o\text{-}ClC_6H_4NO_2 \xrightarrow{Fe,\ H_2O} o\text{-}ClC_6H_4NH_2$$

***p*-Chloroaniline** may be similarly prepared from *p*-chloronitrobenzene ; 240 g. of the latter give 185 g. of *p*-chloroaniline, b.p. 128-131°/20 mm., m.p. 71°.

IV,35. β-PHENYLETHYLAMINE

Saturate commercial absolute methyl alcohol with ammonia (derived from a cylinder) at 0° ; the resulting solution is *ca.* 10*N*. Dissolve 58 g. of benzyl cyanide (Section **IV,147**) (1) in 300 ml. of the cold methyl alcoholic ammonia, and place the solution in a high pressure hydrogenation bomb (Section **VI,4**) ; add 10 ml. of settled Raney nickel catalyst (Section **VI,5**), securely fasten the cap and introduce hydrogen until the pressure is 500-1000 lb. Shake the bomb or set the mechanical stirring device in motion, and heat at 100-125° until absorption of hydrogen ceases (about 2 hours). Allow the bomb to cool, open it, and remove the contents. Rinse the bomb with two 100 ml. portions of anhydrous methyl alcohol and pour the combined liquids through a fluted filter paper to remove the catalyst ; do not permit the catalyst to become dry since it is likely to ignite. Remove the solvent and ammonia by distillation (fume cupboard !), and fractionate the residue through a short column or from a Claisen flask with fractionating side arm (Figs. *II*, *24*, 2-5). Collect the β-phenylethylamine at 92-93°/18 mm. The yield is 54 g. The purity can be checked by conversion into the hydrochloride, m.p. 218-219°.

Note.

(1) Minute amounts of halide have a powerful poisoning effect upon the catalyst ; it is advisable to distil the benzyl cyanide from Raney nickel.

IV,36. α-PHENYLETHYLAMINE

Place 125 g. of ammonium formate, 75 g. of acetophenone (Section **IV, 136**) and a few chips of porous porcelain in a 250 ml. Claisen flask with fractionating side arm (Figs. *II, 24,* 2–5) ; insert a cork carrying a thermometer extending nearly to the bottom of the flask, and attach a short condenser set for downward distillation to the side arm. Heat the flask with a small flame or in an air bath ; the mixture first melts to two layers and distillation occurs. The mixture becomes homogeneous at 150–155° and reaction takes place with slight frothing. Continue the heating, more slowly if necessary, until the temperature rises to 185° (about 2 hours) ; acetophenone, water and ammonium carbonate distil. Stop the heating at 185°, separate the upper layer of acetophenone from the distillate, and return it without drying to the flask. Heat the mixture for 3 hours at 180–185° and then allow to cool ; the acetophenone may be recovered from the distillate by extraction with 20 ml. of benzene (1). Transfer the reaction mixture to a 250 ml. separatory funnel and shake it with 100 ml. of water to remove formamide and ammonium formate. Run off the crude α-phenylethylformamide into the original Claisen flask ; extract the aqueous layer with two 15 ml. portions of benzene, transfer the benzene extracts to the flask, add 75 ml. of concentrated hydrochloric acid and a few chips of porous porcelain. Heat the mixture cautiously until about 30 ml. of benzene are collected, and boil gently for a further 40 minutes ; hydrolysis proceeds rapidly to alpha-phenylethylamine hydrochloride except for a small layer of unchanged acetophenone. Allow the reaction mixture to cool, remove the acetophenone by extraction with 25 ml. of benzene and then with three 15 ml. portions of the solvent (1). Transfer the aqueous acid solution to a 500-ml. round-bottomed flask equipped for steam distillation, cautiously add a solution of 62·5 g. of sodium hydroxide in 125 ml. of water, and steam distil : heat the distillation flask so that the volume remains nearly constant. Most of the amine is contained in the first 500 ml. of distillate ; stop the operation when the distillate is only faintly alkaline. Discard the residue in the flask which contains *inter alia* a little di-(α-phenylethyl)-amine. Extract the distillate with five 25 ml. portions of benzene, dry the extract with sodium hydroxide pellets, and distil off the benzene (Fig. *II, 13,* 4) but use a flask having an inset side arm (compare Fig. *II, 1, 3, d*) * and a soda lime guard tube) ; the amine attacks cork and rubber and absorbs carbon dioxide from the air. Collect the α-phenylethylamine at 184–186° (2). The yield is 45 g.

Notes.

(1) The acetophenone may be recovered by washing the benzene solution with dilute alkali, drying with anhydrous magnesium sulphate and distilling ; the fraction b.p. 198–205° is collected.

(2) The b.p. under diminished pressure has been given as 80–81°/18 mm. To obtain a very pure sample of the amine, dissolve 1 part (by weight) of the above product with a solution of 1·04 parts of crystallised oxalic acid in 8 parts of hot water, add a little decolourising carbon, and filter. The filtered solution deposits crystals of the acid oxalate ; about 5 g. of this salt remains in each 100 ml. of

* An all-glass apparatus is the most satisfactory (compare Sections II,54 *et seq.*).

mother liquor, but most can be recovered by evaporation and further crystallisation. The amine may be liberated from the pure acid oxalate with sodium or potassium hydroxide, steam distillation, and purification as described above. The salt provides a convenient method of obtaining a known weight of the amine in water, since it can be weighed out and decomposed with alkali hydroxide.

IV,37. α-NAPHTHYLAMINE

Into a 3-litre round-bottomed flask place 80 g. of grease-free iron filings, 80 ml. of water and 4 ml. of concentrated hydrochloric acid, and warm the mixture to about 50°. Add 60 g. of α-nitronaphthalene (Section **IV,11**) in small portions at a time, and shake the flask vigorously after each addition. Maintain the temperature throughout the reduction at 70–80°. Follow the experimental details given in Section **IV,34.** The reduction is complete when a test sample is completely soluble in dilute hydrochloric acid. Render the reaction mixture alkaline by the addition of a little sodium carbonate. Add water and filter with suction on a Buchner funnel; wash with a little water, press well, and dry the iron residue containing the naphthylamine in the air (1). Transfer to a distilling or Claisen flask, and distil under reduced pressure until the distillate is highly coloured; use the apparatus depicted in Fig. *II, 19,* 1 or in Fig. *II, 19,* 3–4. The α-naphthylamine solidifies on cooling; it has m.p. 50°, b.p. 300°. The yield is 30 g.

Note.

(1) The α-naphthylamine may also be isolated directly from the neutralised reaction mixture by distillation with superheated steam (Section **I,6**).

IV,38. β-NAPHTHYLAMINE

Pass a stream of sulphur dioxide into 200 ml. of cooled, concentrated ammonia solution (sp. gr. 0·88) until 50 g. of gas have been absorbed. Place this ammonium sulphite solution together with 72 g. of β-naphthol (Section **IV,102**) in an autoclave (see Section **VI,4**) provided with a stirrer or shaking mechanism. Securely fasten the cap and heat at 150° with continual shaking or stirring for 8 hours: allow to cool with shaking or stirring. Remove the reaction mixture from the apparatus with the aid of about 250 ml. of water. Filter on a Buchner funnel. Dissolve the crude material in a boiling mixture of 75 ml. of concentrated hydrochloric acid and 200 ml. of water, and then dilute with 500 ml. of water. Add 5 g. of decolourising carbon, boil for 5 minutes, and filter through a hot water funnel from any undissolved dinaphthylamine ($C_{10}H_7NHC_{10}H_7$). Pour the hot filtrate with stirring into a solution of 60 g. of sodium hydroxide in 250 ml. of water. Make sure that the resulting slurry is alkaline to phenolphthalein; cool it with stirring to 20°, filter with suction, and wash with 1 litre of cold water. Press well. Dry the product to constant weight at 50–60°. The yield of β-naphthylamine, m.p. 111–112°, isolated as a light tan powder, is 68 g.

CAUTION. This compound has carcinogenic properties and great care should be taken to avoid all contact with it during its isolation and drying.

COGNATE PREPARATION

2-*p*-Tolylamino-5-hydroxynaphthalene-7-sulphonic acid. Reflux a mixture of 108 g. of pure *p*-toluidine, 108 g. of " J " acid (2-amino-5-hydroxynaphthalene-7-sulphonic acid), 84 g. of sodium bisulphite and 250 ml. of water for 30 hours in a 1500 ml. three-necked flask, equipped with a reflux condenser and mechanical stirrer. Add sodium carbonate until the mixture is alkaline and remove the excess of *p*-toluidine by steam distillation. Keep the residual solution in a refrigerator until crystallisation is complete, filter with suction on a Buchner funnel, and wash with 25 ml. of saturated sodium chloride solution. Dissolve the product in *ca.* 350 ml. of hot water to which sufficient hydrochloric acid is added to render the mixture acid to Congo red. Keep in a refrigerator until crystallisation is complete, filter with suction, wash with a little ice-cold hydrochloric acid, followed by a small volume of ice-cold water. Dry the residual 2-*p*-tolylamino-5-hydroxynaphthalene-7-sulphonic acid at 100° ; the yield is 95 g.

IV,39. BENZYLAMINE (*Gabriel Synthesis*)

Benzyl phthalimide. Grind together 53 g. of finely-powdered, anhydrous potassium carbonate and 147 g. of phthalimide (Section **IV,169**) in a glass mortar, transfer the mixture to a 750 ml. round-bottomed flask, and treat it with 252 g. (230 ml.) of redistilled benzyl chloride. Heat in an oil bath at 190° under a reflux condenser for 3 hours. Whilst the mixture is still hot, remove the excess of benzyl chloride by steam distillation. The benzyl phthalimide commences to crystallise near the end of the steam distillation. At this point, cool the mixture rapidly with vigorous stirring so that the solid is obtained in a fine state of division. Filter the solid with suction on a Buchner funnel, wash well with water and drain as completely as possible ; then wash once with 200 ml. of 60 per cent. ethanol and drain again. The yield of crude product, m.p. 100–110°, is 180 g. Recrystallise from glacial acetic acid to obtain pure benzyl phthalimide, m.p. 116° : the recovery is about 80 per cent.

Benzylamine. Warm an alcoholic suspension of 118·5 g. of finely-powdered benzyl phthalimide with 25 g. of 100 per cent. hydrazine hydrate (*CAUTION :* corrosive liquid) : a white, gelatinous precipitate is produced rapidly. Decompose the latter (when its formation appears complete) by heating with excess of hydrochloric acid on a steam bath. Collect the phthalyl hydrazide which separates by suction filtration, and wash it with a little water. Concentrate the filtrate by distillation to remove alcohol, cool, filter from the small amount of precipitated phthalyl hydrazide, render alkaline with excess of sodium hydroxide solution, and extract the liberated benzylamine with ether. Dry the ethereal solution with potassium hydroxide pellets, remove the solvent (compare Fig. *II, 13,* 4) on a water bath and finally distil the residue. Collect the benzylamine at 185–187° : the yield is 50 g.

COGNATE PREPARATION

β-Phenylethylamine. Prepare β-phenylethyl phthalimide as above by substituting β-phenylethyl bromide (Section **III,37**) for benzyl

chloride: recrystallise the crude product from glacial acetic acid; m.p. 131–132°. Convert it into β-phenylethylamine by treatment with hydrazine hydrate and hydrochloric acid as described for benzylamine. The yield of β-phenylethylamine, b.p. 200–205°, is about 95 per cent.

IV,40. PURE METHYLANILINE FROM COMMERCIAL METHYLANILINE

***N*-Nitrosomethylaniline (methylphenylnitrosamine).** Place 53·5 g. of pure commercial monomethylaniline, 72·5 ml. of concentrated hydrochloric acid and 200 g. of crushed ice in a 500 ml. beaker equipped with a mechanical stirrer. Support a separatory funnel with a long bent stem (as in Fig. *III*, *35*, 1) containing a solution of 36 g. of sodium nitrite in 125 ml. of water over the beaker. Stir the solution and run in the sodium nitrite solution during 10 minutes; do not allow the temperature to rise above 10° and add more ice if necessary. Continue the stirring for a further hour. Separate the oily layer, wash it once with 50 ml. of water, and dry it with anhydrous magnesium or calcium sulphate. Distil under reduced pressure from a 100 ml. Claisen flask. Collect the *N*-nitrosomethylaniline (a pale yellow liquid) at 120°/13 mm. The yield is about 65 g.

Reduction of *N*-nitrosomethylaniline. Into a 1 litre round-bottomed flask, fitted with a reflux condenser, place 39 g. of *N*-nitrosomethylaniline and 75 g. of granulated tin. Add 150 ml. of concentrated hydrochloric acid in portions of 25 ml. (compare Section **IV,34**); do not add the second portion until the vigorous action produced by the previous portion has subsided, *etc.* Heat the reaction mixture on a water bath for 45 minutes, and allow to cool. Add cautiously a solution of 135 g. of sodium hydroxide in 175 ml. of water, and steam distil (see Fig. *II*, *40*, 1); collect about 500 ml. of distillate. Saturate the solution with salt, separate the organic layer, extract the aqueous layer with 50 ml. of ether and combine the extract with the organic layer. Dry with anhydrous potassium carbonate, remove the ether on a water bath (compare Fig. *II*, *13*, 4), and distil the residual liquid using an air bath (Fig. *II*, *5*, 3). Collect the pure methylaniline at 193–194° as a colourless liquid. The yield is 23 g.

Cognate Preparations

Pure ethylaniline from commercial ethylaniline.

***N*-Nitrosoethylaniline (ethylphenylnitrosoamine).** Use 60·5 g. of pure commercial monoethylaniline, 72·5 ml. of concentrated hydrochloric acid and 200 g. of crushed ice: also 36 g. of sodium nitrite in 125 ml. of water. The yield of *N*-nitrosoethylaniline (a yellow liquid), b.p. 131°/20 mm., is about 65 g.

Reduction of *N*-nitrosoethylaniline. Employ 38 g. of *N*-nitrosoethylaniline, 75 g. of granulated tin and 150 ml. of concentrated hydrochloric acid. After all the acid has been added, heat on a water bath for 75 minutes and allow to cool. Treat the almost solid crystalline mass

with a solution of 135 g. of sodium hydroxide in 175 ml. of water with cooling of the flask in running water : steam distil until no more oily drops pass over (about 500 ml. of distillate). The distillate is first colourless, but gradually assumes a violet colour. Complete the preparation as for methylaniline. Collect the ethylaniline (a practically colourless liquid) at 202–203°. The yield is 24 g.

Note on the laboratory preparation of monoethylaniline. Although the laboratory preparation of monomethyl- or monoethyl-aniline is hardly worth while, the following experimental details may be useful to those who wish to prepare pure monoethylaniline directly from aniline. In a flask, fitted with a double surface reflux condenser, place 50 g. (49 ml.) of aniline and 65 g. of ethyl bromide, and boil gently for 2 hours or until the mixture has almost entirely solidified. Dissolve it in water and boil off the small quantity of unreacted ethyl bromide. Render the mixture alkaline with concentrated sodium hydroxide solution, extract the precipitated bases with three 50 ml. portions of ether, and distil off the ether. The residual oil contains aniline, mono- and di-ethylaniline. Dissolve it in excess of dilute hydrochloric acid (say, 100 ml. of concentrated acid and 400 ml. of water), cool in ice, and add with stirring a solution of 37 g. of sodium nitrite in 100 ml. of water ; do not allow the temperature to rise above 10°. This leads to the formation of a solution of phenyl diazonium chloride, of *N*-nitrosoethylaniline and of *p*-nitrosodiethylaniline. The nitrosoethylaniline separates as a dark coloured oil. Extract the oil with ether, distil off the ether, and reduce the nitrosoamine with tin and hydrochloric acid (see above). The yield of ethylaniline is 20 g.

Notes on the preparation of secondary alkylarylamines. The preparation of ***n*-propyl-, *iso*propyl- and *n*-butyl-anilines** can be conveniently carried out by heating the alkyl bromide with an excess (2·5-4 mols) of aniline for 6-12 hours. The tendency for the alkyl halide to yield the corresponding tertiary amine is thus repressed and the product consists almost entirely of the secondary amine and the excess of primary amine combined with the hydrogen bromide liberated in the reaction. The separation of the primary and secondary amines is easily accomplished by the addition of an excess of 50 per cent. zinc chloride solution : aniline and its homologues form sparingly soluble additive compounds of the type B_2ZnCl_2 whereas the alkylanilines do not react with zinc chloride in the presence of water. The excess of primary amine can be readily recovered by decomposing the zincichloride with sodium hydroxide solution followed by steam distillation or solvent extraction. The yield of secondary amine is about 70 per cent. of the theoretical.

The experimental details for **mono-*n*-propylaniline** are as follows. Reflux a mixture of 230 g. of aniline and 123 g. of *n*-propyl bromide for 8-10 hours. Allow to cool, render the mixture alkaline, and add a solution of 150 g. of zinc chloride in 150 g. of water. Cool the mixture and stir : after 12 hours, filter at the pump and drain well. Extract the thick paste several times with boiling light petroleum, b.p. 60-80° (it is best to use a Soxhlet apparatus), wash the combined extracts successively with water and dilute ammonia solution, and then dry over anhydrous potassium carbonate or anhydrous magnesium sulphate. Remove the solvent on a water bath, and distil the residue from a Claisen flask with fractionating side arm (well lagged). Collect the *n*-propylaniline at 218–220° ; the yield is 80 g. Treat the pasty solid zincichloride with an excess of sodium hydroxide solution and steam distil : 130 g. of pure aniline are recovered.

*iso*Propylaniline, b.p. 206-208°, and *n*-butylaniline, b.p. 235-237°, may be similarly prepared.

Pure dialkylanilines may be prepared by refluxing the monoalkylaniline (1 mol) with an alkyl bromide (2 mols) for 20–30 hours; the solid product is treated with excess of sodium hydroxide solution, the organic layer separated, dried and distilled. The excess of alkyl bromide passes over first, followed by the dialkylaniline. **Di-*n*-propylaniline**, b.p. 242–243°, and **di-*n*-butylaniline** b.p. 269–270°, are thus readily prepared.

Diphenylnitrosamine. Dissolve 8·5 g. of pure diphenylamine in 70 ml. of warm alcohol; also 4 g. of sodium nitrite in 6 ml. of water. Cool each solution in ice until the temperature falls to 5°. Add 6 ml. of concentrated hydrochloric acid slowly and with stirring to the diphenylamine solution, and immediately (otherwise diphenylamine hydrochloride may crystallise out) pour the sodium nitrite solution rapidly into the well-stirred mixture. The temperature soon rises to 20–25° and the diphenylnitrosamine crystallises out. Cool the mixture in ice water for 15–20 minutes, filter with suction on a Buchner funnel, wash with water to remove sodium chloride, and press well with a wide glass stopper. Recrystallise from methylated spirit (for details, see Section **IV,12**). The yield of pure diphenylnitrosamine (pale yellow crystals), m.p. 68°, is 8·5 g.

IV,41. BENZYLANILINE

. Equip a 500 ml. three-necked flask with a separatory funnel, a mechanical stirrer and a reflux condenser; mount the assembly on a water bath. Place 35 g. of pure sodium bicarbonate, 35 ml. of water and 124 g. (121 ml.) of aniline in the flask, and 42 g. (35 ml.) of freshly distilled benzyl chloride (b.p. 177–179°) in the separatory funnel protected by a calcium chloride (or cotton wool) guard tube. Heat the flask and contents to 90–95°, stir vigorously, and run in the benzyl chloride slowly (about 1 hour). Continue the heating and stirring for a further 3 hours. Allow to cool. Filter with suction, separate the organic layer from the filtrate and wash it with 25 ml. of saturated salt solution. Dry with anhydrous magnesium sulphate and filter again with suction. Distil from a Claisen flask with fractionating side arm (Figs. *II*, *24*, 2–5) under reduced pressure: aniline (about 80 g.) distils at 81°/12 mm. and the temperature rises rapidly. Collect the benzylaniline at 170–190°/12 mm. (most of it distils at 178–180°/12 mm.); this solidifies on cooling, melts at 34–36°, and is sufficiently pure for most purposes. The yield is 52 g. If required perfectly pure, it may be recrystallised from about 35 ml. of light petroleum, b.p. 60–80°; cool the solution in a freezing mixture to induce crystallisation, filter at the pump, wash with a little cold light petroleum, press and dry. The recrystallised benzylaniline has m.p. 36°.

$$C_6H_5CH_2Cl + C_6H_5NH_2 \longrightarrow C_6H_5CH_2NHC_6H_5 + HCl$$

IV,42 DIMETHYLANILINE

Place 28 g. (27·5 ml.) of pure aniline and 28 g. (23 ml.) of purified methyl phosphate in a 500 ml. round-bottomed flask equipped with a reflux condenser. Heat gently at first and remove the flame when the vigorous and exothermic reaction commences. When the latter subsides,

two layers are present ; heat under gentle reflux for two hours. Cool the mixture to about 50°, add a solution of 25 g. of sodium hydroxide in 100 ml. of water, reflux the mixture for 1 hour, then pour into a 600 ml. beaker and allow to cool to room temperature. Pour off the oily layer of amine from the solid sodium phosphate, add water to the latter and extract the aqueous solution with ether. Dry the combined oil and ether extract with anhydrous magnesium sulphate, distil off the ether, treat the residue with an equal volume of acetic anhydride and allow to stand overnight. (The acetic anhydride treatment will remove any mono-alkylaniline present.) Then add hydrochloric acid (20 ml. of the concentrated acid and 30 ml. of water), shake until the base dissolves, extract the solution with two 30 ml. portions of ether, and add 25 per cent. sodium hydroxide solution to the water layer to liberate the base. Collect the oil by extracting the mixture with ether, dry the ethereal solution with anhydrous magnesium sulphate, and remove the ether on a water bath. Distil the residue, using an air condenser, and collect the dimethylaniline at 192–193°. The yield is 28 g.

Cognate Preparations

Diethylaniline. Use 28 g. of pure aniline and 36 g. (34 ml.) of purified ethyl phosphate, and proceed exactly as described for dimethylaniline. The reaction is not so vigorous initially. Separation into two layers occurs after 30 to 90 minutes. The yield of diethylaniline, b.p. 215–216°, is 41–5 g.

Pure dimethylaniline from commercial dimethylaniline. Into a 250 ml. round-bottomed flask fitted with a reflux condenser place 50 g. (52·5 ml.) of a good commercial sample of dimethylaniline and 25 g. (23 ml.) of acetic anhydride. Heat under reflux for 3 hours, and allow to cool. Transfer to a 100 ml. Claisen flask equipped for distillation, and distil using a wire gauze or, better, an air bath (Fig. *II*, *5*, 3). Some acetic acid and the excess of acetic anhydride passes over first, followed by pure dimethylaniline (a colourless liquid) at 193–194°. There is a small dark residue in the flask. The yield depends upon the purity of the commercial sample, but is usually 30–40 g.

Pure diethylaniline from commercial diethylaniline. Use 50 g. (53·5 ml.) of a good commercial specimen of diethylaniline and 25 g. (23 ml.) of acetic anhydride, and reflux for 4 hours. Distil and collect the pure diethylaniline at 216–217° as a pale yellow liquid. The yield is 30–40 g.

IV,43. *p*-NITROSODIMETHYLANILINE

Dissolve 30 g. (31·5 ml.) of technical dimethylaniline in 105 ml. of concentrated hydrochloric acid contained in a 600 ml. beaker, and add finely-crushed ice until the temperature falls below 5°. Stir the contents of the beaker mechanically (or, less satisfactorily, with a thermometer) and slowly add (*ca.* 10 minutes) a solution of 18 g. of sodium nitrite in 30 ml. of water from a separatory funnel, the stem of which dips beneath the surface of the liquid. Maintain the temperature below 8° by the

addition of ice, if necessary. When all the nitrite solution has been added, allow the mixture to stand for 1 hour, filter the yellow crystalline *p*-nitrosodimethylaniline hydrochloride at the pump, wash it with 40 ml. of dilute hydrochloric acid (1 : 1), drain well, and finally wash with a little alcohol. The yield is good and depends upon the purity of the original dimethylaniline. If the pure hydrochloride is required, it may be recrystallised from hot water in the presence of a little dilute hydrochloric acid; yellow needles, m.p. 177°. Recrystallisation is, however, unnecessary if the free base is to be prepared.

Transfer 30 g. of the hydrochloride to a 500 ml. separatory funnel, add 100 ml. of water and shake until a thin paste of uniform consistency is obtained; add 10 per cent. aqueous sodium hydroxide solution in the cold with shaking until the whole mass has become bright green (the colour of the free base) and the mixture has an alkaline reaction. Extract the free base by shaking with two 60 ml. portions of benzene (1). Dry the combined benzene extracts with a little anhydrous potassium carbonate, and filter into a distilling flask fitted with a water condenser. Distil off about half of the benzene, and pour the residual hot benzene solution into a beaker. Upon cooling, the *p*-nitrosodimethylaniline crystallises in deep green leaflets. Filter these off and dry them in the air. The yield of *p*-nitrosodimethylaniline, m.p. 85°, from the hydrochloride is almost quantitative.

Note.

(1) The base is only slightly soluble in ether, thus rendering its use uneconomical. It may be extracted with chloroform and precipitated from the dried chloroform solution with carbon tetrachloride.

Cognate Preparation

***p*-Nitroso-*N*-methylaniline.** Dissolve 5 g. of *N*-nitrosomethylaniline (Section **IV,40**) in 10 ml. of anhydrous ether, and add 20 g. of a saturated solution of hydrogen chloride in absolute alcohol. Allow to stand. After some time a mass of crystalline needles of the hydrochloride of 4-nitroso-*N*-methylaniline separates. Filter with suction on a sintered glass funnel and wash with a mixture of alcohol and ether. Dissolve the solid in water and add a slight excess of sodium carbonate solution or dilute ammonia solution. Filter off the blue-green free base, and recrystallise it from benzene. The yield of *p*-nitroso-*N*-methylaniline, m.p. 118°, is 4·5 g.

IV,44. *m*-NITROANILINE

Prepare a solution of sodium polysulphide by dissolving 40 g. of crystallised sodium sulphide, $Na_2S.9H_2O$ (1), in 150 ml. of water, adding 10 g. of finely powdered sulphur, and warming until a clear solution is produced. Heat a mixture of 25 g. of *m*-dinitrobenzene (Section **IV,12**) and 200 ml. of water contained in a 1-litre beaker until the water boils gently: stir the solution mechanically. Place the sodium polysulphide solution in a dropping funnel and clamp the funnel so that the end of the stem is immediately above the beaker. Add the sodium polysulphide solution during 30–45 minutes to the vigorously stirred, boiling mixture, and boil

gently for a further 20 minutes. Allow to cool ; this can be accomplished more rapidly by adding ice. Filter at the pump and wash with cold water. Transfer to a 600 ml. beaker containing 150 ml. of water and 35 ml. of concentrated hydrochloric acid, and boil for 15 minutes ; the *m*-nitroaniline dissolves leaving the sulphur and any unchanged *m*-dinitrobenzene. Filter and precipitate the *m*-nitroaniline from the filtrate by the addition of excess of concentrated aqueous ammonia solution. Filter off the product and recrystallise it from boiling water. The yield of *m*-nitroaniline (bright yellow needles) is 12 g. ; m.p. 114°.

Note.

(1) Crystallised sodium sulphide is very deliquescent and only a sample which has been kept in a tightly-stoppered bottle should be used.

ACETYLATION OF AROMATIC AMINES

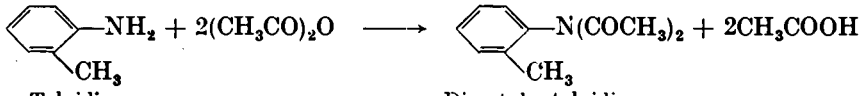
Acetyl derivatives of aromatic amines may be prepared either with acetic anhydride or acetic acid or with a mixture of both reagents. Primary amines react readily upon warming with acetic anhydride to yield, in the first instance, the mono-acetyl derivative, for example :

$$\underset{\text{Aniline}}{C_6H_5NH_2} + (CH_3CO)_2O \longrightarrow \underset{\text{Acetanilide}}{C_6H_5NHCOCH_3} + CH_3COOH$$

If the heating be prolonged and excess of acetic anhydride is employed, variable amounts of the diacetyl derivative are formed :

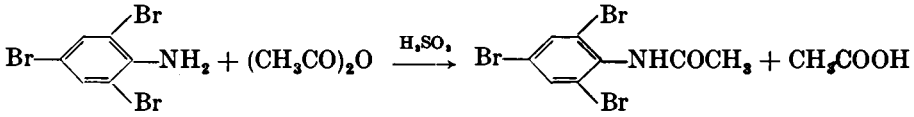
$$RNHCOCH_3 + (CH_3CO)_2O \longrightarrow RN(COCH_3)_2 + CH_3COOH$$

The production of diacetyl derivatives is facilitated by the presence of substituents in the *ortho* position: thus an excellent yield of **diacetyl-*o*-toluidine** results when *o*-toluidine is heated with an excess of the reagent:



o-Toluidine — Diacetyl-*o*-toluidine

In general, however, the diacetyl derivatives are unstable in the presence of water, undergoing hydrolysis to the mono-acetyl compound, so that when they (or a mixture of mono- and di-acetyl derivatives) are crystallised from an aqueous solvent, *e.g.*, dilute alcohol, only the mono-acetyl derivative is obtained. A further disadvantage of the use of acetic anhydride in the absence of a solvent is that all the impurities in the amine are generally present in the reaction product. Heavily substituted amines, *e.g.*, 2 : 4 : 6-tribromoaniline, react extremely slowly with acetic anhydride, but in the presence of a few drops of concentrated sulphuric acid as catalyst acetylation occurs rapidly, for example :



2 : 4 : 6-Tribromoaniline — 2 : 4 : 6-Tribromoacetanilide

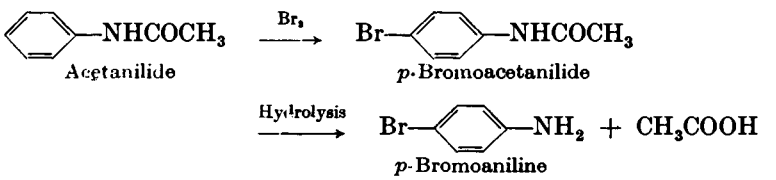
The disadvantages attending the use of acetic anhydride alone are absent when the acetylation is conducted in aqueous solution according to the following procedure. The amine is dissolved in water containing one equivalent of hydrochloric acid, slightly more than one equivalent of acetic anhydride is added to the solution, followed by enough sodium acetate to neutralise the hydrochloric acid, and the mixture is shaken. The free amine which is liberated is at once acetylated. It must be pointed out that the hydrolysis of acetic anhydride at room temperature is extremely slow and that the free amine reacts much more readily with the anhydride than does the water : this forms the experimental basis for the above excellent method of acetylation.

Acetylation with acetic anhydride is comparatively expensive because of the cost of the reagent. The use of the inexpensive glacial acetic acid depends upon the displacement of the reversible equilibrium :

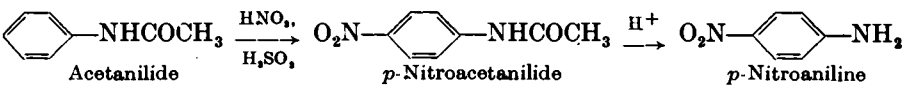
$$RNH_2 + CH_3COOH \rightleftharpoons RNHCOCH_3 + H_2O$$

to the right by removal of the water (and a little acetic acid) by distillation. An alternative technique, suitable for laboratory preparations, is to employ a mixture of acetic acid and acetic anhydride.

Mono-substitution products of primary amines cannot easily be prepared by direct action of the appropriate reagent; for example, bromination of aniline yields largely the 2 : 4 : 6-tribromo derivative and nitration results in much oxidation. If, however, the amino group is protected as in acetanilide, smooth substitution occurs. Thus with bromine, ***p*-bromoacetanilide** is the main product; the small quantity of the *ortho* isomeride simultaneously formed can be easily eliminated by crystallisation. Hydrolysis of *p*-bromoacetanilide gives ***p*-bromoaniline**:



Nitration leads similarly to ***p*-nitroacetanilide**, which can be hydrolysed to ***p*-nitroaniline**:



IV,45. ACETANILIDE

Method 1. In a 1 litre beaker or flask containing 500 ml. of water, introduce 18·3 ml. of concentrated hydrochloric acid and 20·5 g. (20 ml.) of aniline. Stir until the aniline passes completely into solution. (If the solution is coloured, add 3–4 g. of decolourising carbon, warm to about 50° with stirring for 5 minutes, and filter at the pump or through a fluted filter paper.) To the resulting solution add 27·7 g. (25·6 ml.) of redistilled acetic anhydride, stir until it is dissolved, and immediately pour in a solution of 33 g. of crystallised sodium acetate in 100 ml. of water. Stir vigorously and cool in ice. Filter the acetanilide with suction, wash with a little water, drain well, and dry upon filter paper in the air. The yield of colourless, almost pure acetanilide, m.p. 113°, is 24 g. Upon recrystallisation from about 500 ml. of boiling water to which about 10 ml. of methylated spirit has been added (compare *Method 3*), the m.p. is raised to 114°; the first crop weighs 19 g.

Method 2. In a 500 ml. round-bottomed flask, equipped with a reflux condenser, place 20·5 g. (20 ml.) of aniline, 21·5 g. (20 ml.) of acetic anhydride, 21 g. (20 ml.) of glacial acetic acid, and 0·1 g. of zinc dust (1). Boil the mixture gently for 30 minutes, and then pour the hot liquid in a thin stream into a 1 litre beaker containing 500 ml. of cold water whilst stirring continually. When cold (it is preferable to cool in ice), filter the crude product at the pump, wash with a little cold water, drain well and dry upon filter paper in the air. The yield of acetanilide, m.p. 113°, is 30 g. It may be recrystallised as in *Method 1* affording 21 g. of pure acetanilide, m.p. 114°.

Method 3. Fit up the apparatus shown in Fig. *IV, 45*, 1 using a 250-ml. round-bottomed flask. Do not pass water through the glass jacket since the condenser will be employed only as an air condenser: the empty filter flask is used merely as a trap to prevent the escape of vapours into

the atmosphere. Place 20·5 g. (20 ml.) of aniline, 26 g. (25 ml.) of glacial acetic acid, and 0·1 g. of zinc dust (1) in the flask, and boil the mixture over a wire gauze at such a rate that the thermometer reads about 105°. After 2–3 hours, the water formed in the reaction together with a little acetic acid will have been driven off, and the temperature registered by the thermometer will commence to fluctuate: the process is then complete. Pour the hot liquid (2) in a thin stream into a 1 litre beaker containing 500 ml. of water. Stir the mixture well and cool in cold water or, preferably, in ice. Collect the crude acetanilide on a Buchner funnel and wash it with cold water. Place the moist acetanilide in a large beaker or porcelain dish, and add gradually about 750 ml. of boiling water (3). It must be remembered that the crude acetanilide melts slightly below 114°; the substance may therefore melt when heated with water (for theoretical explanation, see Section **I,18**). All the material, liquid or solid, must be dissolved: the addition of a little alcohol will assist the process of solution. Filter, if necessary, through a hot water funnel (Fig. *II*, *1*, 6) or through a Buchner funnel through which boiling water has been poured. If the solution is coloured, add 3–4 g. of decolourising carbon before filtration. Allow the solution to cool, filter when cold, drain well, and dry upon filter paper in the air. The yield of pure acetanilide, m.p. 114°, is 19 g.

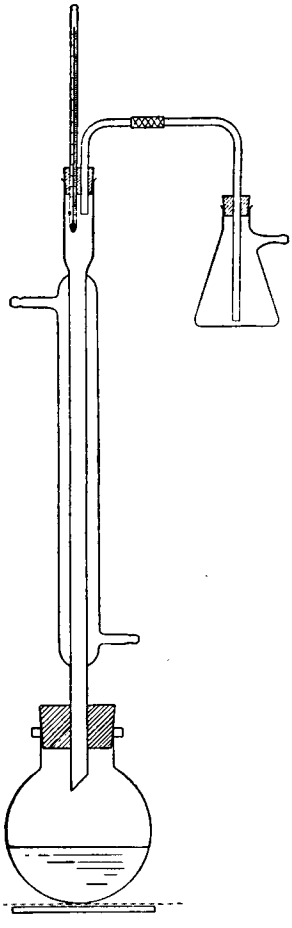


Fig. *IV*, *45*, 1.

Notes.

(1) The zinc reduces the coloured impurities in the aniline and also helps to prevent oxidation of the amine during the reaction.

(2) If the reaction mixture is allowed to cool, it will set to a solid cake in the flask.

(3) The acetanilide may also be recrystallised from toluene (*inflammable*): use a reflux condenser. For practice, recrystallise 5 g. from 50 ml. of toluene.

IV,46. DIACETYL-*o*-TOLUIDINE

Boil a mixture of 10 g. (10 ml.) of *o*-toluidine and 38 g. (35 ml.) of acetic anhydride in a 75 or 100 ml. Claisen flask fitted with a reflux condenser (Fig. *III*, *28*, 1, but with trap replaced by a calcium chloride or cotton wool guard tube) for 1 hour. Arrange the flask for distillation under reduced pressure (compare Fig. *II*, *20*, 1) and distil: acetic acid and the excess of acetic anhydride pass over first, followed by the diacetyl derivative at 152–153°/20 mm.: some mono-acetyl-*o*-toluidine (1·2 g.) remains in the flask. The yield of diacetyl-*o*-toluidine is 14–15 g.; it is a colourless, somewhat unstable liquid, which slowly solidifies to yield crystals, m.p. 18°.

To prepare the (mono-) acetyl-**o**-toluidine, warm a mixture of 5 g.

(5 ml.) of *o*-toluidine and 5·5 g. (5 ml.) of acetic anhydride over a free flame for 2 minutes, and pour the hot mixture into 100 ml. of cold water. Stir the mixture, warm to decompose any excess of acetic anhydride if present, and allow to cool. Filter at the pump, wash with cold water, and recrystallise from alcohol. The yield is 6 g., m.p. 110°.

IV,47. 2 : 4 : 6-TRIBROMOACETANILIDE

2 : 4 : 6-Tribromoaniline. Assemble the apparatus depicted in Fig. *IV*, *47*, 1. The distilling flask *B* has a capacity of 100 ml. and the bolt-head flask *A* (which may be replaced by a flat-bottomed flask) is 1 litre. Into the flask place 10 g. of aniline, 100 ml. of water and 10 ml. of concentrated hydrochloric acid ; shake until the aniline has dissolved and dilute with 400 ml. of water. Charge the distilling flask with 60 g. (19 ml.) of bromine. Surround the flask *A* by an ice bath and immerse the flask *B* in a water bath maintained at 30–40°. Interpose a wash bottle partially filled with water between the reaction flask and a water pump ; this will permit the rate of aspiration to be observed and will also serve to detect the escape of bromine vapours from the reaction flask since a small amount of bromine will impart a distinctly yellow colour to the water. Apply gentle suction by means of a water pump. Continue the passage of bromine vapour until the solution in *A* assumes a distinctly yellow colour (2–3 hours) ; the reaction is then complete. Filter the tribromoaniline on a Buchner funnel, wash it thoroughly with water to remove hydrobromic acid, and suck as dry as possible. Recrystallise from methylated (or rectified) spirit. The yield is 22 g. ; m.p. 120°.

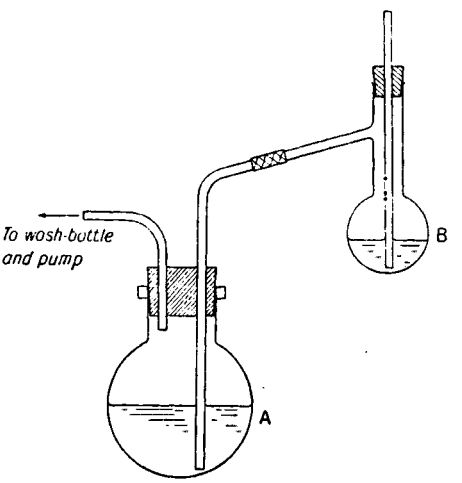


Fig. *IV*, *47*, 1.

$$C_6H_5NH_2 + 3Br_2 \longrightarrow NH_2C_6H_2Br_3 + 3HBr$$

An alternative method of preparation consists in dissolving the aniline in 4 times its weight of glacial acetic acid in a beaker, and running in slowly from a tap funnel, while the solution is well stirred with a mechanical stirrer, the theoretical amount of bromine dissolved in twice its volume of glacial acetic acid. The beaker should be cooled in ice during the addition as the reaction is exothermic. The final product (a pasty mass) should be coloured yellow by the addition of a little more bromine if necessary. Pour into excess of water, filter at the pump, wash well with water, press thoroughly, and dry. The yield of tribromoaniline, m.p. 119–120°, is quantitative. Recrystallise a small portion from methylated (or rectified) spirit ; m.p. 120°.

2 : 4 : 6-Tribromoacetanilide. Dissolve 1 g. of 2 : 4 : 6-tribromoaniline in 20 ml. of acetic anhydride and add 2 drops of concentrated

sulphuric acid. After 10 minutes, pour the reaction mixture into excess of warm water. Filter off the tribromoacetanilide, wash and dry: the m.p. is 231°. Recrystallise from alcohol: the m.p. is raised to 232°.

IV,48. *p*-BROMOACETANILIDE

Dissolve 13·5 g. of finely powdered acetanilide in 45 ml. of glacial acetic acid in a 350 ml. conical flask. In another small flask dissolve 17 g. (5·3 ml.) of bromine in 25 ml. of glacial acetic acid, and transfer the solution to a burette or a separatory funnel supported over the flask. [For precautions attending the use of bromine, see Section **III,35**, *Note 1*. The preparation should be conducted in a fume cupboard.] Add the bromine solution slowly and with constant shaking to ensure thorough mixing: stand the flask in cold water. When all the bromine has been added, the solution will have an orange colour due to the slight excess of bromine; a part of the reaction product may crystallise out. Allow the final reaction mixture to stand at room temperature for 30 minutes with occasional shaking. Pour the reaction product into 400 ml. of water; rinse the flask with about 100 ml. of water. Stir the mixture well and if it is appreciably coloured, add just sufficient sodium bisulphite solution to remove the orange colour. Filter the crystalline precipitate with suction on a Buchner funnel, wash thoroughly with cold water, and press as dry as possible with a wide glass stopper. Recrystallise from dilute methyl alcohol or ethyl alcohol (methylated spirit). The yield of *p*-bromoacetanilide, colourless crystals m.p. 167°, is 18 g.

IV,49. *p*-BROMOANILINE

Method 1 (**Acid hydrolysis**). Dissolve 18 g. of *p*-bromoacetanilide in 35 ml. of boiling ethanol contained in a 500 ml. round-bottomed flask equipped with a reflux condenser. Support a separatory funnel by means of a grooved cork in the top of the condenser, and charge it with 22 ml. of concentrated hydrochloric acid. Add the hydrochloric acid in small portions to the boiling solution. Reflux for 30–40 minutes or until a test portion remains clear when diluted with water. Dilute with 150 ml. of water, and fit the flask with a wide delivery tube leading to a condenser set for downward distillation (compare Fig. *II*, *13*, 3). Distil the mixture from an air bath (Fig. *II*, *5*, 3) or upon an asbestos-centred wire gauze, and collect about 100 ml. of distillate; the latter consists of ethyl acetate, ethyl alcohol and water. Pour the residual solution of *p*-bromoaniline hydrochloride into 100 ml. of ice water, and add, with vigorous stirring, 5 per cent. sodium hydroxide solution until just alkaline. The *p*-bromoaniline separates as an oil, which soon crystallises. Filter the crystals at the pump, wash with cold water, and dry in the air upon pads of filter paper. The yield is 14 g., m.p. 66°. Recrystallisation from dilute alcohol, which results in appreciable loss, is usually unnecessary.

Method 2 (**Alkaline hydrolysis**). Use a solution of 15 g. of *p*-bromoacetanilide in 30 ml. of boiling ethyl alcohol, and add a solution of 7·5 g. of potassium hydroxide in 10 ml. of water. Reflux for 40 minutes, dilute with 120 ml. of water, and distil until 75 ml. of distillate (alcohol and water) are collected; pour the residue into 150 ml. of cold water.

The *p*-bromoaniline separates as an oil, which soon solidifies. Filter at the pump and wash with cold water. Purify the crude *p*-bromoaniline as follows. Dissolve it in a mixture of 120 ml. of water and 75 ml. of concentrated hydrochloric acid, add 1–2 g. of decolourising carbon, and warm on a water bath for 10 minutes. Filter through a fluted paper or through two thicknesses of filter paper on a Buchner funnel. Pour the filtrate *slowly* and with vigorous stirring into a mixture of 60 ml. of 10 per cent. sodium hydroxide solution and 100 g. of crushed ice. The *p*-bromoaniline crystallises out. Filter, etc. as in *Method 1*. The yield is 11·5 g.

IV,50. *p*-NITROACETANILIDE

Add 25 g. of finely-powdered, dry acetanilide to 25 ml. of glacial acetic acid contained in a 500 ml. beaker; introduce into the well-stirred mixture 92 g. (50 ml.) of concentrated sulphuric acid. The mixture becomes warm and a clear solution results. Surround the beaker with a freezing mixture of ice and salt, and stir the solution mechanically. Support a separatory funnel, containing a cold mixture of 15·5 g. (11 ml.) of concentrated nitric acid and 12·5 g. (7 ml.) of concentrated sulphuric acid, over the beaker. When the temperature of the solution falls to 0–2°, run in the acid mixture gradually while the temperature is maintained below 10°. After all the mixed acid has been added, remove the beaker from the freezing mixture, and allow it to stand at room temperature for 1 hour. Pour the reaction mixture on to 250 g. of crushed ice (or into 500 ml. of cold water), whereby the crude nitroacetanilide is at once precipitated. Allow to stand for 15 minutes, filter with suction on a Buchner funnel, wash it thoroughly with cold water until free from acids (test the wash water), and drain well. Recrystallise the pale yellow product from alcohol or methylated spirit (see Section **IV,12** for experimental details), filter at the pump, wash with a little cold alcohol, and dry in the air upon filter paper. [The yellow *o*-nitroacetanilide remains in the filtrate.] The yield of *p*-nitroacetanilide, a colourless crystalline solid of m.p. 214°, is 20 g.

IV,51. *p*-NITROANILINE

Heat a mixture of 15 g. of *p*-nitroacetanilide and 75 ml. of 70 per cent. sulphuric acid (1) under a reflux water condenser for 20–30 minutes or until a test sample remains clear upon dilution with 2–3 times its volume of water. The *p*-nitroaniline is now present in the liquid as the sulphate. Pour the clear hot solution into 500 ml. of cold water and precipitate the *p*-nitroaniline by adding excess of 10 per cent. sodium hydroxide solution or of concentrated ammonia solution. When cold (cool the mixture in ice water, if necessary), filter the yellow crystalline precipitate at the pump, wash it well with water, and drain thoroughly. Recrystallise it from a mixture of equal volumes of rectified (or methylated) spirit and water or from hot water. Filter, wash and dry. The yield of *p*-nitroaniline, m.p. 148°, is 11 g.

Note.

(1) The 70 per cent. sulphuric acid is prepared by adding 60 ml. of concentrated sulphuric acid cautiously and in a thin stream with stirring to 45 ml. of water.

BENZOYLATION OF AROMATIC AMINES

In general, benzoylation of aromatic amines finds less application than acetylation in preparative work, but the process is often employed for the identification and characterisation of aromatic amines (and also of hydroxy compounds). Benzoyl chloride (Section **IV,185**) is the reagent commonly used. This reagent is so slowly hydrolysed by water that benzoylation can be carried out in an aqueous medium. In the **Schotten-Baumann method of benzoylation** the amino compound or its salt is dissolved or suspended in a slight excess of 8–15 per cent. sodium hydroxide solution, a small excess (about 10–15 per cent. more than the theoretical quantity) of benzoyl chloride is then added and the mixture vigorously shaken in a stoppered vessel (or else the mixture is stirred mechanically). Benzoylation proceeds smoothly and the sparingly soluble benzoyl derivative usually separates as a solid. The sodium hydroxide hydrolyses the excess of benzoyl chloride, yielding sodium benzoate and sodium chloride, which remain in solution :

$$C_6H_5COCl + 2NaOH \longrightarrow C_6H_5COONa + NaCl + H_2O$$

The benzoyl compounds frequently occlude traces of unchanged benzoyl chloride, which thus escape hydrolysis by the caustic alkali ; it is therefore advisable, wherever possible, to recrystallise the benzoyl derivatives from methyl, or ethyl alcohol or methylated spirit, since these solvents will esterify the unchanged chloride and so remove the latter from the recrystallised material. Sometimes the benzoyl compound does not crystallise well : this difficulty may frequently be overcome by the use of *p*-nitrobenzoyl chloride or 3 : 5-dinitrobenzoyl chloride, which usually give highly crystalline derivatives of high melting point (see Section **IV,114**).

Examples of benzoylation under Schotten-Baumann conditions are :—

$$\underset{\text{Aniline}}{C_6H_5NH_2} + C_6H_5COCl + NaOH \longrightarrow \underset{\text{Benzanilide}}{C_6H_5NHCOC_6H_5} + NaCl + H_2O$$

$$\underset{p\text{-Toluidine}}{p\text{-}CH_3C_6H_4NH_2} + C_6H_5COCl + NaOH \longrightarrow \underset{\text{Benzoyl } p\text{-toluidide}}{p\text{-}CH_3C_6H_4NHCOC_6H_5} + NaCl + H_2O$$

Benzanilide is more conveniently prepared, particularly on a larger scale, by heating together aniline and benzoic acid :

$$C_6H_5NH_2 + C_6H_5COOH \longrightarrow C_6H_5NHCOC_6H_5 + H_2O$$

Benzoyl compounds are readily hydrolysed by heating with about 70 per cent. sulphuric acid (alkaline hydrolysis is very slow for anilides) :

$$C_6H_5NHCOC_6H_5 + H_2SO_4 + H_2O \longrightarrow C_6H_5NH_3OSO_3H + C_6H_5COOH$$

This procedure is of importance in connexion with the identification of substituted amines.

IV,52. BENZANILIDE (*Schotten-Baumann Reaction*)

Place 5·2 g. (5 ml.) of aniline and 45 ml. of 10 per cent. aqueous sodium hydroxide solution in a wide-necked bottle (or, if not available, a conical flask), and then add 8·5 g. (7 ml.) of benzoyl chloride, stopper, and shake *vigorously* for 10–15 minutes. Heat is evolved in the reaction. The crude benzoyl derivative separates as a white powder. When the reaction is complete (*i.e.*, when the odour of benzoyl chloride can no longer be detected : smell cautiously), make sure that the reaction mixture is

alkaline. Dilute with water. Filter off the product with suction on a Buchner funnel, break up the mass on the filter (if necessary), wash well with water, and drain. Recrystallise from hot alcohol (or methylated spirit); filter the hot solution through a hot water funnel or through a warm Buchner funnel. Collect the crystals which separate and dry in the air or in the steam oven. The yield of benzanilide, m.p. 162°, is 9 g.

Hydrolysis of benzanilide. Place 5 g. of benzanilide and 50 ml. of 70 per cent. sulphuric acid * in a small flask fitted with a reflux condenser, and boil gently for 30 minutes. Some of the benzoic acid will vapourise in the steam and solidify in the condenser. Pour 60 ml. of hot water down the condenser: this will dislodge and partially dissolve the benzoic acid. Cool the flask in ice water; filter off the benzoic acid (aniline sulphate does not separate at this dilution), wash well with water, drain, dry upon filter paper, and identify by m.p. (121°) and other tests. Render the filtrate alkaline by cautiously adding 10 per cent. sodium hydroxide solution, cool and isolate the aniline by ether extraction. Recover the ether and test the residue for aniline (Section **IV,100**).

COGNATE PREPARATION

Benzoyl *p*-toluidide. Use 3·3 g. of *p*-toluidine, 25 ml. of 10 per cent. sodium hydroxide solution and 4·2 g. (3·5 ml.) of benzoyl chloride. Proceed as above. The yield of benzoyl *p*-toluidide, m.p. 158°, is 4·5 g.

IV,53. BENZANILIDE

Into a 500 ml. round-bottomed flask place 150 g. (147 ml.) of aniline and 125 g. of benzoic acid; melt the mixture to reduce the total volume and add a further 75 g. of benzoic acid. Immerse the flask in an oil bath and connect it to a condenser for downward distillation. Raise the temperature of the oil bath rapidly to 180–190°; distillation then commences. Maintain the temperature of the bath at 180–190° until no more aniline and water distils (about 2 hours), then raise the temperature slowly to 225° and hold the bath at this temperature until distillation ceases (1–2 hours). Remove the flask from the oil bath and when the contents have cooled below 180°, add 110 g. (107·5 ml.) of aniline. Repeat the distillation at 180–190° and 225° as before (4–6 hours). Pour the hot mixture into a large evaporating dish and allow it to solidify. Powder the purplish-grey solid very finely, and pour it with vigorous stirring into a 2- or 3-litre beaker containing a mixture of 100 ml. of concentrated hydrochloric acid and 1100 ml. of water. Continue the mechanical stirring for 1 hour. Filter the solid with suction on a Buchner funnel. Repeat the stirring with acid twice in order to remove the aniline as completely as possible. Stir the solid for 1 hour with 1200 ml. of water, and filter. Again stir for 1 hour with 1200 ml. of *ca.* *N*-sodium hydroxide solution to remove the excess of benzoic acid and filter at the pump. Finally stir for 2 hours with 1500 ml. of water, filter, drain, dry in the air upon sheets of filter paper, then dry to constant weight upon large clock glasses at 90–100°. The resulting crude benzanilide is purplish-grey, weighs 260 g. and melts at 158–160°. It is pure enough for most practical purposes, but can be further purified as follows. Dissolve 100 g. in 750 ml.

* Seventy per cent. sulphuric acid is prepared by adding 40 ml. of the concentrated acid cautiously and with stirring and cooling to 30 ml. of water.

of hot ethyl alcohol, add 10 g. of decolourising carbon, and boil for a short time; filter through a hot water funnel and leave to crystallise overnight. Collect the almost colourless crystals on a Buchner funnel and dry them; the yield is 85 g., m.p. 161°.

IV,54. HIPPURIC ACID (BENZOYL GLYCINE)

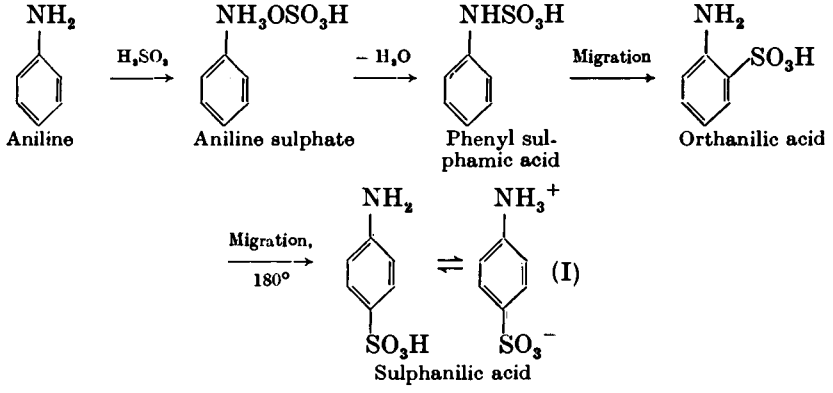
Dissolve 5 g. of glycine (Section **III,129**) in 50 ml. of 10 per cent. sodium hydroxide solution contained in a wide-mouthed bottle or in a conical flask. Add 10·8 g. (9·0 ml.) of benzoyl chloride in five portions to the solution. Stopper the vessel and shake vigorously after each addition until all the chloride has reacted. Transfer the solution to a beaker and rinse the bottle (conical flask) with a little water. Place a few grams of crushed ice in the solution and add concentrated hydrochloric acid slowly and with stirring until the mixture is acid to Congo red paper. Collect the resulting crystalline precipitate of hippuric acid (benzoyl aminoacetic acid), which is contaminated with a little benzoic acid, upon a Buchner funnel, wash with cold water and drain well. Place the solid in a small beaker with 20 ml. of carbon tetrachloride, cover the beaker with a watch glass and boil the mixture gently for 10 minutes (1). Allow the mixture to cool slightly, filter by gentle suction, and wash the hippuric acid on the filter with 3–4 ml. of carbon tetrachloride. Recrystallise from boiling water (about 100 ml.) with the addition of a little decolourising carbon if necessary, filter through a hot water funnel, and allow to crystallise. Collect the pure hippuric acid in a Buchner funnel and dry it in the steam oven. The yield is 9 g., m.p. 187°.

Note.

(1) The carbon tetrachloride extraction removes any benzoic acid which may be present.

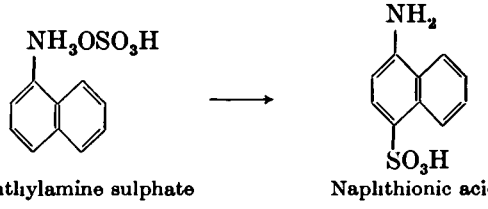
SULPHONATION OF AROMATIC AMINES

If aniline is treated with excess of concentrated sulphuric acid and the resulting mixture, which contains aniline sulphate, is heated at 180° until a test portion when mixed with sodium hydroxide solution no longer liberates aniline, *p*-aminobenzenesulphonic acid or **sulphanilic acid** is formed ; this separates as the dihydrate upon pouring the cooled mixture into water. The reaction probably proceeds as follows :

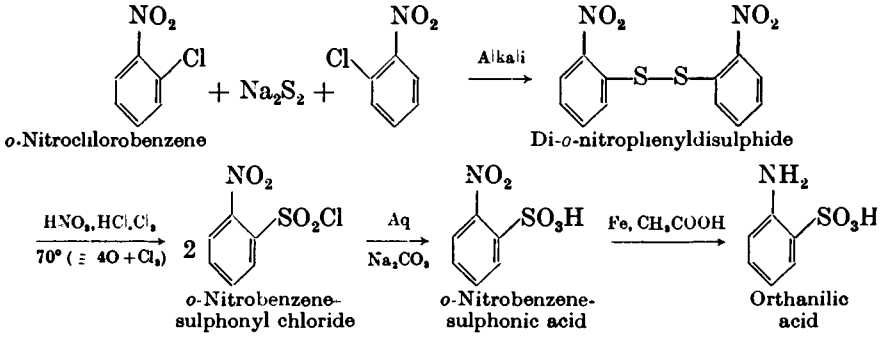


The suggested mechanism involves the initial loss of water from aniline monosulphate with the formation of phenyl sulphamic acid ; upon gentle heating the —SO_3H group migrates first to the *ortho* position to give orthanilic acid, and at a higher temperature (180°) rearranges to sulphanilic acid. It is believed that sulphanilic acid exists largely as the double charged ion (I) in aqueous solution.

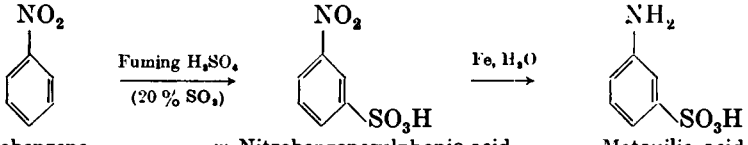
α-Naphthylamine similarly yields 1 - naphthylamine - 4 - sulphonic acid or **naphthionic acid** :



o-Aminobenzenenesulphonic acid or **orthanilic acid** may be prepared from commercial *o*-chloronitrobenzene by the following procedure :



m-Aminobenzenenesulphonic acid or **metanilic acid** is prepared by sulphonating nitrobenzene with fuming sulphuric acid (20 per cent. SO_3) and reducing the resulting *m*-nitrobenzenesulphonic acid with iron filings and water :



Nitrobenzene *m*-Nitrobenzenesulphonic acid Metanilic acid

IV,55. SULPHANILIC ACID

Place 20·4 g. (20 ml.) of aniline in a 250 ml. conical or round-bottomed flask and cautiously add 74 g. (40 ml.) of concentrated sulphuric acid in small portions ; swirl the mixture gently during the addition and keep it cool by occasionally immersing the flask in cold water. Support the flask in an oil bath, and heat the mixture at 180–190° (fume cupboard) for about 5 hours (1). The sulphonation is complete when a test portion (2 drops) is completely dissolved by 3–4 ml. of *ca.* 2*N* sodium hydroxide solution without leaving the solution cloudy. Allow the product to cool to about 50° and pour it carefully with stirring into 400 g. of cold water or of crushed ice. Allow to stand for 10 minutes, and collect the precipitated sulphanilic acid on a Buchner funnel, wash it well with water, and drain. Dissolve the crude sulphanilic acid in the minimum volume of boiling water (450–500 ml.) ; if the resulting solution is coloured, add about 4 g. of decolourising carbon and boil for 10–15 minutes. Filter through a hot water funnel (Fig. *II*, *1*, 6) or through a Buchner funnel and flask which have been preheated by the filtration of boiling distilled water. Upon cooling, the sulphanilic acid dihydrate separates in colourless crystals. When the filtrate is quite cold, filter the crystals with suction, wash with about 10 ml. of cold water, and press thoroughly with a wide glass stopper. Dry between sheets of special absorbent paper or in a desiccator containing anhydrous calcium chloride ; in the latter case, the water of crystallisation (and hence the crystalline form) is lost. The yield of sulphanilic acid is 20–22 g. The substance does not melt sharply and no attempt should be made to determine the melting point ; the crystals are efflorescent.

Note.

(1) If 40 ml. of 10 per cent. oleum be cautiously added to the aniline sulphate mixture, sulphonation proceeds much more rapidly and the time of heating is reduced from 5 hours to 1 hour.

IV,56. NAPHTHIONIC ACID

Place a mixture of 25 g. of α-naphthylamine (Section **IV,37**) and 125 g. (69·5 ml.) of concentrated sulphuric acid in a 250 ml. conical or round-bottomed flask, and heat in an oil bath for 4–5 hours or until a test sample, when made alkaline with sodium hydroxide solution and extracted with ether, yields no naphthylamine upon evaporation of the ether. Pour the warm reaction mixture cautiously and with stirring into 300 ml. of cold

water; the difficultly soluble naphthionic acid, which may be contaminated with a little naphthylamine sulphate, separates out. When cold, filter off the acid at the pump and wash it with cold water until free from sulphuric acid. Dissolve the crude naphthionic acid in the minimum volume (about 350 ml.) of 5 per cent. sodium hydroxide solution (*i.e.*, until about neutral) and saturate the resulting solution of sodium naphthionate with common salt. Allow to stand, when sodium naphthionate separates as white crystals. Filter with suction, drain, and dry in the steam oven. Place the solid in a small beaker with 20 ml. of carbon tetrachloride, cover the beaker with a watch glass and boil the mixture gently on a water bath for 10 minutes, filter by gentle suction, and wash the sodium naphthionate with a little solvent. This process removes any naphthylamine which may be present. The yield of sodium naphthionate is 20–35 g.; this is the form commonly encountered in commerce. To prepare the free acid, dissolve the sodium salt in the minimum volume of boiling water, add the calculated quantity of concentrated hydrochloric acid corresponding to the weight of sodium salt employed (acid to Congo red), and allow to cool. Collect the resulting naphthionic acid hemihydrate upon a Buchner funnel, wash with a little cold water, drain well, and dry upon filter paper or in the steam oven. If desired, it may be recrystallised from boiling water. The yield is 10–18 g.

IV,57. ORTHANILIC ACID

Di-*o*-nitrophenyl disulphide. Place 120 g. of crystallised sodium sulphide (1) and 500 ml. of rectified spirit in a 1-litre round-bottomed flask provided with a reflux condenser. Heat the flask on a water bath until the sulphide dissolves. Then add 16 g. of finely-powdered sulphur and continue the heating until all the sulphur dissolves forming a brownish-red solution of sodium disulphide (2). Prepare a solution of 105 g. of commercial *o*-nitrochlorobenzene in 175 ml. of rectified spirit in a 2-litre round-bottomed flask equipped with a reflux condenser; by means of a dropping funnel, fitted into the top of the condenser with a grooved cork, add the sodium disulphide solution slowly and at such a rate that the reaction is under control. Heat the mixture on a water bath, gently at first until the violent reaction subsides, and then with the water boiling vigorously for 2 hours. Allow to cool. Filter with suction on a Buchner funnel. Transfer the mixture of organic disulphide and sodium chloride to a 400 ml. beaker and stir thoroughly with 175 ml. of water to remove the salt. Filter at the pump, drain well, and wash the crystalline residue on the filter with 35 ml. of alcohol to remove any unreacted *o*-chloronitrobenzene. The residual di-*o*-nitrophenyl disulphide melts at 193–195° and weighs 70 g.

Notes.

(1) Crystallised sodium sulphide $Na_2S,9H_2O$ is very deliquescent, and only a sample which has been kept in a tightly-stoppered bottle should be used; crystals as dry as possible should be selected. Alternatively, an equivalent amount of analysed fused sodium sulphide may be employed; this dissolves somewhat more slowly in alcohol.

(2) If some sodium disulphide separates at the bottom of the flask, this should be dissolved in a little more rectified spirit and added to the chloronitrobenzene solution.

o-Nitrobenzenesulphonyl chloride. Equip a 1-litre three-necked flask with an inlet tube for introducing chlorine well beneath the surface of the liquid (compare Section **III,125**), an efficient liquid-sealed stirrer, and a reflux condenser. Set up the assembly in the fume cupboard and absorb the excess of chlorine in sodium hydroxide solution as detailed under *Chloroacetic Acid* (Section **III,125**). Place 60 g. of di-*o*-nitrophenyl disulphide, 300 ml. of concentrated hydrochloric acid and 60 ml. of concentrated nitric acid in the flask, pass a stream of chlorine from a cylinder into the mixture at the rate of 2 bubbles per second, and warm the solution to 70° on a water bath. After about 30 minutes, the disulphide melts and the solution assumes an orange-red colour; after the melting stage has been reached, the passage of the chlorine and the heating are continued for 1 hour. Immediately separate the sulphonyl chloride from the supernatant liquid by decantation, wash with two 90 ml. portions of water at about 70°, and allow to solidify. Drain the water from the solid mass as completely as possible. Dissolve the sulphonyl chloride in 45 ml. of glacial acetic acid at 50–60°, and rapidly filter the solution at the pump. Cool the filtrate in cold water and stir it vigorously so that the sulphonyl chloride separates in small crystals. Triturate the mixture well with 300 ml. of cold water and decant through a Buchner funnel; repeat the process twice. Finally add 300 ml. of cold water and 3 ml. of concentrated ammonia solution to the mixture, stir well and filter immediately, through a Buchner funnel, wash with 60 ml. of water, drain well, and dry in the air. The yield of moderately pure *o*-nitrobenzenesulphonyl chloride, m.p. 64–65°, is 72 g. The undried material may be used in the preparation of orthanilic acid.

Orthanilic acid. Fit a 1-litre three-necked flask with a liquid-sealed mechanical stirrer and a reflux condenser. Place 60 g. of *o*-nitrobenzenesulphonyl chloride, 30 g. of anhydrous sodium carbonate and 180 ml. of water in the flask. Heat the mixture to boiling, with stirring; the hydrolysis of the sulphonyl chloride to the sulphonic acid is complete within 40 minutes after the compound has melted. Filter the orange-red solution and acidify (to litmus) with acetic acid (about 7·5 ml. are required). Transfer the solution to the original flask (which has been thoroughly rinsed with water) and equipped as before. Heat the solution to boiling, and add 105 g. of finely-divided iron filings (about 20 mesh) with vigorous stirring at the rate of about 7·5 g. every 15 minutes. The mixture soon becomes deep brown and exhibits a tendency to froth. Complete the reaction by stirring for a further 4 hours, *i.e.*, until a test portion when filtered yields an almost colourless filtrate; if the filtrate is orange or red, the heating and stirring must be continued. When the reduction is complete, add 2 g. of decolourising carbon, filter the hot reaction mixture at the pump, and wash the residue with three 15 ml. portions of hot water: combine the washings with the main solution. Cool the filtrate to about 15°, and add 28·5 ml. of concentrated hydrochloric acid slowly, and cool to 12–15°. Filter the acid with suction on a Buchner funnel, wash with a little cold water, followed by a little ethyl alcohol, and dry upon filter paper in the air. The yield is 97 g.; the orthanilic acid has a purity of 97–99 per cent. If required perfectly pure, it may be recrystallised from hot water; it decomposes at about 325°.

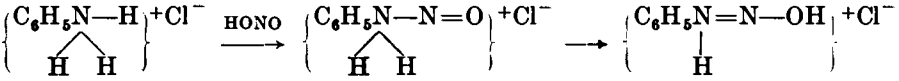
IV,58. METANILIC ACID

In a 500 ml. bolt-head flask, provided with a mechanical stirrer, place 70 ml. of oleum (20 per cent. SO_3) and heat it in an oil bath to 70°. By means of a separatory funnel, supported so that the stem is just above the surface of the acid, introduce 41 g. (34 ml.) of nitrobenzene slowly and at such a rate that the temperature of the well-stirred mixture does not rise above 100–105°. When all the nitrobenzene has been introduced, continue the heating at 110–115° for 30 minutes. Remove a test portion and add it to the excess of water. If the odour of nitrobenzene is still apparent, add a further 10 ml. of fuming sulphuric acid, and heat at 110–115° for 15 minutes : the reaction mixture should then be free from nitrobenzene. Allow the mixture to cool and pour it with good mechanical stirring on to 200 g. of finely-crushed ice contained in a beaker. All the nitrobenzenesulphonic acid passes into solution ; if a little sulphone is present, remove this by filtration. Stir the solution mechanically and add 70 g. of sodium chloride in small portions : the sodium salt of *m*-nitrobenzenesulphonic acid separates as a pasty mass. Continue the stirring for about 30 minutes, allow to stand overnight, filter and press the cake well. The latter will retain sufficient acid to render unnecessary the addition of acid in the subsequent reduction with iron. Spread upon filter paper to dry partially.

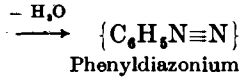
Place 84 g. of iron filings and 340 ml. of water in a 1·5 or 2-litre bolt-head flask equipped with a mechanical stirrer. Heat the mixture to boiling, stir mechanically, and add the sodium *m*-nitrobenzenesulphonate in small portions during 1 hour. After each addition the mixture foams extensively : a wet cloth should be applied to the neck of the flask if the mixture tends to froth over the sides. Replace from time to time the water which has evaporated so that the volume is approximately constant. When all the sodium salt has been introduced, boil the mixture for 20 minutes. Place a small drop of the suspension upon filter paper and observe the colour of the "spot" : it should be a pale brown but not deep brown or deep yellow. If it is not appreciably coloured, add anhydrous sodium carbonate cautiously, stirring the mixture, until red litmus paper is turned blue and a test drop upon filter paper is not blackened by sodium sulphide solution. Filter at the pump and wash well with hot water. Concentrate the filtrate to about 200 ml., acidify with concentrated hydrochloric acid to Congo red, and allow to cool. Filter off the metanilic acid and dry upon filter paper. A further small quantity may be obtained by concentrating the mother liquid. The yield is 55 g.

DIAZONIUM SALTS

Primary aromatic amines differ from primary aliphatic amines in their reaction with nitrous acid. Whereas the latter yield the corresponding alcohols ($RNH_2 \longrightarrow ROH$) without formation of intermediate products {see Section **III,123**, test (i)}, primary aromatic amines yield diazonium salts. Thus aniline gives phenyldiazonium chloride (sometimes termed benzenediazonium chloride) $\{C_6H_5N_2\}^+Cl^-$; the exact mode of formation is not known, but a possible route is through the phenylnitrosoammonium ion thus:



Aniline hydrochloride



Phenyldiazonium chloride

Phenyldiazonium chloride and other similar diazonium compounds are very soluble in water, are completely insoluble in ether and other organic solvents, and are completely dissociated in aqueous solution to organic cations and inorganic anions (*e.g.*, chloride ions): a convenient formulation is therefore, for example, $C_6H_5N_2^+Cl^-$.

The experimental conditions necessary for the preparation of a solution of a diazonium salt, **diazotisation of a primary amine**, are as follows. The amine is dissolved in a suitable volume of water containing 2·5–3 * equivalents of hydrochloric acid (or of sulphuric acid) by the application of heat if necessary, and the solution is cooled in ice when the amine hydrochloride (or sulphate) usually crystallises. The temperature is maintained at 0–5°, an aqueous solution of sodium nitrite is added portion-wise until, after allowing 3–4 minutes for reaction, the solution gives an *immediate* positive test for excess of nitrous acid with an external indicator—moist potassium iodide-starch paper †:

$$2HNO_2 + 2KI + 2HCl \longrightarrow 2KCl + I_2 + 2NO + 2H_2O$$

The precipitated amine hydrochloride (or sulphate), if any, dissolves during the diazotisation to give a clear solution of the highly soluble diazonium salt. The general reaction may be written:

$$ArNH_2 + NaNO_2 + 3HCl \xrightarrow{0°–5°} \{ArN_2\}^+Cl^- + NaCl + 2H_2O + HCl$$

The excess of acid (0·5-1 equivalents) maintains a proper condition of acidity required to stabilise the diazonium salt solution by reducing the secondary

* In those cases where a large excess of acid is harmful, the proportion may be reduced to 2·2 equivalents.

† In actual practice it is found that some time before the theoretical quantity of sodium nitrite has been added, the solution will give a blue colouration (presumably, in part, by atmospheric oxidation) within a few seconds of being placed upon the test paper. It must, however, be remembered that towards the end of the diazotisation the reaction with nitrous acid is somewhat slow, and it is imperative to wait a few minutes before making the test, and furthermore only an *immediate* blue colouration has any significance. It is advisable to dilute the drop of the test solution with a few drops of water on a watch glass before making the test. It is recommended that about 10 per cent. excess of sodium nitrite of good quality (97–98 per cent. $NaNO_2$: *e.g.*, sodium nitrite recryst. or A.R.) be employed; this will serve as an additional check. If a slight excess of sodium nitrite is accidentally added, it may be decomposed by the addition of a little urea or sulphamic acid; alternatively a small amount of the primary amine, dissolved in the acid used, may be added.

changes to a minimum, *e.g.*, the interaction of some of the diazonium salt with unchanged amine to form a diazoamino compound, a reaction which occurs readily in neutral solution :

$$C_6H_5N_2^+Cl^- + HNHC_6H_5 \longrightarrow \underset{\text{Diazoaminobenzene}}{C_6H_5N_2NHC_6H_5} + HCl$$

The amines are comparatively weak bases, so that a certain amount of free amine will be produced by salt hydrolysis unless an excess of acid is present. The reaction mixture must be kept very cold during the process (which is exothermic in character), otherwise the diazonium salt may be partially converted into the corresponding hydroxy compound :

$$ArN_2^+Cl^- + H_2O \longrightarrow ArOH + N_2 + HCl$$

Some amines, such as the nitroanilines and the naphthylamines, give somewhat more stable diazonium compounds and may be diazotised at room temperature, when the reaction proceeds more rapidly. If the amine salt is only sparingly soluble in water, it should be suspended in the acid in a fine state of division (this is generally attained by cooling a hot solution and stirring vigorously), and it passes into solution as the soluble diazonium salt is formed.

To prepare the **solid phenyldiazonium chloride or sulphate**, the reaction is conducted in the absence of water as far as possible. Thus the source of nitrous acid is one of its organic esters (*e.g.*, amyl nitrite) and a solution of hydrogen chloride gas in absolute alcohol ; upon the addition of ether only the diazonium salt is precipitated as a crystalline solid, for example :

$$C_6H_5NH_3^+Cl^- + C_5H_{11}ONO + HCl \longrightarrow C_6H_5N_2^+Cl^- + C_5H_{11}Cl + 2H_2O$$

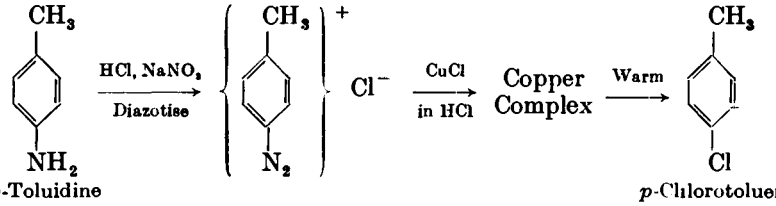
Solid diazonium salts are very sensitive to shock when perfectly dry and detonate violently upon gentle heating : they are, therefore, of little value for preparative work. Happily, most of the useful reactions of diazonium compounds can be carried out with the readily-accessible aqueous solutions, so that the solid (explosive) diazonium salts are rarely required.

When an aqueous solution of phenyldiazonium chloride or of *p*-tolyldiazonium hydrogen sulphate is treated with an equivalent of potassium iodide and warmed on a water bath, **iodobenzene** or ***p*-iodotoluene** is formed in good yield :

$$C_6H_5N_2^+Cl^- + KI \longrightarrow C_6H_5I + N_2 + KCl$$
$$p\text{-}CH_3C_6H_4N_2^+HSO_4^- + KI \longrightarrow p\text{-}CH_3C_6H_4I + N_2 + KHSO_4$$

This simple procedure cannot be applied in the preparation of the corresponding chloro and bromo compounds. Sandmeyer (1884) found that the replacement of the diazonium group by halogen can be successfully accomplished in the presence of the appropriate cuprous salt, thus providing an excellent method for the preparation of nuclear substituted aromatic compounds from the corresponding amines. The reaction has been extended to groups other than halogens, for example, the cyano (—CN) and the thiocyanate (—SCN) radicals. The detailed technique of the **Sandmeyer reaction** may be illustrated by reference to the preparation of ***p*-chlorotoluene** from *p*-toluidine. The amine is diazotised in the presence of hydrochloric acid with sodium nitrite at 0–5°, and a solution of an equimolecular quantity of cuprous chloride in hydrochloric acid is added ; a deep brown, sparingly soluble complex of cuprous chloride and

the diazonium salt is formed (*e.g.*, $CH_3C_6H_4N_2Cl,CuCl$), and when the temperature is raised, decomposition ensues accompanied by the evolution of nitrogen, the disappearance of the solid and the separation of an oily layer of *p*-chlorotoluene:



p-Toluidine — *p*-Chlorotoluene

The following *mechanism* of the Sandmeyer reaction has been proposed as a result of a kinetic study, and incidentally accounts for the formation of the azo compounds as by-products. The catalyst is the $CuCl_2^-$ ion produced in the dissolution of cuprous chloride in the chloride solution:

$$CuCl + Cl^- \rightleftharpoons CuCl_2^-$$

$$ArN_2^+ + CuCl_2^- \longrightarrow [ArN{\equiv}N{\rightarrow}CuCl_2]\,(A) \xrightarrow{(1)} ArCl + CuCl + N_2$$

$$(A) \xrightarrow{(2)\ ArN_2^+} (B)$$

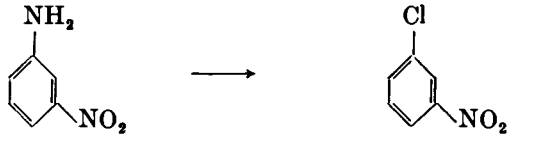
$$2Cu^{++} + ArN{=}NAr + 4Cl^- + N_2 \xleftarrow{(4)\ CuCl_2^-} (B) \xrightarrow{(3)} ArCl + ArN_2^+ + CuCl + N_2$$

The complex (A) is formed by coordination of the terminal diazo nitrogen atom with the copper in $CuCl_2^-$. This complex decomposes into ArCl (1). The complex (A) may also react with more ArN_2^+ to give the complex (B), and this may decompose to give ArCl (3) and the azo compound (4). When ArN_2^+ is present in large concentration (as when all or most is added at the outset), step (2) is faster than step (1), so that most of the ArCl arises from step (3). The yield of azo compound depends upon the $CuCl_2^-$ concentration. If ArN_2^+ is kept low by a gradual addition technique, reaction (1) predominates and, in consequence, the yield of azo compound is small.

The following additional examples of cognate preparations are given:

o-Toluidine ⟶ *o*-Chlorotoluene

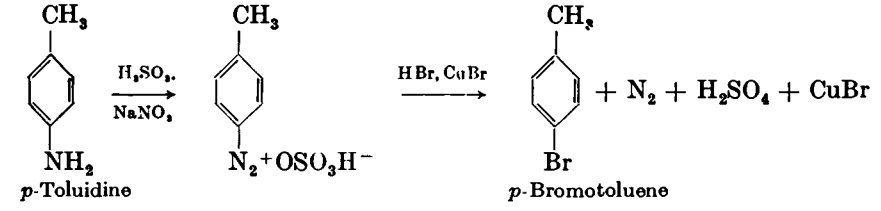
Aniline ⟶ Chlorobenzene



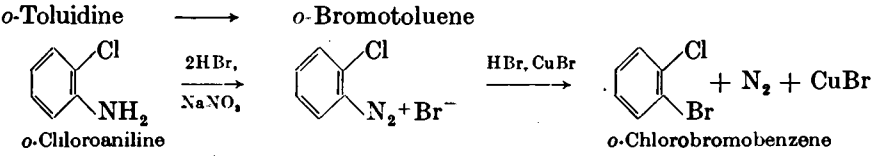
m-Nitroaniline ⟶ *m*-Chloronitrobenzene

In the preparation of bromo compounds by the Sandmeyer reaction, the amine is generally diazotised in sulphuric acid solution (or in hydrobromic acid solution), and the resulting aryldiazonium sulphate (or bromide) is treated with a solution of cuprous bromide in excess of hydrobromic acid; the addition

complex is then decomposed by gentle heating and the bromo compound isolated by steam distillation, for example :

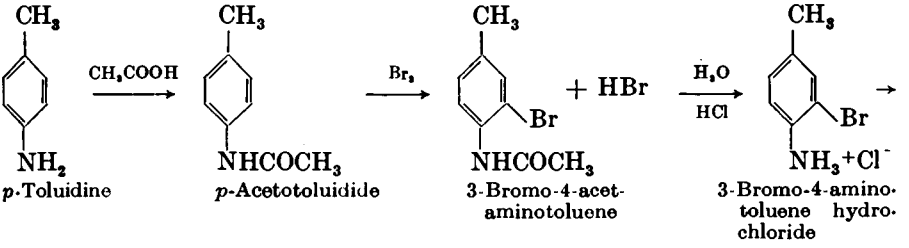


p-Toluidine — *p*-Bromotoluene

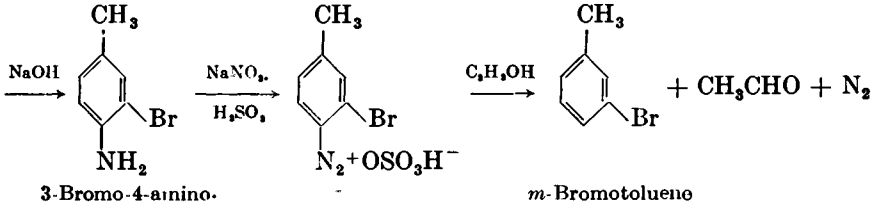


o-Chloroaniline — *o*-Chlorobromobenzene

For the preparation of ***m*-bromotoluene**, the following sequence of reactions from *p*-toluidine may be used :

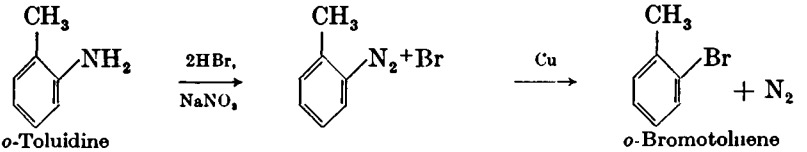


p-Toluidine — *p*-Acetotoluidide — 3-Bromo-4-acetaminotoluene — 3-Bromo-4-aminotoluene hydrochloride



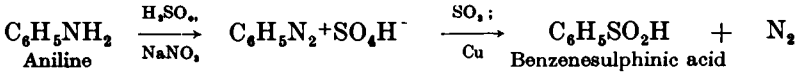
3-Bromo-4-aminotoluene — *m*-Bromotoluene

Gattermann (1890) found that the preparation of the cuprous halide may be avoided by making use of the fact that finely-divided copper (*e.g.*, freshly-precipitated or " reduced by hydrogen " or copper bronze) acts catalytically in the decomposition of solutions of diazonium salts, for example :

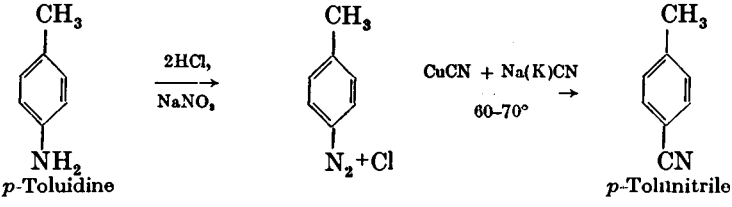


o-Toluidine — *o*-Bromotoluene

The yields by the **Gattermann reaction** are usually not as high as those by Sandmeyer's method. Copper powder is also employed in the preparation of **sulphinic acids**, for example :



The Sandmeyer reaction may also be applied to the preparation of **nitriles.** The solution of the diazonium salt is added to a solution of cuprous cyanide in excess of sodium or potassium cyanide solution (sometimes improved yields are obtained by substituting nickel cyanide for cuprous cyanide), for example :



p-Toluidine *p*-Tolunitrile

Similarly aniline $C_6H_5NH_2$ is converted into **benzonitrile** C_6H_5CN. Hydrolysis of the nitrile with sodium hydroxide solution, followed by acidification, yields the corresponding acid, for example :

$$\underset{p\text{-Tolunitrile}}{p\text{-}CH_3C_6H_4CN} + 2H_2O \longrightarrow \underset{p\text{-Toluic acid}}{p\text{-}CH_3C_6H_4COOH} + NH_3$$

By adding a concentrated solution of sodium borofluoride to a solution of a diazonium salt, the **diazonium fluoborate** is precipitated ; this decomposes into the **aryl fluoride** when cautiously heated, for example :

$$\underset{\text{Aniline}}{C_6H_5NH_2} \longrightarrow C_6H_5N_2{}^+Cl^- \xrightarrow{NaBF_4} C_6H_5N_2{}^+BF_4{}^- \xrightarrow{\text{Heat}} \underset{\text{Fluorobenzene}}{C_6H_5F} + BF_3 + N_2$$

The boron trifluoride is absorbed in sodium hydroxide solution. Similarly *p*-toluidine $p\text{-}CH_3C_6H_4NH_2$ yields ***p*-fluorotoluene** $p\text{-}CH_3C_6H_4F$.

The controlled thermal decomposition of dry aromatic diazonium fluoborates to yield an aromatic fluoride, boron trifluoride and nitrogen is known as the **Schiemann reaction.** Most diazonium fluoborates have definite decomposition temperatures and the rates of decomposition, with few exceptions, are easily controlled. Another procedure for preparing the diazonium fluoborate is to diazotise in the presence of the fluoborate ion. Fluoboric acid may be the only acid present, thus acting as acid and source of fluoborate ion. The insoluble fluoborate separates as it is formed ; side reactions, such as phenol formation and coupling, are held at a minimum ; temperature control is not usually critical and the temperature may rise to about 20° without ill effect ; efficient stirring is, however, necessary since a continuously thickening precipitate is formed as the reaction proceeds. The modified procedure is illustrated by the preparation of *p*-fluoroanisole :

$$\underset{p\text{-Anisidine}}{p\text{-}CH_3O{-}C_6H_4{-}NH_2} \xrightarrow[NaNO_2]{HBF_4,} p\text{-}CH_3O{-}C_6H_4{-}N_2{}^+BF_4{}^- \xrightarrow{\text{Heat}}$$

$$\underset{p\text{-Fluoroanisole}}{p\text{-}CH_3O{-}C_6H_4{-}F} + BF_3 + N_2$$

The *mechanism* of the Schiemann reaction is not known with certainty. Two schemes, which have been proposed, are given below. One involves carbonium ion formation :

$$ArN_2{}^+BF_4{}^- \longrightarrow Ar^+ + N_2 + \left[:\ddot{\underset{\cdot\cdot}{F}}: BF_3\right]^-$$

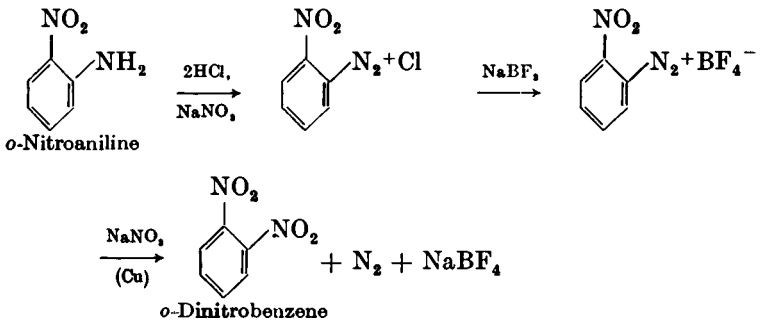
$$Ar^+ + \left[:\ddot{\underset{\cdot\cdot}{F}}: BF_3\right] \longrightarrow Ar:\ddot{\underset{\cdot\cdot}{F}}: + BF_3$$

Another postulates the intermediate formation of a free radical :

$$ArN_2{}^+BF_4{}^- \longrightarrow Ar\cdot + N_2 + \cdot\ddot{\underset{\cdot\cdot}{F}}: + BF_3$$

$$Ar\cdot + \cdot\ddot{\underset{\cdot\cdot}{F}}:F: \longrightarrow :\ddot{\underset{\cdot\cdot}{Ar}}$$

An interesting application of the diazo reaction is to the preparation of the otherwise difficultly accessible ***o-*** and ***p*-dinitrobenzenes**; *o-* or *p*-nitrophenyldiazonium fluoborates react with sodium nitrite in the presence of copper powder to yield *o-* or *p*-dinitrobenzene :



It may be mentioned that diazonium fluoborates containing the nitro group usually decompose suddenly and with violence upon heating, hence if *o-* or *p*-fluonitrobenzene are required, the fluoborates (in 10-20 g. quantities) should be mixed with 3–4 times their weight of pure dry sand (or barium sulphate or sodium fluoride) and heated cautiously until decomposition commences; intermittent heating will be required to complete the reaction.

When a solution of a diazonium salt is heated, the diazo group is replaced by hydroxyl and nitrogen is evolved :

$$ArN_2^+X^- + HOH \xrightarrow{H_2SO_4} ArOH + N_2 + HX$$

The diazonium hydrogen sulphate is used in preference to the diazonium chloride, because the latter gives small quantities of the chloro compound as a by-product :

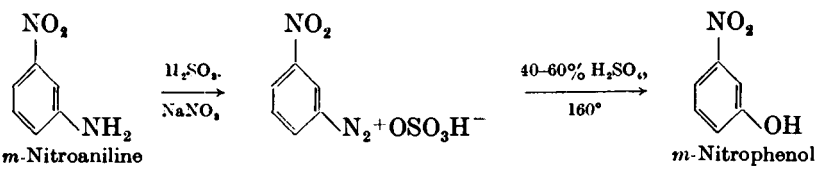
$$ArN_2^+Cl^- \longrightarrow ArCl + N_2$$

The solution must be strongly acid in order to avoid the coupling reaction between the undecomposed diazonium salt and the phenol (see under *Azo Dyes*). For the preparation of **phenol** and the **cresols**, the aqueous solution of the diazonium compound is warmed to about 50°; at higher temperatures the reaction may become unduly vigorous and lead to appreciable quantities of tarry compounds :

$$\underset{\text{Aniline}}{C_6H_5NH_2} \xrightarrow[NaNO_2]{H_2SO_4} C_6H_5N_2^+OSO_3H^- \xrightarrow[50°]{H_2O} \underset{\text{Phenol}}{C_6H_5OH} + N_2 + H_2SO_4$$

Similarly $CH_3C_6H_4NH_2$ (toluidines) $\longrightarrow$ $CH_3C_6H_4OH$ (cresols).

For certain substituted amines, a higher temperature (*e.g.*, boiling 40–60 per cent. sulphuric acid) is necessary to decompose the diazonium salt completely, for example :

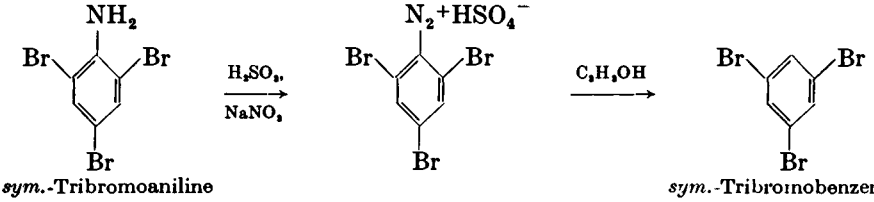


The diazonium group may be replaced by hydrogen, thus effecting the removal of the primary amino group, **deamination**, by the following methods:

(i) By boiling with ethyl alcohol:

$$ArN_2^+X^- + CH_3CH_2OH \longrightarrow ArH + N_2 + CH_3CHO + HX$$

An example of this is given in Section **IV,63**—the conversion of 3-bromo-4-aminotoluene into *m*-bromotoluene. Another application is to the preparation of ***sym.*-tribromobenzene** (Section **IV,72**):



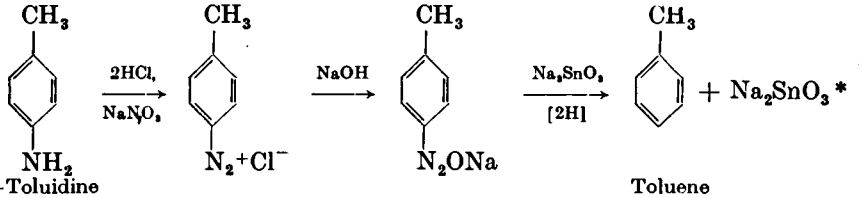
sym.-Tribromoaniline — *sym.*-Tribromobenzene

With simple aromatic compounds, appreciable quantities of the corresponding ethyl ethers are formed as by-products:

$$ArN_2^+Cl^- + C_2H_5OH \longrightarrow ArOC_2H_5 + HCl + N_2$$

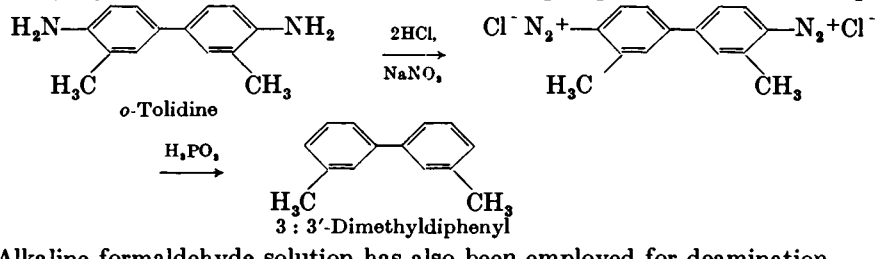
so that deamination with ethyl alcohol does not give a pure product.

(ii) By the use of an alkali stannite solution, for example:



p-Toluidine — Toluene

(iii) By treatment with a large excess of hypophosphorous acid, for example:

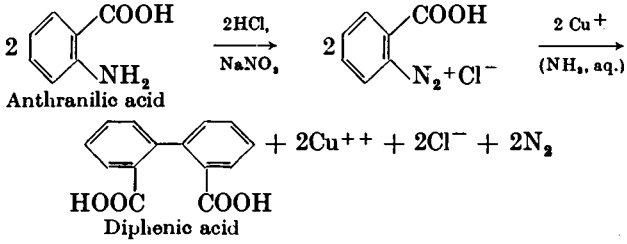


o-Tolidine

3 : 3′-Dimethyldiphenyl

Alkaline formaldehyde solution has also been employed for deamination.

An interesting coupling reaction with the diazonium salt derived from anthranilic acid leads to an excellent method for the preparation of **diphenic acid.** The reaction occurs with cuprous salts in ammoniacal solution:



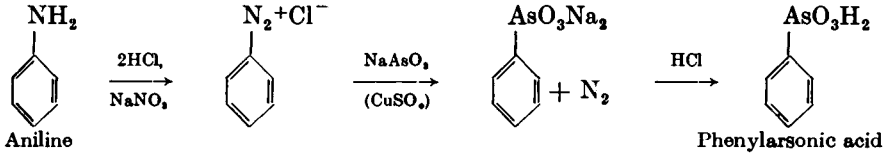
Anthranilic acid

Diphenic acid

* It is possible that an unstable di-imine is first formed and rapidly loses nitrogen:

$$ArN_2^+X^- \longrightarrow ArN{=}NH \longrightarrow ArH + N_2$$

Phenylarsonic acid may be obtained from the reaction between phenyldiazonium chloride and sodium arsenite in the presence of a trace of copper sulphate:



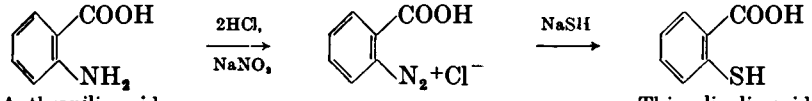
Aniline — Phenylarsonic acid

The conversion of an aromatic diazonium compound into the corresponding arsonic acid by treatment with sodium arsenite in the presence of a catalyst, such as copper or a copper salt, is called the **Bart reaction.** A modification of the reaction employs the more stable diazonium fluoborate in place of the diazonium chloride. This is illustrated by the preparation of ***p*-nitrophenylarsonic acid**:

$$p\text{-}NO_2\text{—}C_6H_4\text{—}N_2{}^+BF_4{}^- + NaAsO_2 + 2NaOH \xrightarrow{CuCl}$$
$$p\text{-}NO_2\text{—}C_6H_4\text{—}AsO_3Na_2 + NaBF_4 + N_2 + H_2O$$

CAUTION. Diazonium compounds have been used for the preparation of:—

(*a*) Mercaptans—by treatment with a solution of sodium hydrogen sulphide, for example:



Anthranilic acid — Thiosalicylic acid

(*b*) Xanthogenates—by reaction with aqueous potassium xanthogenate, and thence to mercaptans by treatment with potassium hydroxide, for example:

$$C_6H_5N_2{}^+Cl^- + C_2H_5OCS.SK \longrightarrow C_6H_5S.CS.OC_2H_5 \longrightarrow C_6H_5SH$$

(*c*) Disulphides—by interaction with a solution of sodium disulphide.

It cannot be too strongly emphasised that in all these reactions violently explosive diazo sulphides and related compounds may be formed, and another less hazardous method for the preparation of the desired compound should be used, if possible. The following reactions are known to lead to dangerous explosions:—

(i) diazotised *o*-nitroaniline, *m*-chloroaniline, 4-chloro-*o*-toluidine or β-naphthylamine and sodium disulphide;

(ii) diazotised *m*-nitroaniline and potassium xanthate; and

(iii) diazotised aniline, *p*-bromoaniline, toluidines and naphthylamines and sodium hydrogen sulphide.

IV,59. SOLID PHENYLDIAZONIUM CHLORIDE

Dissolve 3·5 g. of aniline hydrochloride in 20 ml. of absolute ethyl alcohol contained in a 50 ml. conical flask, and add 0·5 ml. of a saturated solution of hydrogen chloride in absolute ethyl alcohol. Cool in ice and add 4 g. (4·6 ml.) of *iso*-amyl nitrite (compare Section **III,53**) gradually. Allow the mixture to stand for 5–10 minutes at the room temperature, and precipitate the diazonium salt by the gradual addition of ether. Filter off the crystals at the pump on a small Buchner funnel, wash it with 5 ml. of alcohol - ether (1 : 1), and then with 10 ml. of ether. Keep

the phenyldiazonium chloride moist with ether. Do not touch the material, even when it is moist with ether, with a spatula or hard object; it may explode. Allow not more than 0·5 g. to dry on a filter paper, and cautiously warm it in a flame; it will explode. Dissolve all the solid phenyldiazonium chloride in water; it is then rendered harmless.

COGNATE PREPARATION

Solid phenyldiazonium hydrogen sulphate. Dissolve 2·5 g. (2·5 ml.) of aniline in 25 ml. of absolute ethyl alcohol contained in a 50 ml. conical flask. (If rectified spirit, 95 per cent. C_2H_5OH, is used, the yield is somewhat diminished, but the stability of the preparation is increased and consequently the element of danger attending the preparation is slightly decreased.) Add 5 g. (2·75 ml.) of concentrated sulphuric acid very slowly and with continuous shaking; some aniline sulphate may crystallise out, but will dissolve at a later stage. Add 3·25 g. (3·5 ml.) *iso*-amyl nitrite drop by drop from a small tap funnel; throughout the addition keep the mixture well stirred with the thermometer, out of sunlight, and at a temperature of 30–35° (if necessary by gentle warming on a water bath, maintained not above 40°). When all the *iso*-amyl nitrite has been added, allow the solution to stand for 10 minutes to complete the reaction, and then immerse the flask in ice water for at least 15 minutes. The phenyldiazonium sulphate separates as colourless or pale green, needle-shaped crystals. Filter the crystals at the pump using a small Buchner funnel, and wash the solid with 3–4 ml. of absolute ethyl alcohol (or rectified spirit, see note above). Remember that phenyldiazonium sulphate should be not allowed to become quite dry, and should certainly not be touched with a hard object; an explosion may result Immediately the preparation is complete, dissolve the product in water.

$$C_6H_5NH_2 \xrightarrow[HNO_2,\ H_2SO_4]{H_2SO_4,\ \textit{iso}\text{-amyl nitrite}} C_6H_5N_2^+\ HSO_4^-$$

IV,60. IODOBENZENE

Dissolve 20 g. (19·6 ml.) of aniline in a mixture of 55 ml. of concentrated hydrochloric acid (1) and 55 ml. of water contained in a 350 ml. conical flask. Place a thermometer in the solution and immerse the flask in a bath of crushed ice (2); cool until the temperature of the stirred solution falls below 5°. Dissolve 16 g. of sodium nitrite in 75 ml. of water and chill the solution by immersion in the ice bath; add the sodium nitrite solution (3) in small volumes (2–3 ml. at a time) to the cold aniline hydrochloride solution, and keep the latter well stirred with the thermometer. Heat is evolved by the reaction. The temperature should not be allowed to rise above 10° (add a few grams of ice to the reaction mixture if necessary) otherwise appreciable decomposition of the diazonium compound and of nitrous acid will occur. Add the last 5 per cent. of the sodium nitrite solution more slowly (say, about 1 ml. at a time) and, after stirring for 3–4 minutes, test a drop of the solution diluted with 3–4 drops of water with potassium iodide - starch paper (4); if no *immediate* blue colour

is obtained at the point of contact with the paper, add a further 1 ml. of the nitrite solution, and test again after 3–4 minutes. Continue until a slight excess of nitrous acid is present.

To the solution of phenyldiazonium chloride add a solution of 36 g. of potassium iodide in 40 ml. of water slowly and with shaking. Nitrogen is evolved. Allow the mixture to stand for a few hours. Fit the flask with an air condenser (5) and heat it cautiously in a boiling water bath until evolution of gas ceases. Allow to cool. Decant as much as possible of the upper aqueous layer and render the residual aqueous and organic layers alkaline by the cautious addition of 10 per cent. sodium hydroxide solution, *i.e.*, until a drop of the well-shaken mixture withdrawn on a glass rod imparts a blue colour to red litmus paper. The alkali converts any phenol present into sodium phenoxide, which, unlike phenol itself, is not volatile in steam. Immediately transfer the mixture to a steam distillation apparatus (Fig. *II*, *40*, 1) and steam distil until no more oily drops pass over. Transfer the distillate to a separatory funnel and run off the lower layer of iodobenzene into a small conical flask. The crude iodobenzene should have a pale yellow colour ; if it is dark in colour, return it to the separatory funnel and shake it with a little sodium bisulphite solution until a pale yellow colour is obtained, then remove the heavy layer as before. Dry with about 1 g. of anhydrous calcium chloride or anhydrous magnesium sulphate : filter through a fluted filter paper into a small distilling flask equipped with a short air condenser (Fig. *II*, *13*, 2). Distil using an asbestos-centred wire gauze or, better, an air bath (Fig. *II*, *5*, 3) and collect the fraction b.p. 185–190° (6). The yield of iodobenzene (an almost colourless liquid) is 33 g. ; the compound gradually develops a yellow colour upon exposure to light.

Notes.

(1) In computing the volume of acid required in the diazotisation process, it is helpful to remember that 100 ml. of concentrated hydrochloric acid, sp. gr. 1·18, contain 42·4 g. of HCl, and 100 ml. of concentrated sulphuric acid, sp. gr. 1·84, contain 176 g. H_2SO_4.

(2) For preparations on a larger scale, a stoneware vessel may be conveniently employed and the lowering of temperature achieved by the addition of a quantity of crushed ice equal in weight to that of the hydrochloric acid and water. The mixture should be stirred mechanically.

(3) It is advisable to add the sodium nitrite solution, particularly in preparations on a larger scale, through a separatory or dropping funnel with the tip of the stem extending well below the surface of the liquid : this will prevent loss of nitrous acid by surface decomposition into oxides of nitrogen.

(4) It is advisable to test the potassium iodide-starch paper with acidified sodium nitrite solution : the commercial test paper is, particularly if it has been kept for a considerable period, sometimes almost useless. The solution must contain an excess of acid at all times, *i.e.*, it must give a blue colour on Congo red paper.

(5) In large scale preparations, the mixture should be transferred to a large flask before heating.

(6) The iodobenzene is conveniently distilled under reduced pressure and the fraction b.p. 77–80°/20 mm. or 63–64°/8 mm. collected. The product has a higher degree of purity than that obtained directly from benzene (Section IV,21).

Cognate Preparations

***p*-Iodotoluene.** Use 27 g. of *p*-toluidine, 63 ml. of concentrated hydrochloric acid and 63 ml. of water : warm, if necessary, until all the amine dissolves. Cool the solution with vigorous stirring to 0–5° by

immersion in a freezing mixture of ice and salt and the addition of a little crushed ice. Diazotise by the introduction, with stirring (mechanical or with a thermometer), of a solution of 18·5 g. of sodium nitrite in 40 ml. of water; maintain the temperature of the solution at 0–5° if possible, but do not allow it to rise above 10°. Add a solution of 44 g. of potassium iodide in an equal weight of water gradually and with stirring. Allow to stand for 1 hour at the laboratory temperature and then heat cautiously on a water bath until evolution of nitrogen ceases. Allow to cool: a dark-coloured oil settles to the bottom and soon solidifies. Pour off as much of the aqueous layer as possible, add 1–2 g. of sodium bisulphite to remove the dark colour (gentle warming may be necessary), and then render the mixture alkaline with 10 per cent. sodium hydroxide solution in order to fix any cresol which may be formed. Steam distil the mixture and employ a beaker as the receiver; if the *p*-iodotoluidine solidifies in the condenser, turn off the condenser water for a few moments until the solid melts and runs down into the receiver. Filter off the solid in the receiver and recrystallise it from alcohol. The yield of *p*-iodotoluene (colourless plates), m.p. 35°, b.p. 211–212°, is 50 g.

***p*-Iodonitrobenzene.** Stir a mixture of 50 g. of *p*-nitroaniline (Section IV,51), 75 g. (41 ml.) of concentrated sulphuric acid and 300 ml. of water for 1 hour. Cool the mixture to 0–5°, and diazotise with a solution of 25 g. of sodium nitrite in 75 ml. of water. Filter the cold solution, and add the filtrate with stirring to a solution of 100 g. of potassium iodide in 300 ml. of water. Collect the precipitated solid by suction filtration and recrystallise it from ethyl alcohol. The yield of *p*-iodonitrobenzene, m.p. 171°, is 73 g.

IV,61. *p*-CHLOROTOLUENE

In a 1·5 or 2-litre round-bottomed flask, prepare cuprous chloride from 105 g. of crystallised copper sulphate as detailed in Section II,50, *1*. Either wash the precipitate once by decantation or filter it at the pump and wash it with water containing a little sulphurous acid; dissolve it in 170 ml. of concentrated hydrochloric acid. Stopper the flask loosely (to prevent oxidation) and cool it in an ice-salt mixture whilst the diazotisation is being carried out.

Dissolve 36 g. of *p*-toluidine in 85 ml. of concentrated hydrochloric acid and 85 ml. of water contained in a 750 ml. conical flask or beaker. Cool the mixture to 0° in an ice-salt bath with vigorous stirring or shaking and the addition of a little crushed ice. The salt, *p*-toluidine hydrochloride, will separate as a finely-divided crystalline precipitate. Add during 10–15 minutes a solution of 24 g. of sodium nitrite in 50 ml. of water (1); shake or stir the solution well during the diazotisation, and keep the mixture at a temperature of 0–5° by the addition of a little crushed ice from time to time. The hydrochloride will dissolve as the very soluble diazonium salt is formed; when all the nitrite solution has been introduced, the solution should contain a trace of free nitrous acid. Test with potassium iodide-starch paper (see Section IV,60).

Pour the cold diazonium chloride solution slowly and with shaking into the cold cuprous chloride solution (2). The mixture becomes very

thick, owing to the separation of an addition product between the diazonium salt and the cuprous chloride ($CH_3C_6H_4N_2^+Cl^-$,CuCl). Allow the mixture to warm up to room temperature without external heating, and shake occasionally (3). When the temperature reaches about 15°, the solid addition complex commences to break down with the liberation of nitrogen and the formation of an oily layer of *p*-chlorotoluene. Warm the mixture on a water bath to about 60° to complete the decomposition of the double salt ; shake occasionally. When the evolution of nitrogen ceases, steam distil the mixture (compare Fig. *II*, *40*, 1) until no more oily drops are present in the distillate. Transfer the distillate to a separatory funnel, and remove the layer of *p*-chlorotoluene. Wash it successively with 30 ml. of 10 per cent. sodium hydroxide solution (to remove any *p*-cresol which may be present), water, an equal volume of concentrated sulphuric acid (to remove a trace of azo compound that usually colours the crude product and cannot be removed by distillation), and water (to remove the acid). Dry with 3–4 g. of anhydrous calcium chloride or anhydrous magnesium sulphate, decant or filter through a small fluted filter paper into a small distilling flask (Fig. *II*, *13*, 2), and distil on an asbestos-centred gauze or from an air bath (Fig. *II*, *5*, 3). Collect the *p*-chlorotoluene at 158-162° (a colourless liquid ; m.p. 6–7°) ; the yield is 33 g.

Notes.

(1) The sodium nitrite solution is conveniently added from a dropping funnel ; it is recommended, particularly for preparations on a larger scale, that the tip of the stem of the funnel dip well below the surface of the liquid.

(2) The diazonium salt solution decomposes on standing and hence must be mixed with the cuprous chloride solution without delay. Mechanical stirring is an advantage.

(3) For preparations on a larger scale, mechanical stirring is essential and should be continued for 2–3 hours after the solution has attained room temperature.

Cognate Preparations

o-Chlorotoluene. Proceed as for *p*-chlorotoluene, but use 36 g. of *o*-toluidine. Collect the *o*-chlorotoluene at 155–158° ; the yield is 33 g.

Chlorobenzene. Prepare a solution of phenyldiazonium chloride from 31 g. (30·5 ml.) of aniline, 85 ml. of concentrated hydrochloric acid, 85 ml. of water, and a solution of 24 g. of sodium nitrite in 50 ml. of water (for experimental details, see Section **IV,60**). Prepare cuprous chloride from 105 g. of crystallised copper sulphate (Section **II,50**, *1*), and dissolve it in 170 ml. of concentrated hydrochloric acid. Add the cold phenyldiazonium chloride solution with shaking or stirring to the cold cuprous chloride solution ; allow the mixture to warm up to room temperature. Follow the experimental details given above for *p*-chlorotoluene. Wash the chlorobenzene separated from the steam distillate with 40 ml. of 10 per cent. sodium hydroxide solution (to remove phenol), then with water, dry with anhydrous calcium chloride or magnesium sulphate, and distil. Collect the chlorobenzene (a colourless liquid) at 131-133° (mainly 133°). The yield is 29 g.

***m*-Chloronitrobenzene.** This preparation is very similar to that of *p*-chlorotoluene, but certain modifications must be introduced. The quantities required are : 46 g. of *m*-nitroaniline (Section **IV,44**), 85 ml. of concentrated hydrochloric acid, 85 ml. of water, and a solution of 24 g.

of sodium nitrite in 50 ml. of water (if the resulting diazonium salt solution is not clear, it must be filtered); cuprous chloride, from 105 g. of crystallised copper sulphate (Section **II,50,** *1*), dissolved in 170 ml. of concentrated hydrochloric acid. Run the diazonium salt solution into the solution of cuprous chloride while the temperature is kept at 25–30° (water bath); at lower temperatures the decomposition of the unstable addition compound proceeds too slowly and would cause too violent an evolution of nitrogen upon warming, and at a higher temperature the formation of tarry by-products increases. Warm the mixture under a reflux condenser on a water bath until the evolution of nitrogen ceases. Steam distil (1); if the *m*-chloronitrobenzene solidifies in the condenser, turn off the condenser water for a few moments until the solid melts and runs down into the receiver. Allow the steam distillate to cool, decant the water, and shake the solid with 200 ml. of 1 per cent. sodium hydroxide solution at 50° (to remove *m*-nitrophenol, if present). Allow the mixture to cool, filter with suction, wash with a little cold water and dry in the air. Determine the m.p. If this is not satisfactory, *i.e.*, if it is appreciably below 44–45°, purify the product either by recrystallisation from a small volume of alcohol or preferably by distillation under diminished pressure (Figs. *II, 19,* 1 and *II, 19,* 3-4); it boils at 124–125°/18 mm. or 116–117°/12 mm. and the distillate solidifies to a pale yellow solid, m.p. 44–45°. The yield is 50–55 g., depending upon the purity of the original *m*-nitroaniline.

Note.

(1) The steam distillation may be omitted, if desired, by utilising the following method of purification. Allow the reaction mixture to cool, decant the aqueous layer and dissolve the residue in about 150 ml. of benzene. Wash the benzene solution with water, 1 per cent. sodium hydroxide solution, and finally with water; dry with anhydrous magnesium sulphate, distil off the benzene on a water bath, and distil the residue under diminished pressure.

IV,62. *p*-BROMOTOLUENE (*by the Sandmeyer Reaction*)

Method 1. Prepare a **solution of cuprous bromide** by refluxing 31·5 g. of crystallised copper sulphate, 10 g. of clean copper turnings, 77 g. of crystallised sodium bromide, 15 g. (8·2 ml.) of concentrated sulphuric acid and 500 ml. of water contained in a 2·5 litre round-bottomed flask over a flame for 3–4 hours until the solution acquires a yellowish colour; if the blue colour is not discharged, add a few grams of sodium bisulphite to complete the reduction.

In a 1 litre flask mix 53·5 g. of *p*-toluidine and 400 ml. of water, and then add cautiously 98 g. (53·5 ml.) of concentrated sulphuric acid; warm until the *p*-toluidine dissolves. Cool the flask in a bath of ice and salt to 0–5°; add about 100 g. of crushed ice to the contents of the flask in order to accelerate the cooling. Add slowly and with frequent shaking a solution of 35 g. of sodium nitrite in 60 ml. of water until a slight excess of sodium nitrite is present (see Section **IV,60**); keep the temperature of the mixture below 10°.

Equip the 2·5 litre flask holding the cuprous solution for steam distillation (Fig. *II, 40,* 1) with the addition of a third tube (7–8 mm. in diameter) leading almost to the bottom of the flask; attach a short-stemmed,

separatory funnel to this by means of a short length of rubber " pressure " tubing and support the funnel in a ring clamped to a retort stand. Heat the cuprous bromide solution to boiling, add the *p*-tolyldiazonium sulphate solution from the separatory funnel whilst steam is passed rapidly through the mixture. In order to reduce the amount of decomposition of the diazonium salt solution, transfer only about one-fourth to the separatory funnel (the remainder being kept in the freezing mixture) and run this into the cuprous bromide solution : when the funnel is nearly empty, transfer a further portion of the cold diazonium solution to it without interrupting the addition. Add all the diazonium solution in this way during 20–30 minutes. Continue the steam distillation until no more organic matter distils. Render the distillate alkaline with 20 per cent. sodium hydroxide solution (to remove any *p*-cresol present), shake well, and separate the crude *p*-bromotoluene. In order to obtain a colourless product, wash the crude substance with 40-50 ml. of warm (30°) concentrated sulphuric acid, then with water, sodium hydroxide solution, and finally with water. If the *p*-bromotoluene solidifies, warm the wash liquids to 30° before use ; unless this is done, considerable loss may occur. Dry over anhydrous magnesium sulphate or calcium chloride, warm, filter, and distil through an air-cooled condenser (Fig. *II*, *13*, 2). Collect the *p*-bromotoluene at 182–184°. The yield is 60 g. ; m.p. 25–26°.

Method 2. Prepare 40 g. of cuprous bromide according to Section **II,50,2** (about 75 g. of crystallised copper sulphate are required) and dissolve it in 40 ml. of constant boiling point hydrobromic acid (48% HBr) contained in a 2·5 litre round-bottomed flask.

Prepare a solution of *p*-tolyldiazonium chloride from 53·5 g. of *p*-toluidine using the proportions and experimental conditions given under p-*Chlorotoluene* (Section **IV,61**). Add the diazonium chloride solution to the boiling cuprous bromide solution, and proceed as in *Method 1.* The yield of pure, colourless *p*-bromotoluene, b.p. 182–184° (mainly 183°), is 40 g. ; m.p. 26°.

Cognate Preparations

o-Bromotoluene. Use 53·5 g. of *o*-toluidine and the other components as above. The yield of *o*-bromotoluene, b.p. 178–181°, is of the same order.

o-Chlorobromobenzene. Place a mixture of 64 g. of *o*-chloroaniline (Section **IV,34**) and 175 ml. of constant boiling point hydrobromic acid (sp. gr. 1·48 ; 100 ml. contains 71 g. of HBr) in a 1-litre flask set in an ice-salt bath, and cool it to 0–5° by the addition of a little ice. Add, with shaking or stirring, a solution of 35 g. of sodium nitrite in 70 ml. of water until a slight excess of nitrous acid is present (starch-potassium iodide paper test ; Section **IV,60**) ; maintain the temperature below 10° by the addition of ice if necessary. Prepare a solution of 40 g. of cuprous bromide in 40 ml. of 48 per cent. hydrobromic acid contained in a 2·5-litre round-bottomed flask (see *Method 2* above), heat to boiling, and add the *o*-chlorophenyldiazonium bromide solution as above. When all the latter has been introduced, pass steam through the mixture until no more organic material distils. Follow the procedure, including purification, given for p-*Bromotoluene.* Collect the *o*-chlorobromobenzene (a colourless liquid) at 200–202°. The yield is 85 g.

This procedure may be employed for ***m*-chlorobromobenzene**, b.p. 191–194° from *m*-chloroaniline; ***m*-dibromobenzene**, b.p. 215–217°, from *m*-bromoaniline; and **o-bromoanisole**, b.p. 114–116°/29 mm. from *o*-anisidine (the sulphuric acid washing is omitted in the last example).

β-Bromonaphthalene. The preparation from β-naphthylamine, which has carcinogenic properties, is avoided by the use of 2-naphthylamine-1-sulphonic acid ("2-amino-1-naphthalenesulphonic acid"); the latter is obtained commercially by cautious treatment of β-naphthol with sulphuric acid—the SO_3H group first enters the 1-position—followed by the Bucherer reaction. Diazotisation and reaction with cuprous bromide yields 2-bromonaphthalene-1-sulphonic acid; heating with sulphuric acid eliminates the sulphonic acid group to give 2-bromonaphthalene.

Dissolve 223 g. of 2-naphthylamine-1-sulphonic acid, with stirring, in 1700 ml. of 0·6*N* sodium hydroxide solution: add, with stirring, an aqueous solution of 69 g. of sodium nitrite, and filter the resulting solution. Place 500 ml. of concentrated hydrochloric acid and 200 g. of crushed ice in a 2½ gallon battery jar or earthenware crock and equip the latter with a mechanical stirrer. Introduce the filtered solution of sodium nitrite and sodium 2-napthylamine-1-sulphonate * slowly with stirring, and maintain the temperature at 0–5° by adding crushed ice. Collect the reddish-brown precipitate which forms on a large Buchner funnel and wash it with about 1 litre of ice water. Whilst the diazotisation is in progress, suspend 320 g. of cuprous bromide (from 600 g. of crystallised copper sulphate; Section **II,50,2**) in 150 ml. of 48 per cent. hydrobromic acid and 400 ml. of water. Add the damp cake of the diazonium compound portionwise and with vigorous stirring to the cuprous bromide suspension contained in a 2·5 litre battery jar or beaker. After the vigorous evolution of nitrogen has subsided, heat the mixture to 95–100° on a steam bath and then filter the hot mixture through a large Buchner funnel. Pour the filtrate back into the battery jar and add 225 g. of potassium chloride with stirring. Allow the resulting paste to cool to room temperature, filter with suction, and wash with 500 ml. of 20 per cent. aqueous potassium chloride. Dry the reddish-brown precipitate of 2-bromonaphthalene-1-sulphonic acid in the air overnight, and transfer it to a 2·5 litre round-bottomed flask. Add dilute sulphuric acid (prepared from 400 ml. of the concentrated acid and 400 g. of crushed ice), attach a reflux condenser, and reflux the mixture gently, using an electric heating mantle, for 12–16 hours. Cool to room temperature; pour on to about 1 kg. of crushed ice. Transfer the mixture with the aid of 1 litre of benzene to a large separatory funnel, shake well, remove the benzene layer and wash the latter with water until the washings are neutral to litmus. Dry the benzene solution with anhydrous magnesium sulphate, remove the benzene at atmospheric pressure and distil the residue under reduced pressure. Collect the β-bromonaphthalene at 100–101°/2 mm. or at 140°/20 mm.; this solidifies to a pale yellow solid, m.p. 56–57°. The yield is 135 g.

The pale yellow colour cannot be removed by redistillation or recrystallisation; the coloured product probably contains some amino compound rendering it unsuitable for conversion into a Grignard reagent. A pure

* If the solid sodium salt is available, it may be dissolved in 1700 ml. of distilled water and a solution containing 69 g. of sodium nitrite added.

white product may be obtained by the following chromatographic procedure (see Section **II,46**). Dissolve 100 g. of the coloured compound in 350 ml. of *n*-hexane and pass the solution through a 3–4″ column of activated alumina (80–200 mesh); wash the column with 300 ml. of *n*-hexane. Remove the *n*-hexane by distillation: 98 g. of pure β-bromonaphthalene, m.p. 58°, remains. This is sufficiently pure for use in Grignard reactions.

IV,63. *m*-BROMOTOLUENE

The successive stages in the preparation are as follows :—

***p*-Acetotoluidide and *m*-bromo-*p*-acetotoluidide (3-bromo-4-acetaminotoluene).** Prepare a solution of *p*-acetotoluidide in glacial acetic acid by boiling 107 g. of *p*-toluidine with 400 ml. of glacial acetic acid in a 1-litre round-bottomed flask, provided with a reflux condenser, for 2 hours. Remove the reflux condenser, replace it by a mechanical stirrer, and stir the solution vigorously; some *p*-acetotoluidide may separate as small crystals as the temperature falls (1). When the temperature has fallen to about 45°, add 162·5 g. (51 ml.) of bromine from a separatory funnel at such a rate that the temperature of the well-stirred mixture is maintained at 50–55°. A precipitate may separate during the addition which requires 30–40 minutes, but this dissolves later. Continue the stirring for a further 30 minutes after all the bromine has been added. Then pour the reaction mixture in a thin stream into a well-stirred mixture of 1 kilo of crushed ice and 1 kilo of water to which 14 g. of solid sodium bisulphite has been added. If the colour of the bromine persists, add a little more sodium bisulphite. Filter the crystalline 3-bromo-4-acetaminotoluene with suction on a Buchner funnel, wash thoroughly with water and press well. Dry in the air until the weight does not exceed 250 g. (2); further purification is unnecessary before proceeding to the next stage.

3-Bromo-4-aminotoluene hydrochloride. Transfer the partially dried 3-bromo-4-acetaminotoluene to a 1·5-litre round-bottomed flask, add 250 ml. of rectified spirit, and reflux on a water bath until the solid dissolves completely. Introduce through the condenser 250 ml. of concentrated hydrochloric acid to the boiling solution and continue the refluxing for a further 3 hours. During this time crystals of 3-bromo-4-aminotoluene hydrochloride separate. Pour the hot mixture into a 1-litre beaker and cool thoroughly. Filter the crystals of the hydrochloride at the pump through a Buchner funnel and wash rapidly with two 50 ml. portions of chilled rectified spirit. The yield of the hydrochloride is 150 g.

3-Bromo-4-aminotoluene. Suspend the hydrochloride in 400 ml. of water in a 1-litre beaker equipped with a mechanical stirrer. Add a solution of 70 g. of sodium hydroxide in 350 ml. of water. The free base separates as a dark heavy oil. After cooling to 15–20°, transfer the mixture to a separatory funnel and run off the crude 3-bromo-4-aminotoluene. This weighs 125 g. and can be used directly in the next step (3).

***m*-Bromotoluene.** To a cold mixture of 400 ml. of rectified spirit and 100 ml. of concentrated sulphuric acid contained in a 2·5-litre round-bottomed flask, provided with an efficient mechanical stirrer, add 125 g. of crude 3-bromo-4-aminotoluene. Stir the solution and cool to 5°;

then add slowly a solution of 74 g. of pure sodium nitrite in 135 ml. of water from a separatory funnel taking care that the temperature does not rise above 10°. Continue the stirring for 20 minutes after all the nitrite solution has been added in order to complete the diazotisation (test with potassium iodide - starch paper for the presence of free nitrous acid). Add 17·5 g. of copper bronze (which has been washed with ether) or copper powder (Section **II,50,** *4*) to the diazotised solution, and replace the stirrer by a long double surface condenser. Have an ice bath at hand to cool the flask if the reaction becomes too vigorous. Warm the flask *cautiously* on a water bath until a vigorous evolution of gas commences, then immerse at once in an ice bath to prevent loss through the condenser by too rapid evolution of nitrogen and acetaldehyde. When the reaction has subsided, again warm the flask gently, and finally heat on a boiling water bath for 10 minutes. At the end of the reaction, the colour of the solution changes from reddish-brown to yellow. Add 1 litre of water and steam distil the mixture as long as oily drops pass over. Separate the heavy yellow oil, wash it with two 100 ml. portions of 10 per cent. sodium hydroxide solution, once with 50 ml. of water, twice with 75 ml. portions of ice-cold concentrated sulphuric acid, once with 50 ml. of water, and finally with 50 ml. of 5 per cent. sodium carbonate solution. Dry with 2–3 g. of anhydrous magnesium sulphate or calcium chloride, and filter through a little glass wool into a distilling flask. Distil, using an air condenser, and collect the *m*-bromotoluene (a colourless liquid) at 180–183°. The yield is 65 g.

Notes.

(1) If the mixture is cooled in ice, most of the *p*-acetotoluidide separates out in a crystalline form. It may be recrystallised from alcohol.

(2) Unless the material is at least partly dried before hydrolysis, the yield of hydrochloride is reduced because of its solubility. If pure 3-bromo-4-acetaminotoluene is required, the crude material may be recrystallised from 50 per cent. alcohol with the addition of a little decolourising carbon ; it separates as colourless needles, m.p. 116–117° (180 g.).

(3) If pure 3-bromo-4-aminotoluene is required, the crude base may be purified either by steam distillation or, more satisfactorily, by distillation under reduced pressure. The oil is dried with 5 g. of sodium hydroxide pellets, and distilled under reduced pressure from a Claisen flask with a fractionating side arm : a little *p*-toluidine may be present in the low boiling point fraction, and the pure substance is collected at 92–94°/3 mm. or at 120–122°/30 mm. The purified amine solidifies on cooling and melts at 17–18°.

IV,64. *o*-BROMOTOLUENE (*by the Gattermann Reaction*)

In a 1 or 1·5 litre round-bottomed flask prepare a solution of 53·5 g. of *o*-toluidine in 170 ml. of 48 per cent. hydrobromic acid, cool to 5° by immersion in a bath of ice and salt. Diazotise by the gradual addition of a solution of 36·5 g. of sodium nitrite in 50 ml. of water ; stopper the flask after each addition and shake until all red fumes are absorbed. Keep the temperature between 5° and 10°. When the diazotisation is complete, add 2 g. of copper powder or copper bronze, attach a reflux condenser to the flask, and heat very cautiously on a water bath. *Immediately* evolution of gas occurs, cool the flask in crushed ice ; unless the

flask is rapidly removed from the water bath, the reaction may become so violent that the contents may be shot out of the flask. When the vigorous evolution of nitrogen moderates, heat the flask on a water bath for 30 minutes. Then dilute with 400 ml. of water, and steam distil the mixture until about 750 ml. of distillate are collected. Render the distillate alkaline with 10 per cent. sodium hydroxide solution (about 50 ml.) and separate the lower red layer of crude *o*-bromotoluene. Wash it with two 20 ml. portions of concentrated sulphuric acid (which removes most of the colour) and then twice with water. Dry with anhydrous magnesium sulphate or calcium chloride, and distil from a Claisen flask with lagged fractionating side arm. Collect the *o*-bromotoluene at 178–181°.

IV,65. BENZENESULPHINIC ACID

Dissolve 9·3 g. (9·1 ml.) of aniline in a mixture of 19.6 g. (10·7 ml.) of concentrated sulphuric acid and 100 ml. of water, and cool to about 5°. Diazotise by the addition of a solution of 7·0 g. of sodium nitrite in 15 ml. of water to an end point with potassium iodide - starch paper ; maintain the temperature below 10°. Add an ice-cold mixture of 40 g. (22 ml.) of concentrated sulphuric acid and 30 ml. of water, cool in ice and pass sulphur dioxide into the solution until there is no further increase in weight (about 25 g.). The solution should not develop any appreciable colour, during this operation and should remain quite clear. When the solution is saturated with sulphur dioxide, transfer it to a beaker provided with a mechanical stirrer, and add copper powder (Section **II,50**, *4*) or copper bronze (previously washed with ether) gradually until no more nitrogen is evolved (about 50 g. of copper powder are required). Filter at the pump and wash the precipitate with several small amounts of dilute ammonia solution to remove any sulphinic acid which may have separated : add the washings to the filtrate. The combined filtrate and washings should be acid to Congo red paper. Treat it with concentrated ferric chloride solution as long as any precipitate forms. Filter the precipitate of ferric benzenesulphinate, and wash it with a little water. Decompose the ferric salt with a slight excess of 5 per cent. sodium hydroxide solution, and filter the precipitated ferric hydroxide. Acidify the filtrate and extract the sulphinic acid with ether. Upon evaporation of the solvent, pure benzenesulphinic acid, m.p. 84°, is obtained as a colourless crystalline solid. The yield is 10 g. It oxidises in the air.

IV,66. *p*-TOLUNITRILE (*p*-TOLYL CYANIDE)

Cuprous cyandide solution (compare Section **II,50**, *3*). Prepare the following solutions :—

(i) 100 g. of powdered copper sulphate pentahydrate in 320 ml. of water (warming may be necessary), contained in a 1 litre round-bottomed flask ;

(ii) 28 g. of sodium bisulphite in 80 ml. of water (this may require filtering) ; and

(iii) 28 g. of commercial potassium cyanide (98–99 % KCN) in 80 ml. of water.

Warm the copper sulphate solution to 50–60°, and add dilute sulphuric acid until it is acid to Congo red. Add the sodium bisulphite solution,

previously warmed to 60°, during 1–2 minutes with shaking (1), and immediately add the potassium cyanide solution, also warmed to 60°, in five portions with vigorous shaking (1). There is a slight frothing and a white precipitate of cuprous cyanide is formed. After 10 minutes, filter with suction on a Buchner funnel and wash the precipitate with four 25 ml. portions of hot water. Transfer the precipitate to a 1-litre round-bottomed flask, and dissolve it either in a solution of 40 g. of sodium cyanide in 100 ml. of water or in a solution of 52 g. of potassium cyanide in 125 ml. of water.

Diazotise 36 g. of *p*-toluidine, following the method given under p-*Chlorotoluene* (Section **IV,61**). Warm the cuprous cyanide solution on a water bath to about 60°, and add the cold diazonium salt solution in small quantities at a time, shaking vigorously (1) after each addition and taking care to maintain the temperature of the mixture at 60–70°. Attach a reflux condenser to the flask and heat on a boiling water bath for 15–20 minutes in order to complete the reaction. Equip the flask for steam distillation (Fig. *II*, *40*, 1), and pass steam into the mixture until no more yellow oil passes over ; if the oil solidifies in the condenser tube, turn off the condenser water, and, after the material melts and flows through, slowly turn on the water again. Cool the distillate in ice water, and when the crude *p*-tolunitrile has solidified, filter it at the pump and press well to remove liquid impurities. Dry upon filter paper or in a desiccator. Mix the dried product with 2–3 g. of decolourising carbon, transfer to a small distilling flask, and distil using an air condenser (Fig. *II*, *13*, 2). Collect the pure *p*-tolunitrile at 215–219° (2) ; this solidifies on cooling and melts at 29°. The yield is 26 g.

Notes.

(1) Mechanical stirring is preferable.

(2) The crude substance may also be distilled under diminished pressure and the *p*-tolunitrile collected at 104–106°/20 mm.

Hydrolysis of *p*-tolunitrile to *p*-toluic acid. Boil a mixture of 5 g. of *p*-tolunitrile, 80 ml. of 10 per cent. aqueous sodium hydroxide solution and 15 ml. of alcohol under a reflux condenser. (The alcohol is added to prevent the nitrile, which volatilises in the steam, from crystallising in the condenser ; it also increases the speed of hydrolysis. The alcohol may be omitted in the hydrolysis of nitriles which are liquid at the ordinary temperature, *e.g.*, benzonitrile.) The solution becomes clear after heating for about 1 hour, but continue the boiling for a total period of 1·5 hours to ensure complete hydrolysis. Detach the condenser and boil the solution for a few minutes in the open flask to remove dissolved ammonia and incidentally some of the alcohol (*CAUTION !*). Cool, and add concentrated hydrochloric acid until precipitation of the *p*-toluic acid is complete. When cold, filter off the *p*-toluic acid with suction and wash with a little cold water. Recrystallise from a mixture of equal volumes of water and alcohol (methylated spirit) or from benzene. The yield of *p*-toluic acid, m.p. 178°, is 5·5 g.

Cognate Preparations

Benzonitrile (phenyl cyanide). Prepare a cuprous cyanide solution in a 500 ml. round-bottomed flask as above, but use the following quantities : 65 g. of crystallised copper sulphate in 205 ml. of water, 18 g. of sodium bisulphite in 52 ml. of water, and 18 g. of potassium cyanide in

52 ml. of water ; dissolve the precipitated cuprous cyanide in a solution of 26 g. of sodium cyanide in 65 ml. of water or of 33·5 g. of potassium cyanide in 90 ml. of water. Diazotise 20 g. (19·6 ml.) of aniline, following the experimental details given under *Iodobenzene* (Section **IV,60**). Add the cold phenyldiazonium chloride solution to the cuprous cyanide solution warmed at 60–70° and proceed as for p-*Tolunitrile*. Extract the steam distillate with three 30 ml. portions of ether, shake the ethereal solution with 20 ml. of 10 per cent. sodium hydroxide solution (to remove traces of phenol produced by the decomposition of the diazonium chloride solution), then with an equal volume of dilute sulphuric acid (to remove traces of the evil-smelling phenyl *iso*-cyanide C_6H_5NC), and finally with an equal volume of water. Dry the ethereal extract over anhydrous magnesium sulphate or calcium chloride, distil off the ether from a small flask using the apparatus shown in Fig. *II*, *13*, 4 ; then fit a short air condenser to the flask (Fig. *II*, *13*, 2) and distil the benzonitrile. Collect the fraction of b.p. 188–191°. The yield is 16 g.

Hydrolysis of benzonitrile to benzoic acid. Boil 5·1 g. (5 ml.) of benzonitrile and 80 ml. of 10 per cent. sodium hydroxide solution in a 250 ml. round-bottomed flask fitted with a reflux water condenser until the condensed liquid contains no oily drops (about 45 minutes). Remove the condenser, and boil the solution in an open flask for a few minutes to remove free ammonia. Cool the liquid, and add concentrated hydrochloric acid, cautiously with shaking, until precipitation of benzoic acid is complete. Cool, filter the benzoic acid with suction, and wash with cold water ; dry upon filter paper in the air. The benzoic acid (5·8 g.) thus obtained should be pure (m.p. 121°). Recrystallise a small quantity from hot water and redetermine the m.p.

$$C_6H_5CN + 2H_2O \xrightarrow{(NaOH)} C_6H_5COOH + NH_3$$

o-Tolunitrile. The preparation is similar to that described for p-*Tolunitrile* except that *p*-toluidine is replaced by *o*-toluidine. The *o*-tolunitrile is isolated by steam distillation ; the oil, which may be dissolved in a little benzene, is distilled. The *o*-tolunitrile passes over as an almost colourless liquid at 94–96°/20 mm.

IV,67. FLUOROBENZENE

Dissolve 46·5 g. (45·5 ml.) of aniline in a mixture of 126 ml. of concentrated hydrochloric acid and 126 ml. of water contained in a 1-litre beaker. Cool to 0–5° in a bath of ice and salt, and add a solution of 36·5 g. of sodium nitrite in 75 ml. of water in small portions ; stir vigorously with a thermometer (1) and maintain the temperature below 10°, but preferably at about 5° by the addition of a little crushed ice if necessary. The diazotisation is complete when a drop of the solution diluted with 3–4 drops of water gives an immediate blue colouration with potassium iodide - starch paper ; the test should be performed 3–4 minutes after the last addition of the nitrite solution. Prepare a solution of 76 g. of sodium fluoborate (2) in 150 ml. of water, cool, and add the chilled solution slowly to the diazonium salt solution ; the latter must be kept well stirred (1) and the temperature controlled so that it is below 10°. Allow to stand for 10 minutes with frequent stirring. Filter

the precipitated phenyldiazonium fluoborate with suction on a Buchner funnel (3), drain well, and wash the yellow solid with about 30 ml. of ice water, 15 ml. of methyl alcohol, and 30–40 ml. of ether ; suck the solid as free as possible from liquid after each washing. Spread the salt upon absorbent filter paper and dry overnight in a vacuum desiccator or, if possible, in a current of air. The yield of phenyldiazonium fluoborate is 60–65 g. ; the pure salt melts with decomposition at 119–120°.

Assemble the apparatus shown in Fig. *IV*, *67*, 1 ; this is self-explanatory. The distilling flask has a capacity of 250 ml. and the beaker contains 150 ml. of 10 per cent. sodium hydroxide solution. All corks must fit well and should be coated with paraffin wax (by dipping into molten wax, and allowing to drain). Place half of the yield of the dry phenyldiazonium fluoborate in the distilling flask. Heat the solid gently with a small luminous flame at one point near its surface until decomposition begins ; withdraw the flame and allow the reaction to continue

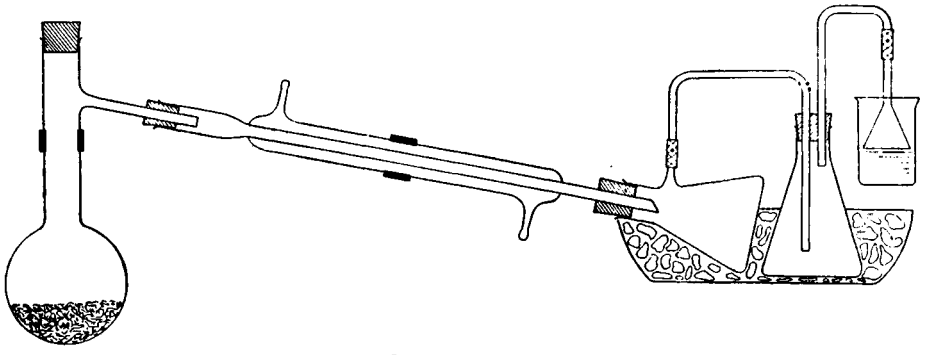


Fig. *IV*, *67*, 1.

as long as it will (4). Continue the cautious heating from time to time as may be necessary to keep the reaction going. When the decomposition appears to be complete, heat the flask more strongly to drive off any remaining fluorobenzene. Allow to cool, add the other half of the borofluoride through a glazed paper funnel, and decompose it as before ; finally heat the flask strongly until no more fumes of boron trifluoride are evolved in order to drive off the last traces of fluorobenzene. Most of the fluorobenzene collects in the first receiver. Wash the combined distillates three times with an equal volume of 10 per cent. sodium hydroxide solution (5) or until the washings are almost colourless ; this will remove any phenol present. Remove the last sodium hydroxide washing as completely as possible, and then shake with an equal volume of almost saturated salt solution. Dry over anhydrous calcium chloride or magnesium sulphate, and distil from 50 ml. distilling flask (Fig. *II*, *13*, 2 but with a Liebig condenser replacing the air condenser). Collect the fluorobenzene (a colourless liquid) at 84–85°. The yield is 24 g.

Notes.

(1) Mechanical stirring, although not essential for small scale preparations, is advantageous and increases the yield slightly.

(2) The use of sodium fluoborate solution supersedes the less convenient fluoboric acid and permits the preparation to be carried out in ordinary glass vessels.

If it is desired to employ fluoboric acid HBF_4, it can be prepared by adding 100 g. of A.R. boric acid in small proportions to 325 g. of A.R. hydrofluoric acid (40 per cent. HF) cooled in ice; the hydrofluoric acid is contained in a Bakelite beaker, a beaker coated with wax or in a lead vessel. A simple container may also be prepared by cutting off the neck of the wax bottle (in which the hydrofluoric acid is supplied) with a large (*e.g.*, a " butcher's ") knife which has been slightly warmed. One-third of the above solution should be employed in the preparation. ***Handle with great care.***

Note on precautions to be adopted when using hydrofluoric acid. Attention is directed to the fact that hydrofluoric acid in contact with the skin produces extremely painful burns. In case of accident, the burned surface, which becomes white, is held under running water until the natural colour returns. A paste made from magnesium oxide and glycerine should be applied immediately; this is said to be helpful in preventing the burn becoming serious. It is advisable to wear acid-resisting rubber gloves and protective goggles.

(3) It is better to employ a large sintered glass funnel for filtering; the fluoborate can then be stirred well after each washing before suction is applied.

(4) If the reaction becomes too vigorous, it may be necessary to cool the flask by covering it with a damp cloth. Normally the decomposition proceeds smoothly under the intermittent heating. If the salt is damp, the reaction may proceed more vigorously and unless the flask is cooled, it may pass beyond control.

(5) The density of fluorobenzene is about 1·025 at room temperature; it is important to use the correct strength of sodium hydroxide solution in order to obtain a clear separation of the two layers.

Cognate Preparations

***p*-Fluorotoluene.** Dissolve 53·5 g. of *p*-toluidine in a mixture of 126 ml. of concentrated hydrochloric acid and 126 ml. of water contained in a 1-litre beaker; warming is generally necessary; Cool the mixture to 0° in a bath of ice and salt with vigorous stirring with a thermometer (or, better, mechanically) and the addition of a little crushed ice. The *p*-toluidine hydrochloride will separate as a finely-divided crystalline precipitate. Add during about 15 minutes, in small portions and preferably from a separatory funnel supported over the beaker, a solution of 36·5 g. of sodium nitrite in 75 ml. of water until a slight excess of nitrous acid is present; commence testing when about 5 ml. of nitrite solution remains. Maintain the temperature preferably below 5–7° during the diazotisation by the addition of a little crushed ice if necessary; stir vigorously all the time (compare Section **IV,61**). Add a chilled solution of 76 g. of sodium borofluoride in 150 ml. of water slowly and with good stirring to the cold diazonium salt solution. Continue stirring for about 15 minutes. Filter the *p*-tolyldiazonium fluoborate on a Buchner or sintered glass funnel, wash with about 30 ml. of ice water, 15 ml. of methyl alcohol, and 30–40 ml. of ether. Dry overnight upon absorbent paper in a vacuum desiccator or, if possible, in a current of air. The yield of *p*-tolyldiazonium borofluoride is 78 g.; it melts with decomposition at 114°. Decompose the salt in two equal lots, and work up as for *Fluorobenzene*. The yield of pure *p*-fluorotoluene (a colourless liquid), b.p. 116–117 is 27 g.

***p*-Fluoroanisole.** To 105 ml. of *ca.* 42 per cent. fluoboric acid (*CAUTION:* corrosive chemical) (1) diluted with an equal volume of water, contained in a 600 ml. beaker, add 31 g. of *p*-anisidine. Place the beaker in an ice bath and stir the solution mechanically. Add a solution of 17·5 g. of sodium nitrite in 35 ml. of water slowly and maintain the

temperature at about 10°. Stir the solution vigorously towards the end of the reaction, cool the mixture to 0°, and filter with suction on a sintered glass funnel. Wash the precipitate successively with 30-40 ml. of cold 5 per cent. fluoboric acid, 40 ml. of ice-cold methanol, and several times with ether. Dry overnight by spreading the salt thinly on absorbent paper supported upon a screen or wire netting allowing circulation underneath. The yield of *p*-methoxyphenyldiazonium fluoborate is 54 g. Decompose the dry salt as detailed for *Fluorobenzene*. Return the small amount of product in the receiver to the distilling flask and steam distil. Extract the steam distillate with two 50 ml. portions of ether, wash the ethereal solution with 50 ml. of 10 per cent. sodium hydroxide solution, followed by water, and dry over anhydrous magnesium sulphate. Remove the ether on a steam bath and distil the residue. Collect the *p*-fluoroanisole at 156–157°. The yield is 16 g.

Note.

(1) The fluoboric acid may be prepared by adding 92 g. of A.R. boric acid slowly and with constant stirring to 250 g. of hydrofluoric acid (40–48 per cent.) in a copper, lead or a waxed-lined beaker. A lead rod may be used for stirring. All operations should be carried out in a fume cupboard.

4 : 4′-Difluorodiphenyl. Bis-diazotise a solution of 46 g. of benzidine (Section **IV,88**) in 150 ml. of concentrated hydrochloric acid and 150 ml. of water by means of a solution of 35 g. of sodium nitrite in 60 ml. of water ; add about 200 g. of crushed ice during the process (compare p-*Fluorotoluene* above). Filter the solution and add it to a filtered solution of 85 g. of sodium borofluoride in 150 ml. of water. Stir for several minutes, collect the precipitated bis-diazonium borofluoride by suction filtration, wash with 5 ml. of ice-cold water, and dry at 90–100°. Place the dry salt in a flask fitted with an air condenser, immerse the flask in an oil bath, and slowly raise the temperature to 150° (*Fume Cupboard !*). When decomposition of the salt is complete, steam distil the mixture ; collect the 4 : 4′-difluorodiphenyl which passes over and recrystallise it from ethanol. The yield is 21 g., m.p. 92–93°.

IV,68. o-DINITROBENZENE

Dissolve 34 g. of *o*-nitroaniline in a warm mixture of 63 ml. of concentrated hydrochloric acid and 63 ml. of water contained in a 600 ml. beaker. Place the beaker in an ice-salt bath, and cool to 0–5° whilst stirring mechanically ; the *o*-nitroaniline hydrochloride will separate in a finely-divided crystalline form. Add a cold solution of 18 g. of sodium nitrite in 40 ml. of water slowly and with stirring to an end point with potassium iodide-starch paper ; do not allow the temperature to rise above 5–7°. Introduce, whilst stirring vigorously, a solution of 40 g. of sodium borofluoride in 80 ml. of water. Stir for a further 10 minutes, and filter the solid diazonium fluoborate with suction on a sintered glass funnel. Wash it immediately once with 25 ml. of cold 5 per cent. sodium borofluoride solution, then twice with 15 ml. portions of rectified (or methylated) spirit and several times with ether ; in each washing stir

the fluoborate well before applying suction. The *o*-nitrophenyldiazonium fluoborate weighs about 50 g.; the pure substance melts with decomposition at 135°.

Dissolve 200 g. of sodium nitrite in 400 ml. of water in a 2-litre beaker provided with an efficient mechanical stirrer, and add 40 g. of copper powder (either the precipitated powder or copper bronze which has been washed with a little ether). Suspend the fluoborate in about 200 ml. of water and add it slowly to the well-stirred mixture. Add 4–5 ml. of ether from time to time to break the froth. The reaction is complete when all the diazonium compound has been added. Transfer the mixture to a large flask and steam distil until no more solid passes over (about 5 litres of distillate). Filter off the crystalline solid in the steam distillate and dry upon filter paper in the air; this *o*-dinitrobenzene (very pale yellow crystals) has m.p. 116° (*i.e.*, is practically pure) and weighs 29 g. It may be recrystallised from alcohol; the recrystallised solid melts at 116·5°.

COGNATE PREPARATION

p-Dinitrobenzene. Use 34 g. of *p*-nitroaniline (Section **IV,51**) and proceed exactly as above to the point where all the suspension of *p*-nitrophenyldiazonium fluoborate has been added. Filter the reaction mixture with suction, wash the residue well with water, twice with 25 ml. of 5 per cent. sodium hydroxide solution, and finally with water. Dry the solid at 100–110°, powder it, and extract it with four 150 ml. portions of boiling benzene. Distil off the benzene on a water bath, and recrystallise the residue from about 120 ml. of boiling glacial acetic acid. The yield of *p*-dinitrobenzene (reddish-yellow crystals), m.p. 173°, is 30 g. Further recrystallisation from alcohol affords pale yellow crystals of the same m.p.

IV,69. PHENOL (*from Aniline*)

Add 49 g. (27 ml.) of concentrated sulphuric acid cautiously and with stirring to 200 ml. of water in a 1 litre round-bottomed flask, and to the resulting hot solution add 23 g. (22·5 ml.) of aniline; warm the mixture gently until all the aniline dissolves. Add 200 ml. of cold water and cool the mixture in ice until the temperature falls below 5°. During the cooling process, keep the mixture well shaken. This will ensure that any aniline sulphate which separates will be in a finely-divided crystalline form; this dissolves rapidly as the diazotisation proceeds. Add a cold solution of 18 g. of sodium nitrite in 35 ml. of water slowly and with constant shaking to an end point with potassium iodide-starch paper; follow the precautions given under *Iodobenzene*, Section **IV,60**. When all the sodium nitrite solution has been introduced, allow the solution to stand at room temperature for 15–20 minutes to ensure complete diazotisation. Place the flask in a water bath, and heat the latter until the temperature of the diazotised solution reaches 50°. Continue the heating for 15 minutes or until the evolution of nitrogen ceases, taking care that the temperature of the solution does not exceed 55°. Steam distil (see Fig. *II, 40*, 1) the reaction mixture until 400 ml. of distillate are collected. Transfer the distillate to a separatory funnel, add about 20 g. of salt and

shake until it has dissolved. Extract with three 50 ml. portions of ether; remember to run off the lower aqueous layer and to decant the ethereal solution through the mouth of the funnel into a 250 ml. conical flask at each extraction. Dry the combined ether extracts with 3–4 g. of anhydrous potassium carbonate or magnesium sulphate. Distil off the ether in a 50 or 75 ml. distilling flask using the apparatus depicted in Fig. *II,13*,4. When all the ether has been removed, fit the distilling flask with a thermometer and an air condenser (Fig. *II*, *13*, 2), and distil from a wire gauze or an air bath. A little ether passes over first (*CAUTION* against fire) and the temperature rises rapidly. Collect the phenol at 179–183° (pure phenol boils at 182° and melts at 43°) in a small weighed specimen tube or flask. It should crystallise on cooling; if it remains supercooled, crystallisation may be induced by scratching the vessel with a glass rod whilst cooling in ice water or by seeding with a small crystal of pure phenol. The yield is 14 g.

Note.

Phenol should not be allowed to come into contact with the skin for it causes painful burns. The best antidote for phenol burns is a saturated solution of bromine in glycerine: if all undissolved bromine is allowed to settle out before the solution is used, there is no danger of bromine burns. Lime water may also be employed.

COGNATE PREPARATION

p-Cresol. Use 27 g. of *p*-toluidine, but otherwise proceed exactly as for phenol. Collect the *p*-cresol at 197–202°; this solidifies on cooling. The yield is 15 g. Pure cresol has m.p. 36°, b.p. 202°.

IV,70. *m*-NITROPHENOL

Add 101 g. (55 ml.) of concentrated sulphuric acid cautiously to 75 ml. of water contained in a 1 litre beaker, and introduce 35 g. of finely-powdered *m*-nitroaniline (Section **IV,44**). Add 100–150 g. of finely-crushed ice and stir until the *m*-nitroaniline has been converted into the sulphate and a homogeneous paste results. Cool to 0–5° by immersion of the beaker in a freezing mixture, stir mechanically, and add a cold solution of 18 g. of sodium nitrite in 40 ml. of water over a period of 10 minutes until a permanent colour is immediately given to potassium iodide-starch paper: do not allow the temperature to rise above 5–7° during the diazotisation. Continue the stirring for 5–10 minutes and allow to stand for 5 minutes; some *m*-nitrophenyldiazonium sulphate may separate. Decant the supernatant liquid from the solid as far as possible.

While the diazotisation is in progress, cautiously add 165 ml. of concentrated sulphuric acid to 150 ml. of water in a 1-litre round-bottomed flask. Heat the mixture just to boiling. Add the supernatant liquid (diazonium solution) from a separatory funnel supported over the flask at such a rate that the mixture boils very vigorously (about 30 minutes). Then add the residual damp solid (or suspension) in small portions; avoid excessive frothing. When all the diazonium salt has been introduced, boil for a further 5 minutes and pour the mixture into a 1-litre beaker

set in ice water, and stir vigorously to obtain a homogeneous crystal magma. When cold, filter at the pump, drain well and wash with four 20 ml. portions of ice water. Recrystallise by dissolving the crude product in hot dilute hydrochloric acid (1 : 1 by volume), decant from any residual dark oil, filter and cool to 0°, when light yellow crystals separate (1). Spread these upon a large sheet of filter paper, and dry in the air in a warm room. The mother liquid deposits a further crop (about 2 g.) upon standing for 24 hours. The yield of *m*-nitrophenol, m.p. 96°, is 23 g.

Note.

(1) When working with larger quantities of material, it is more convenient (and a better yield is obtained) to purify the air-dried product by distillation under diminished pressure. Use the apparatus pictured in Fig. *II*, *19*, 4, and add a few fragments of porous porcelain to the solid. No air inlet can be employed to prevent bumping since this may lead to explosive decomposition. Collect the pure *m*-nitrophenol at 160–165°/12 mm.; always allow the flask to cool before admitting air otherwise the residue may decompose with explosive violence. The recovery is over 90 per cent. of the pure *m*-nitrophenol.

IV,71. TOLUENE (*from* p-*Toluidine*)

Diazotise 10·7 g. of *p*-toluidine, following the procedure given under p-*Chlorotoluene* (Section **IV,61**). Pour the cold solution of *p*-tolyldiazonium chloride very slowly into a solution of 15 g. of sodium hydroxide in 45 ml. of water cooled to about 5°. While the diazotisation is in progress, prepare a solution of 30 g. of stannous chloride in 75 ml. of water in a 500 ml. round-bottomed flask, and add a solution of 30 g. of sodium hydroxide in 30 ml. of water with shaking until the initial precipitate of stannous hydroxide nearly redissolves. Fit the flask with a reflux condenser, and cool the resulting solution of sodium stannite in ice. Add the cold, alkaline diazonium salt solution through the top of the condenser in small quantities at a time. After each addition there is a vigorous evolution of nitrogen and a brown oil (impure toluene) separates: do not add a further portion of the diazonium solution until effervescence due to the preceding portion has ceased. Steam distil the mixture (Fig. *II*, *40*, 1), separate the toluene from the distillate, dry it with a little anhydrous magnesium sulphate, and distil from a small distilling flask. Pure toluene passes over at 110°. The yield is 6 g.

Note.

Benzene may be prepared similarly from phenyldiazonium chloride (Section IV,60).

IV,72. *sym.*-TRIBROMOBENZENE

Dissolve 10 g. of *sym.*-tribromoaniline (Section **IV,47**) in 60 ml. of rectified spirit and 15 ml. of benzene in a 200 ml. bolt-head flask by heating on a water bath. Add, from a burette or small graduated pipette, 5·3 g. (3·5 ml.) of concentrated sulphuric acid to the hot solution and gently swirl the liquid. Attach a reflux condenser to the flask and heat on a water bath until the clear solution boils. Detach the condenser, remove the flask from the water bath, and add 3·5 g. of powdered sodium

nitrite in two approximately equal portions ; after each addition, fit the condenser to the flask and shake the flask vigorously. The heat of reaction will cause the solution to boil vigorously ; when the reaction subsides, add the second portion of the sodium nitrite. Heat the flask on a boiling water bath as long as gas is evolved ; shake well from time to time. Allow the solution to cool for ten minutes, and then immerse the flask in an ice bath. A mixture of tribromobenzene and sodium sulphate crystallises out. Filter with suction on a Buchner funnel, wash with a small quantity of alcohol, and then repeatedly with water to remove all the sodium sulphate. Dissolve the crude tribromobenzene (7·5 g.) in a boiling mixture of 120 ml. of glacial acetic acid and 30 ml. of water (1), boil the solution with 2·5 g. of decolourising carbon, and filter through a hot water funnel or a preheated Buchner funnel : allow the solution to cool. Collect the crystals on a Buchner funnel and wash with a small quantity of chilled rectified spirit to remove the acetic acid. Dry in the air upon filter paper. The yield of *sym.*-tribromobenzene (colourless crystals), m.p. 122°, is 6·5 g.

Note.

(1) Methylated spirit may also be employed for recrystallisation.

IV,73. 3 : 3′-DIMETHYLDIPHENYL

Make a thin paste of 21·5 g. of finely-powdered *o*-tolidine (a commercial product) with 300 ml. of water in a 1-litre beaker, add 25 g. (21 ml.) of concentrated hydrochloric acid, and warm until dissolved. Cool the solution to 10° with ice, stir mechanically, and add a further 25 g. (21 ml.) of concentrated hydrochloric acid (1) ; partial separation of *o*-tolidine dihydrochloride will occur. Add a solution of 15 g. of sodium nitrite in 30 ml. of water as rapidly as possible, but keep the temperature below 15° : a slight excess of nitrous acid is not harmful in this preparation. Add the clear, orange tetrazonium solution to 175 ml. of 30 per cent. hypophosphorous acid (2), and allow the mixture to stand, loosely stoppered, at room temperature for 16–18 hours. Transfer to a separatory funnel, and remove the upper red oily layer. Extract the aqueous layer with 50 ml. of benzene. Dry the combined upper layer and benzene extract with anhydrous magnesium sulphate, and remove the benzene by distillation (compare Fig. *II*, *13*, 4) from a Widmer or similar flask (Figs. *II*, *24*, 3–5) : heat in an oil bath to 150° to ensure the removal of the last traces of benzene. Distil the residue at *ca.* 3 mm. pressure and a temperature of 155°. Collect the 3 : 3′-dimethyldiphenyl as a pale yellow liquid at 114–115°/3 mm. ; raise the bath temperature to about 170° when the temperature of the thermometer in the flask commences to fall. The yield is 14 g.

Notes.

(1) If the hydrochloric acid is added all at once instead of in two portions as detailed, a solid will be obtained consisting of *o*-tolidine coated with its dihydrochloride, and the diazotisation will proceed slowly.

(2) If the quantity of hypophosphorous acid is doubled, the yield is increased by 1 g.

IV,74. DIPHENIC ACID (*from Anthranilic Acid*)

The special reducing agent (a solution containing cupro-ammonia ions) is first prepared. Dissolve 63 g. of crystallised copper sulphate in 250 ml. of water in a 1-litre beaker, add 100 ml. of concentrated ammonium hydroxide solution (sp. gr. 0·88), and cool the solution to 10°. Dissolve 17·8 g. of hydroxylammonium chloride or 21 g. of hydroxylammonium sulphate in 60 ml. of water, cool to 10°, and add 42·5 ml. of 6*N* sodium hydroxide solution; if the resulting solution of hydroxylamine is not clear, filter it at the pump. Without delay add the hydroxylamine solution, with stirring, to the ammoniacal cupric sulphate solution. Reduction occurs at once, a gas is evolved, and the solution assumes a pale blue colour. Protect the reducing agent from the air if it is not used immediately.

Grind 25 g. of anthranilic acid with 46 ml. of concentrated hydrochloric acid and 75 ml. of water in a glass mortar, and transfer the suspension to a 500 ml. round-bottomed flask which is provided with a mechanical stirrer. Cool the contents of the flask in an ice bath to 0–5°, and add a solution of 13·2 g. of sodium nitrite in 175 ml. of water from a dropping funnel during about 20 minutes. Keep the diazonium solution below 5° and, if it is not clear, filter it by suction through a chilled Buchner funnel immediately before use.

Surround the reducing solution in the 1-litre beaker (which is equipped with a mechanical stirrer) with a bath of crushed ice so that the temperature of the solution is about 10°. Attach, by means of a short length of rubber " pressure " tubing, to the stem of a dropping funnel a glass tube which dips well below the surface of the solution and is bent upwards at the end and constricted so that the opening is about 2 mm. (this arrangement ensures that the diazonium solution reacts with the ammoniacal solution in the beaker and prevents the latter rising in the stem of the funnel). Place about 45 ml. of the cold diazonium solution in the funnel and add it at the rate of about 10 ml. per minute whilst the mixture is stirred. Add the remainder of the diazonium solution at the same rate ; continue the stirring for 5 minutes after the addition is complete. Heat the solution rapidly to boiling and carefully acidify with 125 ml. of concentrated hydrochloric acid ; the diphenic acid precipitates as pale brown crystals. Allow to stand overnight and filter with suction ; wash the crude diphenic acid with about 25 ml. of cold water. Suspend the crude acid in 100 ml. of water and add 20 g. of solid sodium bicarbonate. Filter the resulting solution by gravity, and then boil with about 0·5 g. of decolourising carbon ; filter and acidify the filtrate while still hot with excess of dilute hydrochloric acid (1 : 1). Collect the precipitated diphenic acid on a Buchner funnel, wash it with 20 ml. of cold water, and dry at 100°. The yield of diphenic acid is 18 g. ; it melts at 227–228° and usually possesses a light cream colour.

IV,75. PHENYLARSONIC ACID

In a 1500 ml. beaker, provided with a mechanical stirrer, place 46·5 g. (45·5 ml.) of aniline, 101 ml. of concentrated hydrochloric acid and 250 ml. of water, and enough finely crushed ice to make a volume of about

750 ml. ; stir vigorously and add slowly (during *ca.* 20 minutes) a solution of 36·5 g. of sodium nitrite in 125 ml. of water.

Concurrently with the preparation of the phenyldiazonium chloride solution, prepare a cold suspension of sodium arsenite. Place 250 ml. of water in a 3-litre round-bottomed flask equipped with a mechanical stirrer. Heat the water to boiling, add 125 g. of anhydrous sodium carbonate, and, as soon as the carbonate has dissolved, introduce 62·5 g. of pure arsenious oxide and 3 g. of crystallised copper sulphate with stirring. When all the solids have dissolved, cool the solution with stirring under a stream of tap water until the temperature has fallen to 15°.

Continue the stirring and cool the suspension of sodium arsenite to 0° in a freezing mixture of ice and salt. Add the cold phenyldiazonium chloride solution, following the method given under p-*Bromotoluene* (Section IV,62), during about 20 minutes : hold the temperature below 5° if possible, but do not allow it to rise above 10°. Frothing occurs due to the escape of nitrogen ; it can easily be controlled by the occasional addition of a little benzene. Continue the stirring for 1 hour after the diazonium solution has been added, and filter the mixture to remove the solid material which separates. Wash the solid with 125 ml. of cold water ; concentrate the combined filtrate and washings over a free flame to about 400 ml. Add concentrated hydrochloric acid (about 25 ml.) to the hot, concentrated, deep brown solution until no more tarry material separates. Filter the tar through a fluted filter paper, and add more hydrochloric acid until, after filtering, a pale yellow solution is obtained. Precipitate the phenylarsonic acid by the addition of concentrated hydrochloric acid (about 63 ml.) ; avoid too large an excess of hydrochloric acid for this will dissolve some of the product. Filter the cold mixture at the pump on a Buchner funnel and wash it with 50 ml. of cold water. Dissolve the pale yellow crystals in 125 ml. of boiling water, add 5 g. of decolourising carbon, filter the solution through a hot water funnel and allow the filtrate to cool. Collect the crystals and dry in a steam oven. The yield of phenylarsonic acid (white crystals) is 45 g. ; they melt at 155–158° with decomposition into the anhydride $C_6H_5AsO_2$.

Cognate Preparation

p-Nitrophenylarsonic acid. Dissolve 52 g. of sodium meta-arsenite ($NaAsO_2$) and 16 g. of sodium hydroxide in 600 ml. of water (1) contained in a 2-litre beaker and suspend 6 g. of cuprous chloride in the solution. Suspend the *p*-nitrophenyldiazonium fluoborate obtained from 34 g. of *p*-nitroaniline (2) in 300 ml. of cold water and add the suspension, with vigorous mechanical stirring, during 1 hour to the mixture. Control the foaming that accompanies the evolution of nitrogen by the occasional addition of small volumes of amyl alcohol or ethyl ether. As the reaction proceeds, introduce 100 ml. of 10 per cent. sodium hydroxide solution in 20 ml. portions in order to maintain the correct alkalinity. Continue the stirring for a further hour, warm the mixture at 60° for 30 minutes, filter with suction through a sintered glass funnel, and wash the residue on the funnel with two 40 ml. portions of water. Add concentrated hydrochloric

acid to the combined filtrate and washings until the solution is acid to litmus paper, filter, add activated charcoal to the filtrate and concentrate the solution over a flame to about 200 ml. Filter the hot solution at the pump and render the filtrate acid to Congo red with concentrated hydrochloric acid. Upon cooling, finally in ice, the *p*-nitrophenylarsonic acid separates. Filter the crystals with suction and dissolve them in 10 per cent. ammonia solution. Filter the solution, render acid to Congo red with concentrated hydrochloric acid and set aside to cool, preferably overnight. Collect the pure *p*-nitrophenylarsonic acid, wash with small volumes of ice-cold water, and dry in the steam oven. The yield is 47 g., m.p. 298–300° (decomp.).

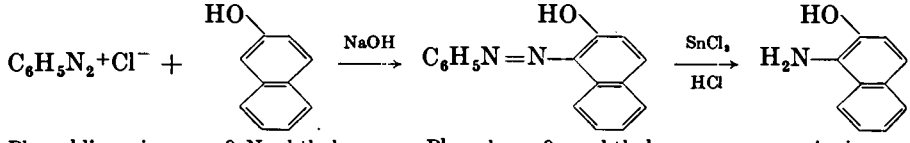
Notes.

(1) Alternatively, prepare the sodium meta-arsenite solution by dissolving 39·6 g. A.R. arsenious oxide and 32 g. of A.R. sodium hydroxide in 600 ml. of water.

(2) Prepare the diazonium fluoborate from 34 g. of *p*-nitroaniline as detailed in Section IV,68 for o-*Nitroaniline*.

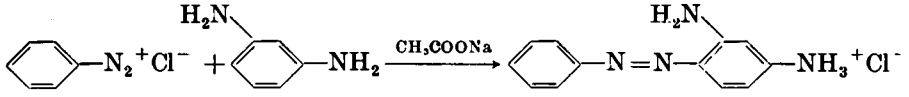
SOME AZO DYESTUFFS

Azo compounds (ArN=NAr) are prepared by the interaction of a diazonium salt with a phenol in the presence of sodium hydroxide, for example :



Phenyldiazonium chloride — β-Naphthol — Phenyl-azo-β-naphthol — α-Amino-β-naphthol

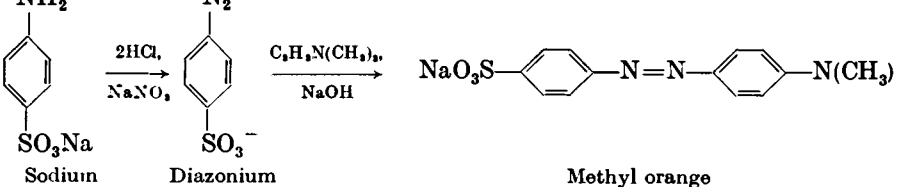
or from a diazonium salt and an amine in the presence of sodium acetate, for example :



m-Phenylenediamine — Chrysoidine

The azo dyes are not of any great practical value owing to their slight solubility in water. The introduction of a sulphonic acid group into the molecule has no effect upon the colour, but renders the dye water-soluble—a fact of great commercial value. The simplest way of achieving this is to employ an amine, *e.g.*, sulphanilic acid, in which the —SO_3H group is already present.

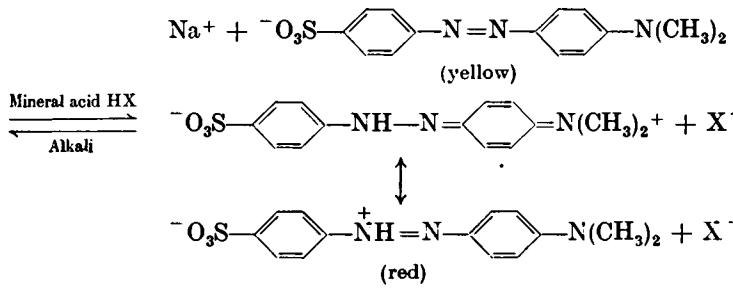
Sulphanilic acid, which is conventionally represented as *p*-$H_2NC_6H_4SO_3H$ and is designated more correctly as the internal salt or zwitterion *p*-$^+H_3NC_6H_4SO_3^-$, is sparingly soluble in water. It is best diazotised by bringing it into solution as the sodium salt by adding the calculated quantity of sodium carbonate, introducing the requisite quantity of sodium nitrite, and pouring the solution on to a mixture of hydrochloric acid and ice ; nitrous acid and the dipolar sulphanilic acid are liberated together and immediately react, and after a short time the internal diazonium salt (*p*-diazoniumphenylsulphonic acid) separates from the solution. This condenses with a solution of, say, dimethylaniline in acetic acid (hydrochloric acid should not be used, because the coupling reaction is rendered difficult by a high concentration of hydrogen ions) to give a product, which on treatment with sodium hydroxide yields the sodium salt, known as **methyl orange** :



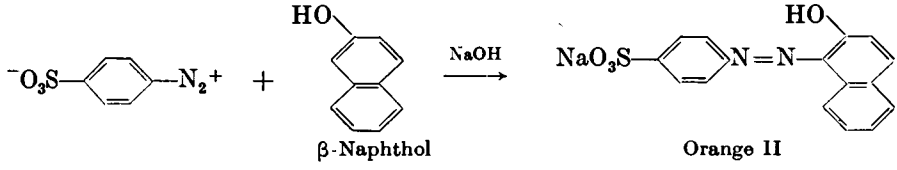
Sodium sulphanilate — Diazonium inner salt — Methyl orange

This substance is more useful as an indicator than as a dye, for it changes colour at a certain concentration of hydrogen ions (*p*H 3·1–4·4). Treatment

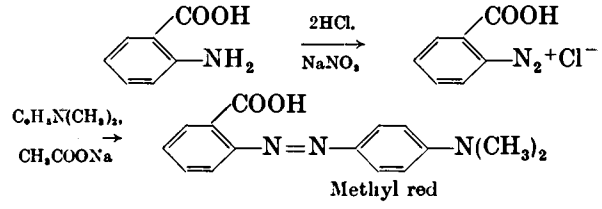
of a solution of methyl orange with a strong acid gives rise to a red form—this is essentially an internal salt, which is stabilised by resonance.



By condensation of diazotised sulphanilic acid with β-naphthol in the presence of sodium hydroxide, the useful dyestuff **Orange II** (*p*-sulphobenzene-azo-β-naphthol) is obtained :

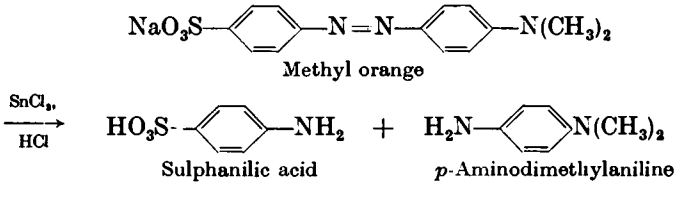


The valuable indicator **methyl red** (*o*-carboxybenzene-azo-dimethylaniline) is obtained by coupling diazotised anthranilic acid with dimethylaniline :



The colour change is red (pink) to yellow over the *p*H range 4·2–6·3.

It is interesting to note that azo dyestuffs may be conveniently reduced either by a solution of stannous chloride in hydrochloric acid or by sodium hyposulphite. Thus phenyl-azo-β-naphthol yields both aniline and α-amino-β-naphthol (see formula above), and methyl orange gives *p*-aminodimethylaniline and sulphanilic acid :



The general reaction may be written in the form :

$$RN{=}NR' + 4H \longrightarrow RNH_2 + H_2NR' \text{ *}$$

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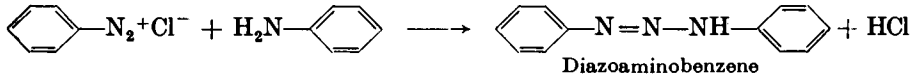
* The equations are :—

$$RN{=}NR' + 2SnCl_2 + 4HCl \longrightarrow RNH_2 + R'NH_2 + 2SnCl_4$$
$$RN{=}NR' + 2Na_2S_2O_4 + 4H_2O \longrightarrow RNH_2 + R'NH_2 + 4NaHSO_3$$

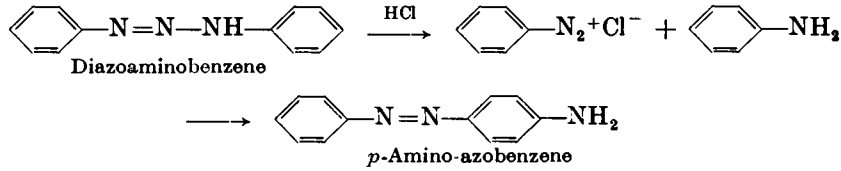
and is of great importance in determining the constitutions of azo compounds. If RNH_2 contains a sulphonic acid group, the reaction product may be neutralised and $R'NH_2$ extracted with ether.

Attention has previously (see *Diazonium Salts*) been drawn to the fact that unless an excess of hydrochloric (or mineral) acid is used in the diazotisation process, coupling occurs between the diazonium salt and the amine to give diazoamino compounds. Thus phenyldiazonium chloride and aniline yield **diazoaminobenzene.** This substance may be conveniently prepared by dissolving two equivalents of aniline in three equivalents of hydrochloric acid, and adding one equivalent of sodium nitrite in aqueous solution followed by two equivalents of sodium acetate :



Diazoaminobenzene

If diazoaminobenzene is dissolved in aniline with a small quantity of aniline hydrochloride and the mixture kept at about 40° for a short time, it is converted in good yield into ***p*-amino-azobenzene** :



Diazoaminobenzene

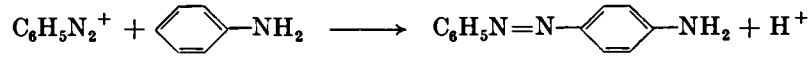
p-Amino-azobenzene

The *mechanism* of the **diazoamino-aminoazo rearrangement** is dependent upon :—

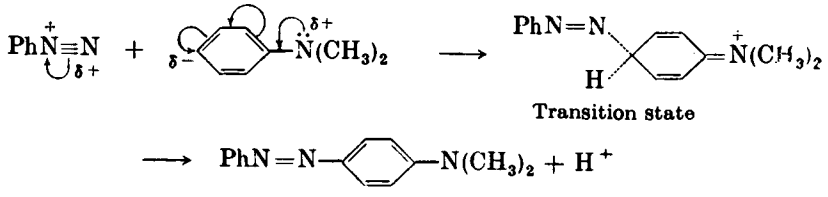
(*a*) an equilibrium involving the diazoamino compound, the acid, phenyldiazonium chloride and aniline :

$$C_6H_5N{=}N{-}NHC_6H_5 + H^+Cl^- \rightleftharpoons C_6H_5N_2{}^+Cl^- + H_2NC_6H_5$$

(*b*) a reaction, under the weakly acid conditions, of the phenyldiazonium ion and the *p*-position of aniline :



This view is supported by the fact that if diazominobenzene is dissolved in dimethylaniline in the presence of the hydrochloride of the latter, the main product is *p*-dimethylamino-azobenzene, $C_6H_5N{=}NC_6H_4N(CH_3)_2$; this is because dimethylaniline couples in the nucleus more readily than does aniline. The reaction is an electrophilic displacement of hydrogen by the diazonium ion :



Transition state

IV,76. PHENYL-AZO-β-NAPHTHOL *

Dissolve 5·0 g. (4·9 ml.) of aniline in 16 ml. of concentrated hydrochloric acid and 16 ml. of water contained in a small beaker or conical flask. Diazotise by the addition of a solution of 4·0 g. of sodium nitrite

* Also termed benzene-azo-β-naphthol.

in 20 ml. of water ; follow the method given in Section **IV,60.** Prepare a solution of 7·8 g. of β-naphthol in 45 ml. of 10 per cent. sodium hydroxide solution in a 250 ml. beaker ; cool the solution to 5° by immersion in an ice bath, assisted by the direct addition of about 25 g. of crushed ice. Stir the naphthol solution vigorously and add the cold diazonium salt solution *very slowly* : a red colour develops and red crystals of phenyl-azo-β-naphthol soon separate. When all the diazonium salt solution has been added, allow the mixture to stand in an ice bath for 30 minutes with occasional stirring. Filter the solution through a Buchner funnel with *gentle suction*, wash well with water, and drain thoroughly by pressing the crystals with the back of a large glass stopper. Recrystallise one-fourth of the product from glacial acetic acid (30–35 ml.) : retain the remainder for reduction by stannous chloride. Filter the recrystallised product with suction, wash with a little alcohol (or methylated spirit) to eliminate acetic acid, and dry upon filter paper. The yield of deep red crystals is about 3 g. Pure phenyl-azo-β-naphthol has m.p. 131° ; if the m.p. is low, recrystallise the dry product from alcohol.

Reduction with stannous chloride. α-Amino-β-naphthol hydrochloride. Into a 350 or 500 ml. round-bottomed flask, provided with a reflux condenser and containing 100 ml. of methylated spirit, place the crude phenyl-azo-β-naphthol reserved above and boil gently until most of the azo compound has dissolved. Meanwhile dissolve 20 g. of a good grade of stannous chloride in 60 ml. of concentrated hydrochloric acid (warming is necessary to produce a clear solution),* add this to the contents of the flask and boil under reflux for a further 30 minutes. All the azo compound dissolves rapidly and is reduced by the stannous chloride ; the solution acquires a very pale brown colour. Decant the solution to a beaker and cool in ice : the α-amino-β-naphthol hydrochloride separates as fine greyish-white crystals. Filter with suction, and wash with dilute hydrochloric acid (1 : 4). Recrystallise from the minimum volume of hot water which contains a few drops of stannous chloride solution in an equal weight of hydrochloric acid (this reduces atmospheric oxidation), cool the clear solution in an ice bath, and collect the recrystallised product as before. Dry the colourless crystals in a desiccator. The yield is 3–4 g. The compound will remain colourless, or nearly so, if protected from light during storage.

IV,77. CHRYSOIDINE

Prepare a solution of phenyldiazonium chloride from 5·0 g. (4·9 ml.) of aniline as detailed in Section **IV,60**, and keep it in an ice bath. Meanwhile dissolve 6·0 g. of a good grade of *m*-phenylene diamine, preferably redistilled before use (Section **IV,93**), in 60 ml. of 2*N* hydrochloric acid in a 600 ml. beaker, cool, and add the phenyldiazonium chloride solution rapidly and with vigorous stirring. Then add sodium acetate solution (say, 20 g. of the trihydrate in 50 ml. of water) slowly and with stirring until precipitation of the dyestuff is complete ; continue stirring for 1 hour. Heat to the boiling point and filter through a heated funnel, if necessary. Add 40 g. of sodium chloride to the filtrate, heat on a steam bath until the precipitated dyestuff becomes crystalline, allow to cool, filter, wash with a little water, and dry in the air. The yield of chrysoidine is 10 g.

* Sodium hyposulphite (dithionite) $Na_2S_2O_4$ may also be employed for the reduction : see under *Methyl Orange*, Section IV,78.

IV,78. METHYL ORANGE

In a 250 ml. conical flask place 10·5 g. of sulphanilic acid dihydrate, 2·65 g. of anhydrous sodium carbonate and 100 ml. of water, and warm until a clear solution is obtained. Cool the solution under the tap to about 15°, and add a solution of 3·7 g. of sodium nitrite in 10 ml. of water. Pour the resulting solution slowly and with stirring into a 600 ml. beaker containing 10·5 ml. of concentrated hydrochloric acid and 60 g. of crushed ice (1). Test for the presence of free nitrous acid with potassium iodide - starch paper after 15 minutes. Fine crystals of the diazobenzene sulphonate will soon separate ; do not filter these off as they will dissolve during the next stage of the preparation. Dissolve 6·05 g. (6·3 ml.) of dimethylaniline in 3·0 ml. of glacial acetic acid, and add it with vigorous stirring to the suspension of diazotised sulphanilic acid. Allow the mixture to stand for 10 minutes ; the red or acid form of methyl orange will gradually separate. Then add slowly and with stirring 35 ml. of 20 per cent sodium hydroxide solution : the mixture will assume a uniform orange colour due to the separation of the sodium salt of methyl orange in fine particles. Direct filtration of the latter is slow, hence, whilst stirring the mixture with a thermometer, heat it almost to the boiling point. Most of the methyl orange will dissolve. Add about 10 g. of sodium chloride (to assist the subsequent separation of the methyl orange) and warm at 80–90° until the salt has dissolved. Allow the mixture to cool undisturbed for 15 minutes and then cool in ice water ; this gives a fairly easily filterable product. Filter off the methyl orange at the pump, but apply only gentle suction so as to avoid dragging the particles into the pores of the filter paper ; rinse the beaker with a little saturated salt solution and drain well. Recrystallise from hot water (about 150 ml. are required) ; filter the hot solution, if necessary, through a hot water funnel or through a preheated Buchner funnel (prepared by pouring boiling water through it). Reddish-orange crystals of methyl orange separate as the solution cools. Filter these at the pump, drain well, wash with a little alcohol, and finally with a small volume of ether. The yield is 13 g. Methyl orange, being a salt, has no well-defined m.p.

Note.

(1) An alternative procedure is to cool the solution containing the sodium sulphanilate and sodium nitrite in a bath of crushed ice to about 5° and then add 10·5 ml. of concentrated hydrochloric acid diluted with an equal volume of water slowly and with stirring ; the temperature must not be allowed to rise above 10° and an excess of nitrous acid should be present (the solution is tested after standing for 5 minutes). The subsequent stages in the preparation—addition of dimethylaniline solution, *etc.*—are as above.

Reduction of methyl orange to *p*-aminodimethylaniline. *Method 1.* Dissolve 2·0 g. of methyl orange in the minimum volume of hot water and to the hot solution add a solution of 8 g. of stannous chloride in 20 ml. of concentrated hydrochloric acid until decolourisation takes place ; gentle boiling may be necessary. Cool the resulting solution in ice ; a crystalline precipitate consisting of sulphanilic acid and some *p*-aminodimethylaniline hydrochloride separates out. In order to separate the free base, add 10 per cent. sodium hydroxide solution until the precipitate of tin hydroxide redissolves. Extract the cold solution with three or four 20 ml. portions of ether, dry the extract

with anhydrous potassium carbonate, and remove the ether by distillation. The residual base soon crystallises, particularly if it is stirred with a glass rod; it melts at 41°.

Method 2. Suspend 2·0 g. of methyl orange in 4 ml. of water, and add a small quantity of sodium hyposulphite ($Na_2S_2O_4$). Heat the mixture and add more sodium hyposulphite until the colour is discharged. The sulphanilic acid remains in the solution as sodium sulphanilate and the *p*-aminodimethylaniline may be extracted with ether as in *Method 1.*

IV,79. ORANGE II (β-NAPHTHOL ORANGE)

Diazotise 10·5 g. of sulphanilic acid dihydrate as described under *Methyl Orange* (Section **IV,78**), and keep the suspension of the diazonium compound in ice water until required. Dissolve 7·2 g. of a good grade of β-naphthol in 40 ml. of cold 10 per cent. sodium hydroxide solution in a 600 ml. beaker, cool to 5°, and pour in, with stirring, the well-mixed suspension of diazotised sulphanilic acid. Coupling takes place readily and the dyestuff separates as a crystalline paste. Stir well and, after 10 minutes, heat the mixture until all the solid has dissolved. Add 20 g. of sodium chloride (to decrease the solubility of the product further) and warm until this dissolves. Allow the solution to cool spontaneously in the air for 1 hour, and then cool in ice until crystallisation is complete. Collect the product on a Buchner funnel and apply gentle suction; wash with a little saturated salt solution, and dry at 80°. The product weighs about 22 g., and contains about 20 per cent. of sodium chloride; further purification is unnecessary for dyeing purposes. To obtain pure, crystalline Orange II, dissolve the crude substance in the minimum volume of boiling water, allow to cool to about 80°, add about twice the volume of rectified (or methylated) spirit, and allow crystallisation to proceed spontaneously. When cold, filter at the pump, wash the pure dyestuff (it is a dihydrate) with a little alcohol, and dry in the air. The yield is 14 g.

IV,80. METHYL RED

Dissolve 65 g. of pure anthranilic acid (1) in a mixture of 50 ml. of concentrated hydrochloric acid and 150 ml. of water by heating; filter off any insoluble impurities. Transfer the solution to a 2-litre beaker, surrounded by an ice bath and provided with a mechanical stirrer. Add 250 g. of crushed ice and 75 ml. of concentrated hydrochloric acid, and stir continuously. When the temperature has fallen to about 3°, slowly introduce a cold solution of 36 g. of sodium nitrite in 70 ml. of water to a permanent end point with potassium iodide - starch paper. This is best done by attaching to the stem of a 50 ml. dropping funnel a glass tube which dips well below the surface of the solution and is bent upwards at the end and constricted so that the opening is about 2 mm.; this arrangement ensures that the entrance of the acid liquor into the nitrite solution is prevented. It is essential that the temperature be kept between 3° and 5° during the diazotisation, otherwise tarry by-products are formed. To the resulting solution of the diazonium salt, add fairly rapidly 84·8 g. (88·5 ml.) of dimethylaniline. Continue the stirring for 1 hour and maintain the temperature at about 5°.

Dissolve 68 g. of crystallised sodium acetate in 100 ml. of water, and dilute to 120 ml. Add 50 ml. of this solution to the reaction mixture and stir for a further 4 hours; eliminate any appreciable amount of foamy solid by the addition of a few drops of ethyl acetate. Allow the mixture to stand overnight in an ice box or in a refrigerator: the temperature must be kept below 7°. Then add the remainder of the sodium acetate solution with stirring to the mixture cooled in an ice bath, stir for an additional period of 2–3 hours, and allow the temperature to rise to 20–25° during 24 hours. Introduce just sufficient sodium hydroxide solution with stirring to cause the mixture to have a distinct odour of dimethylaniline (24 ml. of a 40 per cent. solution are usually required), and allow to stand at room temperature (20–25°) for 48 hours or longer. (The formation of the azo compound is a very slow reaction, but is accelerated by increasing the *p*H of the solution.) Filter off the solid at the pump, wash it first with water, then with 40 ml. of 10 per cent. acetic acid (to remove the dimethylaniline), and finally with water (the last filtrate is pale pink); drain well. Dry the solid in the air for 24 hours. Suspend the solid in 400 ml. of methyl alcohol in a 1500 ml. bolt-head flask: stir the mixture on a water bath under a reflux condenser for 1 hour, cool in ice and filter. Wash with 400 ml. of cold methyl alcohol and dry in the air. The yield of crude methyl red is 85 g. (2). Purify by extraction with 700 ml. of boiling toluene (3) in a Soxhlet apparatus (Fig. *II*, *44*, 5 or 6). When the extraction is complete, remove the flask containing the almost boiling toluene to a bath containing water at 90–100° and arrange that the level of the water is slightly above that of the toluene in the flask. The temperature thus falls slowly and large crystals are obtained. Finally allow to cool to room temperature. Filter off the crystals and wash with a little toluene. The yield of methyl red, m.p. 181–182°, is 79 g.

Notes.

(1) If crude anthranilic acid is employed, it should be titrated against standard alkali with phenolphthalein as indicator, and the weight adjusted in accordance with the purity.

(2) The sodium salt of methyl red may be prepared by dissolving the crude product in an equal weight of 35 per cent. sodium hydroxide which has been diluted to 350 ml., filtering, and evaporating under diminished pressure (Fig. *II*, *37*, 1). The resulting sodium salt forms orange leaflets. This water-soluble product is very convenient for use as an indicator. Incidentally, the toluene extraction is avoided.

(3) Methyl red may also be recrystallised from glacial acetic acid.

IV,81. DIAZOAMINOBENZENE

In a 250 ml. flask place 75 ml. of water, 24 g. (20 ml.) of concentrated hydrochloric acid and 14 g. (13·7 ml.) of aniline. Shake vigorously (1) and then add 50 g. of crushed ice. Run in a solution of 5·2 g. of sodium nitrite in 12 ml. of water, with constant shaking, during a period of 5–10 minutes. Allow to stand with frequent shaking (1) for 15 minutes, and add a solution of 21·0 g. of crystallised sodium acetate in 40 ml. of water during 5 minutes. A yellow precipitate of diazoaminobenzene begins to form immediately; allow to stand with frequent shaking for 45 minutes and do not allow the temperature to rise above 20° (add ice,

if necessary). Filter the yellow diazoaminobenzene on a Buchner funnel, wash with it 250 ml. of cold water, drain as completely as possible, and spread it on a sheet of filter paper to dry. The yield of crude diazoaminobenzene, m.p. 91°, is 15 g. (2). Recrystallise a small portion from light petroleum, b.p. 60–80° : the pure compound, m.p. 97°, is obtained.

Notes.

(1) For preparations on a larger scale, mechanical stirring is recommended : a beaker or bolt-head flask should be used.

(2) About 200 ml. of light petroleum is required for recrystallisation. It is therefore advisable, for the sake of economy when the preparation is conducted by a large class of students, that only about 1 g. of the crude material be recrystallised from this solvent. The crude compound may be employed in the preparation of *p*-amino-azobenzene.

IV,82. *p*-AMINO-AZOBENZENE

Dissolve 5 g. of finely-powdered diazoaminobenzene (Section **IV,81**) in 12–15 g. of aniline in a small flask and add 2·5 g. of finely-powdered aniline hydrochloride (1). Warm the mixture, with frequent shaking, on a water bath at 40–45° for 1 hour. Allow the reaction mixture to stand for 30 minutes. Then add 15 ml. of glacial acetic acid diluted with an equal volume of water : stir or shake the mixture in order to remove the excess of aniline in the form of its soluble acetate. Allow the mixture to stand, with frequent shaking, for 15 minutes : filter the amino-azobenzene at the pump, wash with a little water, and dry upon filter paper Recrystallise the crude *p*-amino-azobenzene (3·5 g. ; m.p. 120°) from 15–20 ml. of carbon tetrachloride to obtain the pure compound, m.p. 125°. Alternatively, the compound may be recrystallised from dilute alcohol, to which a few drops of concentrated ammonia solution have been added.

To prepare the **hydrochloride**, dissolve about 1 g. of the compound (which need not be perfectly dry) in about 8 ml. of alcohol. Add this solution to boiling dilute hydrochloric acid (10 ml. of the concentrated acid and 80 ml. of water). Boil for 5 minutes, filter the hot solution if necessary, and allow to cool. *p*-Amino-azobenzene hydrochloride separates in steel-blue crystals. Filter, wash with a little dilute hydrochloric acid, and dry.

To recover the free base, dissolve the hydrochloride in the minimum volume of boiling alcohol, add concentrated ammonia solution dropwise until a clear solution results and the blue colour has become light brown. Add water carefully until a cloudiness appears, warm on a water bath until the cloudiness just disappears, and allow to cool. Yellow crystals of *p*-amino-azobenzene separate on cooling.

Note.

(1) The aniline hydrochloride may be prepared by treating 2 g. of aniline with an excess (about 3 ml.) of concentrated hydrochloric acid in a small beaker, cooling, filtering at the pump, washing with a *small* volume of ether, and drying between filter paper.

INTERMEDIATE PRODUCTS IN THE REDUCTION OF NITRO COMPOUNDS

The reduction of an aromatic nitro compound with a powerful reducing agent (tin or stannous chloride and hydrochloric acid ; iron and dilute hydrochloric acid ; hydrogen and a platinum catalyst) leads to a good yield of the corresponding primary amine, *e.g.*, nitrobenzene → aniline. The process is by no means a simple one : by the use of milder reducing agents and by the control of the hydrogen ion concentration (*p*H) of the solution, a number of intermediate products may be isolated, some of which are products of direct reduction and others are formed through secondary changes. Particularly fine control may be obtained by electrolytic reduction, *e.g.*, it can be carried out in solutions of varying *p*H, and the size and material of the electrodes as well as the current density may be varied within wide limits. Haber (1900) thus established that the reduction of nitrobenzene proceeds in the following stages :—

$$\underset{\text{Nitrobenzene}}{C_6H_5NO_2} \xrightarrow{2H} \underset{\text{Nitrosobenzene}}{C_6H_5NO} \xrightarrow{2H} \underset{\beta\text{-Phenylhydroxylamine}}{C_6H_5NHOH} \xrightarrow{2H} \underset{\text{Aniline}}{C_6H_5NH_2}$$

The initial product, nitrosobenzene, is so easily reduced to β-phenylhydroxylamine that it has never been isolated in the free state, but its presence has been established by reaction in solution with hydroxylamine to yield a phenyldiazonium salt, which couples readily with a α-naphthylamine to form the dyestuff phenyl-azo-α-naphthylamine (compare Section IV,77) :

$$C_6H_5NO + H_2NOH + HX \longrightarrow C_6H_5N_2^+X^- + 2H_2O$$

Under the catalytic influence of alkali, nitrosobenzene and β-phenylhydroxylamine react to yield azoxybenzene :

$$C_6H_5NO + HN(OH)C_6H_5 \xrightarrow[(-H_2O)]{OH^-} \underset{\text{Azoxybenzene}}{C_6H_5N{=}\overset{\overset{O}{\uparrow}}{N}C_6H_5}$$

Further reduction in alkaline solution (say, with zinc powder) leads to azobenzene and hydrazobenzene :

$$\underset{\text{Azoxybenzene}}{C_6H_5N{=}\overset{\overset{O}{\uparrow}}{N}C_6H_5} \xrightarrow{2H} \underset{\text{Azobenzene}}{C_6H_5N{=}NC_6H_5} \xrightarrow{2H} \underset{\text{Hydrazobenzene}}{C_6H_5NH{-}NHC_6H_5}$$

Electrolytic reduction of hydrazobenzene gives aniline :

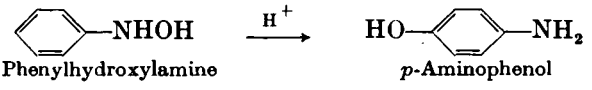
$$C_6H_5NH{-}NHC_6H_5 \xrightarrow{2H} C_6H_5NH_2 + H_2NC_6H_5$$

The various intermediate compounds may be prepared in the laboratory, and convenient methods are described below.

β-Phenylhydroxylamine is formed when aniline is treated with a "neutral" reducing agent, *e.g.*, zinc powder and aqueous ammonium chloride solution :

$$C_6H_5NO_2 + 2Zn + H_2O \longrightarrow C_6H_5NHOH + 2ZnO$$

This extremely reactive substance rearranges, in the presence of acids, with the production of ***p*-aminophenol** :



β-Phenylhydroxylamine *p*-Aminophenol

Nitrosobenzene may be obtained by the oxidation of β-phenylhydroxylamine with acid dichromate solution at 0° :

$$C_6H_5NHOH + O \longrightarrow C_6H_5NO + H_2O$$

The solid is colourless and is probably dimolecular : it dissociates to a green monomer upon melting or in solution.

Azoxybenzene is readily prepared by reduction of nitrobenzene in an alkaline medium with dextrose or sodium arsenite :

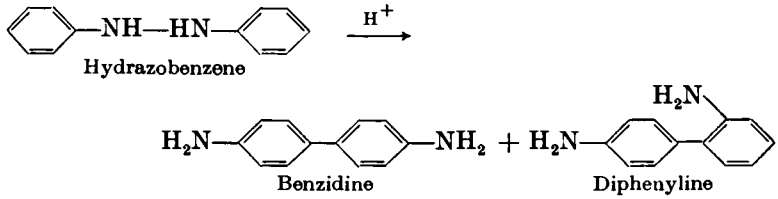
$$2C_6H_5NO_2 + 6H \longrightarrow C_6H_5\overset{\overset{O}{\uparrow}}{N}{=}NC_6H_5 + 3H_2O$$

Reduction of nitrobenzene in methyl or ethyl alcoholic sodium hydroxide solution with zinc powder leads to **azobenzene** or **hydrazobenzene** according to the proportion of zinc powder employed :

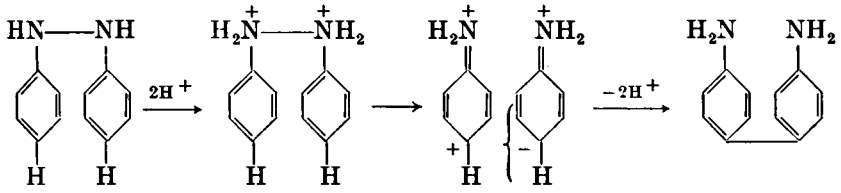
$$2C_6H_5NO_2 + 4Zn + 8NaOH \longrightarrow C_6H_5N{=}NC_6H_5 + 4Na_2[ZnO_2] + 4H_2O$$
$$2C_6H_5NO_2 + 5Zn + 10NaOH \longrightarrow C_6H_5NHNHC_6H_5 + 5Na_2[ZnO_2] + 4H_2O$$

Hydrazobenzene may be oxidised to azobenzene by sodium hypobromite solution at 0°.

In the presence of acids, hydrazobenzene rearranges to give about 70 per cent. of **benzidine** (4 : 4′-diaminodiphenyl) and about 30 per cent. of *diphenyline* (2 : 4′-diaminodiphenyl) :



The conversion of a hydrazobenzene into a diaminodiphenyl upon treatment with acid is termed the **benzidine rearrangement.** The following *mechanism* for the formation of benzidine from hydrazobenzene appears reasonable :



The rearranging entity has been shown to be the bivalent cation ; the adjacent charges may so weaken the N—N link that charges of nearly integral size may be built up in the 4 and 4′ positions. In the bent, but strainless, cation the minimum separation of the two *p*-positions would suffice for the establishment of a largely electrostatic bond, which could pass smoothly into the covalent rearrangement product (benzidine).

IV,83. β-PHENYLHYDROXYLAMINE

In a 2 litre beaker, equipped with a thermometer and mechanical stirrer, place 25 g. of ammonium chloride, 800 ml. of water and 50 g. (41·6 ml.) of nitrobenzene (1). Stir the mixture vigorously, and add 59 g. of

zinc powder of 90 per cent. purity (2) during about 15 minutes ; the rate of addition should be such that the temperature rapidly rises to 60–65° and remains in this range until all the zinc has been added. Continue the stirring for a further 15 minutes, by which time the reduction is complete as is shown by the fact that the temperature commences to fall. Filter the warm reaction mixture at the pump to remove the zinc oxide, and wash it with 100 ml. of hot water. Place the filtrate in a conical flask, saturate it with common salt (about 300 g.), and cool in an ice bath for at least one hour to ensure maximum crystallisation of the desired product. Filter the pale yellow crystals of β-phenylhydroxylamine with suction and drain well. The yield of crude, dry product is about 38 g. ; this contains a little salt and corresponds to about 29 g. of pure phenylhydroxylamine as determined by its separation from inorganic materials by dissolution in ether. The substance deteriorates upon storage and is therefore used immediately for a secondary preparation (*e.g.*, nitrosobenzene, Section **IV,84** or cupferron, Section **VII,6**). If required perfectly pure, it may be recrystallised from benzene - light petroleum (b.p. 40–60°) or from benzene alone ; the resulting pure compound is somewhat more stable and has a melting point of 81°.

Notes.

(1) Redistilled or A.R. nitrobenzene should be used. It must not be acid in reaction.

(2) The zinc powder should be analysed (for method, see, for example, Vogel, *Quantitative Inorganic Analysis : Theory and Practice*, Second Edition ; 1952, p. 812; Longmans, Green and Co., Ltd.), and a proportional quantity employed if the zinc content is not 90 per cent.

Conversion of β-phenylhydroxylamine into *p*-aminophenol. Add 4·4 g. of recrystallised β-phenylhydroxylamine to a mixture of 20 ml. of concentrated sulphuric acid and 60 g. of ice contained in a 1 litre beaker cooled in a freezing mixture. Dilute the solution with 400 ml. of water, and boil until a sample, tested with dichromate solution, gives the smell of quinone and not of nitrosobenzene or nitrobenzene (*ca.* 10–15 minutes). Neutralise the cold reaction mixture with sodium bicarbonate, saturate with salt, extract twice with ether, and dry the ethereal extract with anhydrous magnesium or sodium sulphate. Distil off the ether ; *p*-aminophenol, m.p. 186°, remains. The yield is 4·3 g.

IV,84. NITROSOBENZENE

In a 2 litre bolt-head flask, equipped with an efficient mechanical stirrer, place 60·5 g. (50 ml.) of pure nitrobenzene and a solution of 30 g. of ammonium chloride in 1 litre of water. Stir vigorously and add 75 g. of a good quality zinc powder (about 90 per cent. purity) in small portions over a period of 5 minutes. The main reaction occurs about 5 minutes after the addition and the temperature rises. When the temperature reaches about 65°, add enough ice to the well-stirred mixture to reduce the temperature to 50–55°. Filter the solution through a Buchner funnel twenty minutes after the first portion of zinc powder was introduced; wash the zinc oxide residues with 600–700 ml. of boiling water.

Transfer the filtrate and washings to a 4 litre round-bottomed flask or beaker and cool *immediately* to 0–1° by the addition of sufficient crushed ice and leave at least 250 g. unmelted. Without delay, add with stirring a cold solution of concentrated sulphuric acid (150 ml. of the concentrated acid to which sufficient ice has been added to reduce the temperature to − 5°). Then add an ice-cold solution of 34 g. of crystallised sodium dichromate in 125 ml. of water as rapidly as possible to the stirred solution. After 2–3 minutes, filter the straw-coloured precipitate of nitrosobenzene on a Buchner funnel and wash it with 200 ml. of water. Steam distil the nitrosobenzene, preferably from an all-glass apparatus (compare Fig. *II*, *61*, 5) since cork and rubber are readily attacked, as rapidly as possible ; the nitrosobenzene tends to decompose at the elevated temperature. Cool the receiver in ice because the compound has a high vapour pressure at room temperature. The nitrosobenzene condenses to a green liquid, which solidifies to a white solid ; care should be taken that the solid does not clog the condenser by turning off the water supply from time to time. Stop the distillation when yellow oily material appears in the condenser. Filter ; grind the nitrosobenzene in a glass mortar with a little water. Filter at the pump, wash it with water until the washings are no longer brown, and drain as completely as possible. Dry the solid between layers of filter paper. The yield of nitrosobenzene, m.p. 66–67°, is 30 g. A pure product, m.p. 68°, may be obtained by recrystallisation from a small volume of alcohol with good cooling : the compound should be dried over anhydrous calcium chloride at atmospheric pressure. The substance may be kept for 1–2 days at room temperature and for longer periods at 0°.

IV,85. AZOXYBENZENE

Equip a 500 ml. three-necked flask with an efficient stirrer (*e.g.*, a Hershberg stirrer, Fig. *II*, 7, 8) and a reflux condenser ; stopper the third neck. Place a solution of 30 g. of sodium hydroxide in 100 ml. of water, and also 20·5 g. (17·1 ml.) of pure nitrobenzene in the flask, immerse it in a water bath maintained at 55–60°, and add 21 g. of anhydrous dextrose in small portions, with continuous stirring, during 1 hour. Then heat on a boiling water bath for 2 hours. Pour the hot mixture into a 1 litre round-bottomed flask and steam distil (Fig. *II*, *40*, 1) to remove aniline and nitrobenzene. When the distillate is clear (*i.e.*, after about 1 litre has been collected), pour the residue into a beaker cooled in an ice bath. The azoxybenzene soon solidifies. Filter with suction, grind the lumps of azoxybenzene in a mortar, wash with water, and dry upon filter paper or upon a porous plate. The yield of material, m.p. 35–35·5°, is 13 g. Recrystallise from 7 ml. of rectified spirit or of methyl alcohol ; the m.p. is raised to 36°.

IV,86. AZOBENZENE

Method 1 (from nitrobenzene). Support a 1 litre three-necked flask, equipped with a mercury-sealed stirrer and a reflux condenser, on a water bath, and place a solution of 65 g. of sodium hydroxide in 150 ml. of

water, 50 g. (41·5 ml.) of pure nitrobenzene and 500 ml. of methyl alcohol in the flask. Add 53 g. of zinc powder (1) to the mixture, start the stirrer, and reflux for 10 hours (2). Filter the mixture while hot, and wash the precipitate of sodium zincate with a little methyl alcohol. The strongly alkaline filtrate is not always clear : render it neutral to litmus by the cautious addition of concentrated hydrochloric acid, and filter again. Distil off the methyl alcohol from the filtrate, cool the residue in ice, and filter off the solid azobenzene. The crude azobenzene contains occluded zinc salts. To remove these, add the crude product to 100 ml. of 2 per cent. hydrochloric acid, warm to about 70° in order to melt the azobenzene, and stir mechanically for 5 minutes ; continue the stirring whilst the mixture is immersed in ice water in order to solidify the azobenzene. Filter, wash well with water, drain thoroughly, and recrystallise from a mixture of 145 ml. of rectified spirit and 12 ml. of water ; collect the azobenzene and dry in the air. The yield of pure azobenzene (reddish-orange crystals), m.p. 67–68°, is 31 g. (3).

Notes.

(1) This weight assumes 100 per cent. purity. The zinc powder should be analysed and a proportional quantity employed according to the zinc content (see Section IV,83, *Note 2*).

(2) At the end of this time, the reddish mixture should be free from the odour of nitrobenzene ; if it is not, reflux for 2–3 hours longer.

(3) Frequently the recrystallized azobenzene has m.p. 61°, which is unaffected by recrystallisation from alcohol. Upon distillation from a 50 ml. distilling flask fitted with a short air condenser, the m.p. is raised to 67·5° and the recovery is about 90 per cent. : one recrystallisation from diluted alcohol (as above) then gives perfectly pure azobenzene of m.p. 68·5°.

Method 2 (from hydrazobenzene). Prepare a solution of sodium hypobromite by adding 10 g. (3·2 ml.) of bromine dropwise to a cold solution of 6·0 g. of sodium hydroxide in 75 ml. of water immersed in an ice bath. Dissolve 9·5 g. of hydrazobenzene (Section **IV,87**) in 60 ml. of ether contained in a separatory funnel, and add the cold sodium hypobromite solution in small portions. Shake for 10 minutes, preferably mechanically. Separate the ether layer, pour it into a 100 ml. distilling flask, and distil off the ether by warming gently on a water bath. Dissolve the warm liquid residue in about 30 ml. of alcohol, transfer to a small beaker, heat to boiling on a water bath, add water dropwise to the hot solution until the azobenzene just commences to separate, render the solution clear again with a few drops of alcohol, and cool in ice water. Filter the orange crystals at the pump, and wash with a little 50 per cent. alcohol. Dry in the air. The yield is 8 g.

IV,87. HYDRAZOBENZENE (*sym.*DIPHENYLHYDRAZINE)

Support a 1500 ml. three-necked flask, equipped with a mercury-sealed stirrer and a double surface reflux condenser, on a water bath, and place a solution of 84 g. of sodium hydroxide in 185 ml. of water, 50 g. (41·5 ml.) of nitrobenzene and 500 ml. of methyl alcohol in the flask. Add 70 g. of zinc powder (1), start the stirrer, and reflux for 10 hours. The solution gradually assumes the reddish colour of azobenzene and then on further

reduction, turns to a pale yellow (due to hydrazobenzene). If the colour is not almost completely discharged at the end of the refluxing period, add a further 10 g. of zinc powder, and reflux for 2–3 hours longer. Filter the hot solution through a pre-heated Buchner funnel and wash the sodium zincate upon the filter with a little hot methanol. Pour the filtrate into a large flask (2), stopper it loosely, and cool it in a freezing mixture of ice and salt to accelerate crystallisation. After 1 hour filter off the almost colourless crystals of hydrazobenzene at the pump as rapidly as possible (take care not to draw air through them unnecessarily), wash with 50 per cent. methyl alcohol to which a little sulphurous acid has been added until the filtrate is no longer alkaline. Dry in a vacuum desiccator. The resulting almost colourless hydrazobenzene (15 g.; m.p. 125°) is sufficiently pure for the preparation of benzidine or of azobenzene. If it is required pure (m.p. 126° with production of a yellow colour), it may be recrystallised from hot alcohol containing a little ammonium sulphide or sulphurous acid (these assist in preventing atmospheric oxidation).

Owing to the great tendency of hydrazobenzene to undergo oxidation, all operations involving filtration should be carried out as rapidly as possible and air should not be drawn through it unnecessarily. The substance should be dried in a vacuum desiccator: it can only be preserved in a colourless condition if it is kept in an atmosphere of carbon dioxide or nitrogen or in sealed vessels.

Notes.

(1) This weight of zinc powder assumes 100 per cent. purity. The zinc content should be determined (see Section IV,83, *Note 2*) and a corresponding adjustment made.

(2) If the methyl alcohol is distilled off before thorough cooling in a freezing mixture, the yield of hydrazobenzene is appreciably increased, but the product is considerably more coloured due to admixture with a trace of azobenzene. About 12 g. of impure hydrazobenzene may be recovered by distilling off the methyl alcohol from the filtrate after the colourless hydrazobenzene has been collected.

IV,88. BENZIDINE

Dissolve 9·5 g. of hydrazobenzene (Section **IV,87**) in the minimum volume of ether (about 90 ml. are usually required), and add this solution in small portions from a separatory funnel to 100 ml. of ice-cold dilute hydrochloric acid (1 : 1) contained in a 350 ml. conical flask: stopper the flask and shake after each addition. Benzidine hydrochloride separates out during the reaction. After all the hydrazobenzene has been introduced, add 50 ml. of concentrated hydrochloric acid and allow the mixture to stand for 30 minutes in ice water. Filter the benzidine hydrochloride at the pump, wash it first with 20 ml. of dilute hydrochloric acid (1 : 1) and then with two or three 20 ml. portions of ether (to dissolve any unchanged hydrazobenzene) (1).

To obtain the free base, dissolve the crude hydrochloride in 150–200 ml. of water, filter, and cool rapidly to about 20°. Pour the solution with stirring into a mixture of 150 g. of crushed ice and 50 ml. of 10 per cent. sodium hydroxide solution contained in a litre beaker. Filter off the

benzidine, which separates as greyish-white flocks, with suction on a Buchner funnel, and wash it thoroughly with water. Recrystallise from hot water (about 40 ml.) or from alcohol (about 15 ml.); collect the crystals and dry them in a steam oven or in a vacuum desiccator (2). The yield of pure, anhydrous benzidine, m.p. 128°, is 5 g.

Note.

(1) The hydrochloride (about 9 g.) may be recrystallised by dissolving in hot water and adding concentrated hydrochloric acid to the slightly cooled solution, but this is generally unnecessary. The diphenyline may be isolated by rendering the filtrate from the benzidine hydrochloride strongly alkaline with sodium hydroxide solution, cooling in ice, filtering, and recrystallising from alcohol; the yield is 0·5 g., m.p. 45°.

(2) Benzidine crystallises from water as the monohydrate; the m.p. of the latter is unsatisfactory, since water is lost gradually above about 95°.

REDUCTION OF DIAZONIUM COMPOUNDS. ARYL HYDRAZINES

Phenylhydrazine may be prepared by reducing phenyldiazonium chloride solution with excess of warm sodium sulphite solution, followed by acidification with hydrochloric acid, when the hydrochloride crystallises out on cooling. Treatment of the latter with excess of sodium hydroxide solution liberates the free base. The reaction is believed to proceed through the following stages :—

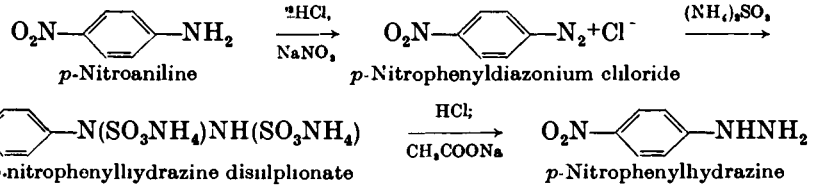
$$\underset{\text{Phenyldiazonium chloride}}{C_6H_5N_2{}^+Cl^-} \xrightarrow{Na_2SO_3} \underset{\text{Sodium phenyldiazosulphonate}}{C_6H_5N{=}NSO_3Na} \xrightarrow[(2H)]{NaHSO_3} \underset{\text{Sodium phenylhydrazine sulphonate}}{C_6H_5NHNHSO_3Na}$$

$$\xrightarrow{HCl} \underset{\text{Phenylhydrazine hydrochloride}}{C_6H_5NHNH_2,HCl} \xrightarrow{NaOH} \underset{\text{Phenylhydrazine}}{C_6H_5NHNH_2}$$

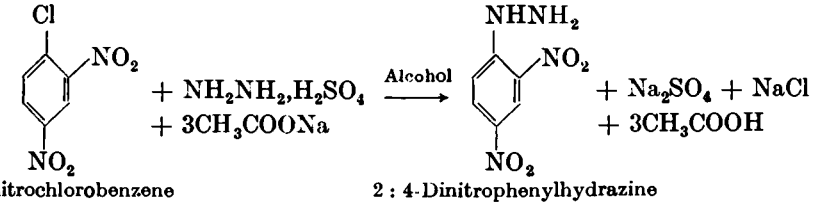
It may also be prepared by the reduction of phenyldiazonium chloride with the calculated amount of a solution of stannous chloride in hydrochloric acid, but the yield is not so high as that obtained by the above sulphite method :

$$C_6H_5N_2{}^+Cl^- + 2SnCl_2 + 4HCl \longrightarrow C_6H_5NHNH_2,HCl + 2SnCl_4$$

***p*-Nitrophenylhydrazine** may be similarly prepared from *p*-nitrophenyldiazonium chloride by reduction with sodium or ammonium sulphite :



This method cannot be applied to polynitro amines, since these are so weakly basic that they can be diazotised only under special conditions in strongly acidic solutions. In such cases use may, however, be made of the mobility conferred upon halogen atoms by the presence of nitro groups in the *ortho* and *para* positions. Thus the valuable reagent **2 : 4-dinitrophenylhydrazine** is readily prepared by the condensation of 2 : 4-dinitrochlorobenzene with hydrazine :



The reaction represented is that with hydrazine solution, produced from hydrazine sulphate and sodium acetate in the presence of aqueous alcohol. Excellent results are also obtained by interaction of the commercially available 60–64 per cent. hydrazine solution with a solution of 2 : 4 dinitrochlorobenzene in triethylene glycol or in diethylene glycol at about 20°.

IV,89. PHENYLHYDRAZINE

Place 130 ml. of concentrated hydrochloric acid in a 1·5 litre round-bottomed flask, equipped with a mechanical stirrer and immersed in a freezing mixture of ice and salt. Start the stirrer and, when the temperature has fallen to about 0°, add 60 g. of finely-crushed ice (1), run in 47·5 g. (46·5 ml.) of pure aniline during about 5 minutes, and then add another 60 g. of crushed ice. Dissolve 35 g. of sodium nitrite in 75 ml. of water, cool to 0–3°, and run in the cold solution from a separatory funnel, the stem of which reaches nearly to the bottom of the flask. During the addition of the nitrite solution (*ca.* 20 minutes), stir vigorously and keep the temperature as near 0° as possible by the frequent addition of crushed ice. There should be a slight excess of nitrous acid (potassium iodide-starch paper test) at the end of 10 minutes after the last portion of nitrite is added.

In the meantime, prepare a sodium sulphite solution as follows. In a 2-litre beaker or bolt-head flask place 50 g. of sodium hydroxide (2) and add 500 ml. of water. When the sodium hydroxide has dissolved, add 112·5 g. of recrystallised sodium bisulphite (3), and stir mechanically until the solid has dissolved. Cool the resulting solution to about 25° and add a few drops of phenolphthalein indicator solution. Introduce small quantities of sodium bisulphite until the pink colour of the solution just disappears, then stir in a further 12 g. of sodium bisulphite (the total weight required should not exceed 135–140 g.). Cool this solution, with stirring, to about 5° by immersion in an ice bath, then add about 60 g. of crushed ice. Run in the ice-cold diazonium solution as rapidly as possible, while stirring vigorously. The reaction mixture immediately acquires a bright orange-red colour. Slowly heat the solution to 60–70° on a water bath and maintain this temperature for 30–60 minutes, *i.e.*, until the colour becomes quite dark. Acidify the solution to litmus with concentrated hydrochloric acid (40–50 ml. are required); continue the heating on a boiling water bath until the colour becomes much lighter and in any case for 4–6 hours. If any solid is present, filter the solution. To the hot, clear solution add, with stirring, 500 ml. of concentrated hydrochloric acid; cool, first in running water, and then in a freezing mixture to 0°. The phenylhydrazine hydrochloride separates as yellowish or pinkish crystals. Collect them on a Buchner funnel, drain, wash with 25 ml. of dilute hydrochloric acid (1 : 3), and press well with a large glass stopper (4).

Liberate the free base by adding to the phenylhydrazine hydrochloride 125 ml. of 25 per cent. sodium hydroxide solution. Extract the phenylhydrazine with two 40 ml. portions of benzene, dry the extracts with 25 g. of sodium hydroxide pellets or with anhydrous potassium carbonate: thorough drying is essential if foaming in the subsequent distillation is to be avoided. Most of the benzene may now be distilled under atmospheric pressure, and the residual phenylhydrazine under reduced pressure. For this purpose, fit a small dropping funnel to the main neck of a 100 ml. Claisen flask (which contains a few fragments of porous porcelain) and assemble the rest of the apparatus as in Fig. *II*, *20*, 1, but do not connect the " Perkin triangle " to the pump. Run in about 40 ml. of the benzene, solution into the flask, heat the latter in an air bath (Fig. *II*, *5*, 3) so that

the benzene distils over steadily. Allow the remainder of the benzene solution to run in from the dropping funnel as fast as the benzene itself distils over. When all the benzene solution has been introduced into the flask, close the stopcock on the funnel, and continue the heating until the temperature on the thermometer reads about 90°. Allow to cool. Replace the dropping funnel by a rubber stopper carrying a capillary tube reaching to the bottom of the flask, and distil under diminished pressure. Collect the phenylhydrazine at 137–138°/18 mm. (or at 119–120°/12 mm.). The yield of almost colourless liquid is 70 g.; it crystallises on cooling in ice and then melts at 23°. Phenylhydrazine slowly darkens on exposure to light.

CAUTION. Phenylhydrazine is highly poisonous and produces unpleasant burns in contact with the skin. Wash off immediately any liquid which has come into contact with the skin first with 2 per cent. acetic acid, then with soap and water.

Notes.

(1) External cooling may be dispensed with if more ice is added.

(2) This weight assumes 100 per cent. purity of the sodium hydroxide. If the commercial solid is used, its purity should be determined and a corresponding adjustment made in the weight.

(3) The sodium sulphite solution may also be prepared by dissolving 100 g. of pure (or a corresponding quantity of commercial) sodium hydroxide in about 125 ml. of water, and then diluting to 750 ml. The flask is cooled in running water, a few drops of phenolphthalein indicator are added, and sulphur dioxide passed in until the pink colour just disappears (it is advisable to add a further 1–2 drops of the indicator at this point) and then for 2–3 minutes longer. It is best to remove a sample for test from time to time, dilute with 3–4 volumes of water, and test with 1 drop of phenolphthalein.

(4) If desired, the phenylhydrazine hydrochloride may be purified by recrystallisation. The crude hydrochloride is boiled with 6 times its weight of water and a few grams of decolourising carbon. After filtering, a volume of concentrated hydrochloric acid equal in volume to one-third of the solution is added, and the mixture cooled to 0°. Pure white crystals are obtained in 85–90 per cent. yield.

IV,90. *p*-NITROPHENYLHYDRAZINE

Dissolve 10 g. of *p*-nitroaniline (Section **IV,51**) in a mixture of 21 ml. of concentrated hydrochloric acid and an equal volume of water, and cool rapidly to 0° in order to obtain the hydrochloride of the base in a fine state of division. Diazotise in the usual way (see Section **IV,68**) by the gradual addition of a solution of 6·0 g. of sodium nitrite in 12 ml. of water. Continue the stirring for a few minutes, filter the solution rapidly, and add it from a separatory funnel to an ice-cold solution of 41 g. of sodium sulphite (90 per cent. $Na_2SO_3,7H_2O$) in 100 ml. of water containing 4 g. of sodium hydroxide (1); stir the mixture during the addition which requires about 5 minutes. (If the diazonium solution is added too rapidly, an orange-red precipitate of sodium *p*-nitrodiazobenzene sulphonate is produced, and is apt to form a resin.) Allow the solution to stand for 5 minutes, acidify with 70 ml. of concentrated hydrochloric acid, and heat on a water bath at 25° for 3 minutes, when yellow needles commence to separate. Allow to stand overnight, filter off the crystals, heat them with 20 ml. of concentrated hydrochloric acid on a water bath for 7 minutes, and allow to cool. Filter off the precipitate, consisting of

p-nitrophenylhydrazine hydrochloride and sodium salts, dissolve it in water and treat the solution with a concentrated solution of sodium acetate : the free base will separate out in an almost pure state (7–8 g.). The *p*-nitrophenylhydrazine may be recrystallised from alcohol and is obtained as light brown crystals, m.p. 158° (decomp.).

Note.

(1) The alkaline sodium sulphite solution may be replaced by saturated ammonium sulphite solution prepared as follows. Pass sulphur dioxide into a mixture of 1 part of concentrated ammonia solution (sp. gr. 0·88) and two parts of crushed ice in a freezing mixture until the liquid smells strongly of sulphur dioxide, and then neutralise with ammonia solution. This solution slowly deposits ammonium sulphite crystals and contains about 0·25 g. of SO_2 per ml. Use 60 ml. of this ice-cold ammonium sulphite solution to which 8 ml. of concentrated ammonia solution are added. After the addition of the solution of *p*-nitrophenyldiazonium chloride, allow the mixture to stand for 1 hour in a freezing mixture, filter off the yellow precipitate of ammonium *p*-nitrophenylhydrazine disulphonate, heat it on a water bath with 20 ml. of concentrated hydrochloric acid at 70–80° for 7 minutes, cool the blood-red solution, and dissolve the resulting precipitate of *p*-nitrophenylhydrazine hydrochloride and ammonium salts in water, and isolate the base as above.

IV,91. 2 : 4-DINITROPHENYLHYDRAZINE

Suspend 35 g. of finely-powdered hydrazine sulphate in 125 ml. of hot water contained in a 400 ml. beaker, and add, with stirring, 118 g. of crystallised sodium acetate or 85 g. of potassium acetate. Boil the mixture for 5 minutes, cool to about 70°, add 80 ml. of rectified spirit, filter at the pump and wash with 80 ml. of hot rectified spirit. Keep the filtered hydrazine solution for the next stage in the preparation.

Equip a 1 litre three-necked flask or a 1 litre bolt-head flask with a reflux condenser and a mercury-sealed stirrer. Dissolve 50·5 g. of commercial 2 : 4-dinitro-1-chlorobenzene in 250 ml. of rectified spirit in the flask, add the hydrazine solution, and reflux the mixture with stirring for an hour. Most of the condensation product separates during the first 10 minutes. Cool, filter with suction, and wash with 50 ml. of warm (60°) rectified spirit to remove unchanged dinitrochlorobenzene, and then with 50 ml. of hot water. The resulting 2 : 4-dinitrophenylhydrazine (30 g.) melts at 191–192° (decomp.), and is pure enough for most purposes. Distil off half the alcohol from the filtrate and thus obtain a less pure second crop (about 12 g.) : recrystallise this from *n*-butyl alcohol (30 ml. per gram). If pure 2 : 4-dinitrophenylhydrazine is required, recrystallise the total yield from *n*-butyl alcohol or from dioxan (10 ml. per gram) : this melts at 200° (decomp.).

The following alternative method of preparation is recommended. Dissolve 50 g. of purified 2 : 4-dinitrochlorobenzene (1) in 100 ml. of triethylene glycol (gentle warming may be necessary; alternatively, 125 ml. of warm diethylene glycol may be used) in a 600 ml. beaker and cool, with mechanical stirring, in an ice bath to 15–18°. Place 15 ml. of commercial 60–65 per cent. hydrazine solution in a small separatory funnel supported over the beaker. Add the hydrazine solution to the stirred solution in the beaker at such a rate that the temperature is maintained between 15° and 20° (20–30 minutes). When

the exothermic reaction is over, digest the paste on a boiling water bath with 50 ml. of methanol for 15–20 minutes. Cool the reaction mixture, filter with suction and wash with a little methanol. Dry at 100°. The yield of 2:4-dinitrophenylhydrazine, m.p. 192–193° (decomp.), is 46 g. The product is pure enough for most purposes: the pure compound may be obtained by recrystallisation from *n*-butyl alcohol or from dioxan as described above.

Cognate Preparation

2 : 4-Dinitroaniline. This preparation is another illustration of the mobile character of the chlorine atom in 2 : 4-dinitro-1-chlorobenzene:

$$(NO_2)_2C_6H_3Cl + 2NH_3 \longrightarrow (NO_2)_2C_6H_3NH_2 + NH_4Cl$$

Place a mixture of 18 g. of ammonium acetate and 50 g. of commercial 2 : 4-dinitro-1-chlorobenzene (1) in a 250 ml. bolt-head flask, and fit it with a reflux condenser and inlet tube (at least 2 cm. diameter in order to prevent clogging) which terminates just above the surface of the reaction mixture. Half immerse the flask in an oil bath. Pass ammonia gas (from a cylinder) through a bubble counter, which contains a solution of 3 g. of potassium hydroxide in 2·5 ml. of water, into the mixture. Heat the oil bath to 170°, and pass the ammonia gas at the rate of 3–4 bubbles per second for 6 hours. Allow the reaction mixture to cool, break up the solid cautiously with a glass rod, add 100 ml. of water, heat to boiling and filter while hot. Dissolve the residue in 500 ml. of boiling rectified (or methylated) spirit, and add water (*ca.* 150 ml.) until the solution becomes turbid; heat until the turbidity disappears and allow the clear solution to cool overnight. Filter the crystals at the pump and dry in the steam oven. The yield is 35 g., m.p. 176–177°. To obtain a perfectly pure product, recrystallise again from alcohol and water; use 20 ml. of alcohol per gram of solid: 31·5 g. of pure 2 : 4-dinitroaniline, m.p. 180°, are thus obtained.

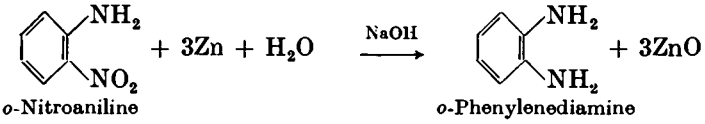
Note.

(1) It is advisable to recrystallise the commercial dinitrochlorobenzene from alcohol; m.p. 51–52.°

AROMATIC DIAMINES

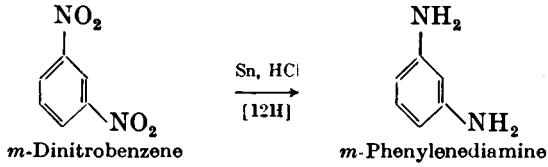
Compounds containing two primary amino groups attached to a benzene ring can be prepared by the reduction of dinitro compounds and of nitroanilines, usually with tin or stannous chloride and hydrochloric acid or with iron and very dilute hydrochloric acid. *Para*-diamines may also be obtained by the reduction of aromatic amino-azo compounds (*e.g.*, *p*-aminodimethylaniline from methyl orange, see Section **IV,78**). *p*-Phenylenediamine may also be prepared from *p*-nitroacetanilide: reduction with iron and acid yields *p*-aminoacetanilide, which may be hydrolysed to the diamine.

Experimental details are given for ***o*-phenylenediamine**, which is conveniently prepared by the reduction of *o*-nitroaniline in alcoholic sodium hydroxide solution with zinc powder:



o-Nitroaniline *o*-Phenylenediamine

and for ***m*-phenylenediamine**:



m-Dinitrobenzene *m*-Phenylenediamine

IV,92. *o*-PHENYLENEDIAMINE

Equip a 750 ml. three-necked flask with a reflux condenser and a liquid-sealed mechanical stirrer, and place in it 46 g. of *o*-nitroaniline, 27 ml. of 20 per cent. sodium hydroxide solution and 170 ml. of rectified spirit. Stir the mixture vigorously and heat it on a water bath to gentle boiling. Remove the source of heat from beneath the bath, and introduce 5 g. portions of zinc powder at such a rate that the solution is kept boiling (1); add 90 g. of zinc powder (2) in all. Reflux the mixture, with stirring, for 1 hour; the colour of the solution changes from deep red to nearly colourless. Filter the hot mixture at the pump; return the zinc residue to the flask and extract it with two 100 ml. portions of hot rectified spirit. Combine the extracts with the filtrate, add 2 g. of sodium hyposulphite ($Na_2S_2O_4$), and concentrate the solution under reduced pressure (water pump) on a steam bath to a volume of 80–100 ml.; use the apparatus shown in Fig. *II*, *37*, 1. Cool the solution in a freezing mixture of ice and salt, collect the pale yellow crystals on a Buchner funnel, wash once with 10–15 ml. of ice water, and dry in a vacuum desiccator. The yield of crude *o*-phenylenediamine, m.p. 98–100°, is 33 g. This is sufficiently pure for most practical purposes. If a pure material is required (3), dissolve the crude product in 100–115 ml. of hot water containing 1 g. of sodium hyposulphite and add a few grams of decolourising carbon, filter, and cool in an ice-salt mixture. Collect the colourless crystals of pure *o*-phenylenediamine on a Buchner funnel, wash with 10 ml. of

ice water, and dry in a vacuum desiccator; the yield is 28·5 g., m.p. 100-101°. It darkens rapidly upon exposure to light.

Notes.

(1) Sometimes the reaction stops suddenly; it is then necessary to add a further 10 ml. of 20 per cent. sodium hydroxide solution and warm to the boiling point: this causes the reaction to continue. Occasionally, the reduction becomes very vigorous: a wet towel and a bath of ice water should be kept close at hand.

(2) This weight of zinc powder assumes 100 per cent. purity: an equivalent amount of less pure material may be used (see Section IV,83, *Note 2*).

(3) The crude *o*-phenylenediamine may be converted into the dihydrochloride and the salt purified in the following manner. Dissolve it in 60 ml. of concentrated hydrochloric acid and 40 ml. of water containing 2 g. of stannous chloride, and treat the hot solution with 2–3 g. of decolourising carbon. Filter, add 100 ml. of concentrated hydrochloric acid to the hot colourless filtrate, and cool in a freezing mixture of ice and salt. Collect the colourless crystals of the dihydrochloride on a Buchner or sintered glass funnel, wash with a small volume of concentrated hydrochloric acid, and dry in a vacuum desiccator over sodium hydroxide. The yield is 51 g.

IV,93. *m*-PHENYLENEDIAMINE

In a 2-litre round-bottomed flask, provided with a reflux condenser, place 25 g. of *m*-dinitrobenzene (Section **IV,12**) and 100 g. of granulated tin; add 200 ml. of concentrated hydrochloric acid in 15 ml. portions according to the procedure described under *Aniline* (Section **IV,34**, *Method 1*). When all the acid has been introduced, complete the reduction by heating on a water bath for 1 hour. Dilute with 750 ml. of water, heat nearly to boiling, and pass hydrogen sulphide into the liquid until all the tin is precipitated as the sulphide. Filter a small quantity from time to time and test for completeness of precipitation with hydrogen sulphide. Allow the precipitate to settle overnight, decant the clear liquid, and filter the residue with suction through two or three filter papers (1). Add sodium hydroxide solution to the filtrate until the latter is strongly alkaline, and extract several times with ether. Dry over anhydrous potassium carbonate or sodium hydroxide pellets, remove the ether, and then distil the residue: use an air condenser after all the ether has passed over. Collect the portion boiling between 280° and 284°: this solidifies on standing to crystalline *m*-phenylenediamine, m.p. 63°. The yield is 13 g.

Note.

(1). The dihydrochloride may be obtained by evaporating the filtrate on a water bath until crystals appear, and then cooling in ice. The crystals are filtered at the pump, washed with a little concentrated hydrochloric acid, and dried in a vacuum desiccator over sodium hydroxide.

MISCELLANEOUS COMPOUNDS DERIVED FROM PRIMARY AMINES

IV,94. THIOCARBANILIDE (*sym.*-DIPHENYLTHIOUREA)

Thiocarbanilide is prepared by heating a mixture of aniline and carbon disulphide in absolute ethyl alcohol :

$$CS_2 + 2C_6H_5NH_2 \xrightarrow{C_2H_5OH} CS(NHC_6H_5)_2 + H_2S$$

The mechanism of the reaction is probably as follows :

$$C_6H_5NH_2 \xrightarrow{CS_2} \underset{\text{Phenyldithiocarbamic acid}}{C_6H_5NHC(=S)SH} \xrightarrow{-H_2S} \underset{\text{Phenyl } iso\text{-thiocyanate}}{C_6H_5N=C=S} \xrightarrow{+C_6H_5NH_2} \underset{\text{Thiocarbanilide}}{(C_6H_5NH)_2CS}$$

In a 1 litre round-bottomed flask provided with an efficient double surface condenser, place 40 g. (39 ml.) of aniline, 50 g. (40 ml.) of carbon sulphide (*CAUTION :* inflammable) (1), and 50 g. (63·5 ml.) of absolute ethyl alcohol (2). Set up the apparatus in the fume cupboard or attach an absorption device to the top of the condenser (see Fig. *II*, *8*, 1) to absorb the hydrogen sulphide which is evolved. Heat upon an electrically-heated water bath or upon a steam bath for 8 hours or until the contents of the flask solidify. When the reaction is complete, arrange the condenser for downward distillation (Fig. *II*, *13*, 3), and remove the excess of carbon disulphide and alcohol (*CAUTION :* inflammable; there must be no flame near the receiver). Shake the residue in the flask with excess of dilute hydrochloric acid (1 : 10) to remove any aniline present, filter at the pump, wash with water, and drain well. Dry in the steam oven. The yield of crude product, which is quite satisfactory for the preparation of phenyl *iso*-thiocyanate (Section **IV,95**), is 40–45 g. Recrystallise the crude thiocarbanilide by dissolving it, under reflux, in boiling rectified spirit (filter through a hot water funnel if the solution is not clear), and add hot water until the solution just becomes cloudy and allow to cool. Pure *sym.*-diphenylthiourea separates in colourless needles, m.p. 154°.

Notes.

(1) No flames may be present in the vicinity : read Section **II,14**.

(2) The addition of powdered potassium hydroxide (about 20 per cent. of the weight of the carbon disulphide) reduces the refluxing period necessary to complete the reaction.

IV,95. PHENYL *iso*-THIOCYANATE * (*from Thiocarbanilide*)

Upon heating thiocarbanilide with concentrated hydrochloric acid, it is partly converted into phenyl *iso*-thiocyanate :

$$C_6H_5NHCSNHC_6H_5 \xrightarrow{\text{Conc. HCl}} \underset{\text{Phenyl } iso\text{-thiocyanate}}{C_6H_5N=C=S} + C_6H_5NH_2$$

* Also termed phenyl mustard oil or phenyl thiocarbimide.

A little hydrogen sulphide is evolved in the reaction and triphenylguanidine is formed as a by-product, probably in accordance with the following scheme:

$$C_6H_5NHCSNHC_6H_5 \xrightarrow{-H_2S} \underset{\text{Carbodiphenylimide}}{C_6H_5N{=}C{=}NC_6H_5} \xrightarrow{+C_6H_5NH_2} \underset{\text{Triphenylguanidine}}{C_6H_5N{=}C(NHC_6H_5)}$$

Place 25 g. of crude thiocarbanilide (Section **IV,94**) and 100 ml. of concentrated hydrochloric acid in a 250 ml. distilling flask; plug the side arm of the flask, and fit a reflux condenser into the neck (Fig. *III*, *28*, 1 but with the trap omitted). Reflux gently in the fume cupboard for 30 minutes. Arrange the flask for distillation (compare Fig. *II*, *13*, 1) and distil the mixture until the oily phenyl *iso*-thiocyanate has all passed over; the volume remaining in the flask will be 25–30 ml. Crystals of triphenylguanidine hydrochloride may appear in the distilling flask during the latter part of the distillation. Dilute the distillate with an equal volume of water, and extract the mustard oil with ether; wash the extract with a little sodium carbonate solution, and dry over anhydrous calcium chloride or magnesium sulphate. Remove the ether using a small distilling flask (Fig. *II*, *13*, 4) and then distil the residual oil. Collect the phenyl *iso*-thiocyanate at 217–220° (1). The yield is 10 g.

To isolate the **triphenylguanidine**, dilute the residue in the flask with 50 ml. of water, add 2–3 g. of decolourising carbon, warm, and filter. Cool the solution in ice, and filter off the hydrochloride at the pump. Dissolve it in the minimum volume of hot water, render the solution alkaline with sodium hydroxide, and allow to cool. Filter off the free base (triphenylguanidine), and recrystallise it from alcohol; it separates in colourless crystals, m.p. 144°. The yield is 3 g.

Note.

(1) It may also be distilled under diminished pressure; see Section **IV,96.**

IV,96. PHENYL *iso*-THIOCYANATE (*from Aniline*)

Phenyl *iso*-thiocyanate may be prepared in quantity directly from aniline. Aniline, carbon disulphide and concentrated aqueous ammonia react to form the sparingly soluble ammonium phenyldithiocarbamate; this is decomposed by lead nitrate to produce phenyl *iso*-thiocyanate:

$$C_6H_5NH_2 + CS_2 \xrightarrow{NH_3(H_2O)} \underset{\text{Ammonium phenyldithiocarbamate}}{C_6H_5NHC(=S)SNH_4}$$

$$C_6H_5NHCS_2NH_4 + Pb(NO_3)_2 \longrightarrow \underset{\text{Phenyl-}iso\text{-thiocyanate}}{C_6H_5N{=}C{=}S} + NH_4NO_3 + HNO_3 + PbS$$

Equip a 500 ml. three-necked flask with a powerful mechanical stirrer and a separatory funnel; leave the third neck open or loosely stoppered. Introduce, while the flask is cooled in a freezing mixture of ice and salt, 90 ml. of concentrated ammonia solution (sp. gr. 0·88) and 54 g. (43 ml.) of pure (*e.g.*, A.R.) carbon disulphide. Stir the mixture and run in 56 g. (55 ml.) of pure aniline from the separatory funnel during about 20 minutes; stir for a further 30 minutes, and allow to stand for another 30 minutes. A heavy precipitate of ammonium phenyldithiocarbamate separates. Transfer the salt to a 5 litre round-bottomed flask by four extractions with 200 ml. portions of water. Add to the resulting solution, with

constant stirring, a solution of 200 g. of lead nitrate in 400 ml. of water; lead sulphide precipitates. Steam distil the mixture into a receiver containing 10 ml. of *ca.* *N*-sulphuric acid as long as organic material passes over (2–3 litres of distillate). Separate the oil, dry it over anhydrous calcium chloride or magnesium sulphate, and distil under diminished pressure. Collect the phenyl *iso*-thiocyanate at 120–121°/35 mm. or at 95°/12 mm. The yield is 62 g.

COGNATE PREPARATION

p-Bromophenyl *iso*-thiocyanate, p-BrC_6H_4NCS. Add 41 ml. of concentrated ammonia solution (sp. gr. 0·88) slowly to a solution of 45 g. of p-bromoaniline (Section **IV,49**), 30 g. (24 ml.) of A.R. carbon disulphide and 40 ml. of rectified spirit (95 % C_2H_5OH) at 10–15° contained in a flask. Stopper the flask, cover it with a damp towel, and shake the milky suspension occasionally until a clear solution is obtained: do not allow the temperature to rise above 30°. Considerable heat is evolved, and the intermediate dithiocarbamate soon crystallises out. Allow to stand overnight, filter the crystals, wash with a little ether, dissolve in 1500 ml. of water, and stir mechanically while a solution of 87 g. of lead nitrate in 175 ml. of water is slowly added. Continue the stirring for 20 minutes, and isolate the p-bromophenyl *iso*-thiocyanate by steam distillation into a receiver containing 5 ml. of *ca.* *N* sulphuric acid; if the substance solidifies in the condenser, stop the cooling water until the solid has melted and run into the receiver. Filter the cold solid product, wash with a little water, and dry in the air upon filter paper. The yield is 15 g., m.p. 61°.

In this modified procedure the presence of alcohol is essential otherwise no *iso*-thiocyanate is obtained. The process may be applied to other substituted anilines.

IV,97. PHENYLUREA * (*Cyanate Method*)

Salts of primary aromatic amines react with solutions of alkali cyanates to yield first the amine cyanate, which then undergoes molecular rearrangement to the arylurea, for example:

$$\{C_6H_5NH_3\}Cl + NaCNO \longrightarrow \underset{\text{Anilinium cyanate}}{\{C_6H_5NH_3\}CNO} + NaCl \longrightarrow \underset{\text{Phenylurea}}{C_6H_5NHCONH_2}$$

The monoarylurea may be prepared directly from the amine by heating it in aqueous solution with an equivalent quantity of alkali cyanate and excess of acetic acid, for example:

$$\underset{\text{A toluidine}}{CH_3C_6H_4NH_2} \longrightarrow \{CH_3C_6H_4NH_3\}C_2H_3O_2 \longrightarrow \{CH_3C_6H_4NH_3\}CNO$$
$$\longrightarrow \underset{\text{A tolylurea}}{CH_3C_6H_4NHCONH_2}$$

Method 1 (**from the amine hydrochloride**). Dissolve 13·0 g. of aniline hydrochloride in 200 ml. of water and filter, if necessary, from any insoluble matter into a 350 ml. beaker or conical flask. Add a solution of 6·5 g. of pure sodium cyanate in 50 ml. of warm water. Allow to stand for a few hours until crystallisation is complete. Filter with suction on a Buchner funnel, and wash with a little cold water. Dry in the steam

* Also termed monophenylurea.

oven. The phenylurea is usually colourless and melts at 148°, *i.e.*, is pure: the yield is 9 g. If the m.p. is somewhat low or if the product is slightly discoloured, dissolve it in 9–10 times its weight of boiling water, add cautiously 1–2 g. of decolourising carbon, and filter with the aid of a hot water funnel or a Buchner funnel and flask which have been preheated by the filtration of some boiling distilled water. Allow to cool, collect and dry the crystals as above.

Method 2 (**from the free amine**). Dissolve 9·3 g. (9·1 ml.) of aniline in 10 ml. of glacial acetic acid diluted to 100 ml. contained in a 250 ml. beaker or conical flask, and add with stirring or shaking a solution of 6·5 g. of pure sodium cyanate in 50 ml. of warm water. Allow to stand for 30 minutes, then cool in ice, and allow to stand for a further 30 minutes. Filter at the pump, wash with water and dry in the steam oven. The resulting phenylurea is generally colourless and has a m.p. of 148° (*i.e.*, is pure): the yield is 11 g. If the colour or the m.p. of the product is not quite satisfactory, recrystallise it from boiling water (10 ml. per gram) as in *Method 1*.

COGNATE PREPARATION

p-Tolylurea. Dissolve 10·7 g. of *p*-toluidine in a warm mixture of 10 ml. of glacial acetic acid and 50 ml. of water, and then dilute with 150 ml. of hot water. Introduce, with stirring or shaking, a solution of 6·5 g. of pure sodium cyanate in 50 ml. of hot water. The *p*-tolylurea precipitates almost immediately. Allow to stand several hours, filter at the pump, wash with water, and dry in the steam oven. The yield of *p*-tolylurea, m.p. 180–180·5°, is 14 g. Recrystallise by dissolving the crude product under reflux in about 95 ml. of methylated spirit and adding hot water in small portions until the solution is just turbid: warm until the solution is clear and allow to cool; filter and dry. The resulting *p*-tolylurea melts sharply at 181°.

p-Bromophenylurea. Proceed as for *p-Tolylurea*, but use 17·2 g. of *p*-bromoaniline dissolved in a mixture of 50 ml. of glacial acetic acid and 100 ml. of water at 35°; add gradually a solution of 6·5 g. of sodium cyanate in 50 ml. of water at 35°. The yield of crude *p*-bromophenylurea is 19 g.; m.p. 227°. Recrystallise from aqueous alcohol (240 ml. ethanol and 30 ml. of water); m.p. 228°. The m.p. depends somewhat upon the rate of heating.

IV,98. PHENYLUREA (*Urea Method*)

Salts of primary aromatic amines react with a solution of urea to give the corresponding arylureas, for example:

$$\{C_6H_5NH_3\}Cl + NH_2CONH_2 \longrightarrow C_6H_5NHCONH_2 + NH_4Cl$$

The *mechanism* of the reaction involves the intermediate formation of an amine cyanate (see previous Section); in aqueous solution urea behaves as an equilibrium mixture with ammonium cyanate:

$$NH_2CONH_2 \rightleftharpoons NH_4CNO$$

Some *sym.*-diphenylurea is also formed and the quantity increases with continued refluxing:

$$C_6H_5NHCONH_2 + \{C_6H_5NH_3\}Cl \longrightarrow (C_6H_5NH)_2CO + NH_4Cl$$

The diarylurea is insoluble in boiling water and is therefore easily separated from the monoarylurea, which is readily soluble. The proportion of diarylurea is highest for aniline and decreases with substituted anilines.

Dissolve 65 g. of aniline hydrochloride and 120 g. of urea in 200 ml. of water contained in a 1-litre round-bottomed flask; filter the solution, if necessary. Add 4 ml. of concentrated hydrochloric acid and 4 ml. of glacial acetic acid. Fit a reflux condenser to the flask, introduce a few fragments of broken porcelain, and boil the mixture for 30 minutes. Fine white crystals (largely *sym.*-diphenylurea) appear after about 15 minutes and gradually increase in amount as the refluxing is continued. Cool the flask in ice and filter with suction. Separate the mixture of phenylurea and diphenylurea (*ca.* 42 g.) by boiling with 500 ml. of water and filter at the pump through a preheated Buchner funnel into a warm flask; cool the filtrate, collect the phenylurea, drain well and dry in the steam oven. The phenylurea melts at 146–147° and weighs 30 g.; recrystallisation from hot water raises the m.p. to 148°. The crude diphenylurea (residue from first recrystallisation after drying at 100°) has m.p. 241° and weighs 10 g.; recrystallisation from glacial acetic acid or ethyl acetate with the addition of a little decolourising carbon gives a colourless product, m.p. 242°.

Cognate Preparations

***p*-Tolylurea.** Reflux a mixture of 18 g. *p*-toluidine hydrochloride, 30 g. of urea, 50 ml. of water, 1 ml. of concentrated hydrochloric acid and 1 ml. of glacial acetic acid contained in a 250 ml. bolt-head flask for 1 hour. The mixture becomes cloudy after about 10 minutes and a solid gradually collects at the surface of the liquid. Cool the reaction mixture in ice, filter with suction and wash with two 25 ml. portions of cold water. Drain well and dry the crude product at 120° for 2 hours; the yield is 18 g., m.p. 175°. Recrystallise as follows: dissolve the solid in 125 ml. of absolute industrial spirit, add hot water until the solution is just turbid, warm until the solution is clear (filter, if necessary, through a preheated Buchner funnel) and allow to cool. Filter; dry at 120°. The yield of *p*-tolylurea, m.p. 181°, is 12 g. Concentrate the mother liquor to about half the original volume, cool and filter; a further 2·5 g. of *p*-tolylurea, m.p. 180°, is obtained.

***p*-Methoxyphenylurea.** Proceed as for *Phenylurea* but use 79 g. of *p*-anisidine hydrochloride in place of 65 g. of aniline hydrochloride; reflux the mixture for 1 hour. Cool the reaction mixture slowly to 0°, filter and recrystallise from boiling water. The yield of *p*-methoxyphenylurea, m.p. 168°, is 60 g.

***p*-Ethoxyphenylurea.** Proceed as for *Phenylurea* but use 87 g. of *p*-phenetidine hydrochloride; reflux the mixture for 45–90 minutes. The product commences to separate after 20–30 minutes and increases rapidly until the entire contents of the flask suddenly set to a solid mass: withdraw the source of heat *immediately* at this point. Cool to room temperature, add 150 ml. of water, stir, filter with suction, and wash with cold water. Suspend the solid in 2 litres of boiling water, add 1 g. of decolourising carbon, boil for 5 minutes, and filter through a hot water funnel;

cool the colourless filtrate slowly to 0°, collect the solid which separates and dry at 100°. The yield of *p*-ethoxyphenylurea, m.p. 174°, is 60 g.

IV,99. *p*-IODOANILINE

This preparation illustrates the direct iodination of a primary aromatic amine by iodine; the sodium bicarbonate removes the hydrogen iodide as formed:

$$\underset{\text{Aniline}}{C_6H_5NH_2} + I_2 + NaHCO_3 \longrightarrow \underset{p\text{-Iodoaniline}}{p\text{-}IC_6H_4NH_2} + NaI + CO_2 + H_2O$$

Into a 1-litre beaker, provided with a mechanical stirrer, place 36·8 g. (36 ml.) of aniline, 50 g. of sodium bicarbonate and 350 ml. of water; cool to 12–15° by the addition of a little crushed ice. Stir the mixture, and introduce 85 g. of powdered, resublimed iodine in portions of 5–6 g. at intervals of 2–3 minutes so that all the iodine is added during 30 minutes. Continue stirring for 20–30 minutes, by which time the colour of the free iodine in the solution has practically disappeared and the reaction is complete. Filter the crude *p*-iodoaniline with suction on a Buchner funnel, drain as completely as possible, and dry it in the air. Save the filtrate for the recovery of the iodine (1). Place the crude product in a 750 ml. round-bottomed flask fitted with a reflux double surface condenser add 325 ml. of light petroleum, b.p. 60–80°, and heat in a water bath maintained at 75–80°. Shake the flask frequently and after about 15 minutes, slowly decant the clear hot solution into a beaker set in a freezing mixture of ice and salt, and stir constantly. The *p*-iodoaniline crystallises almost immediately in almost colourless needles; filter and dry the crystals in the air. Return the filtrate to the flask for use in a second extraction as before (2). The yield of *p*-iodoaniline, m.p. 62–63°, is 60 g.

Notes.

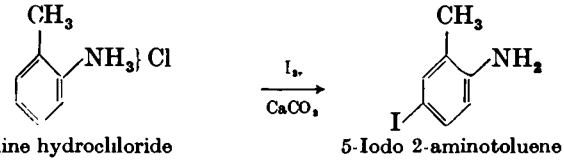
(1) The Iodine may be recovered from the aqueous filtrate, containing sodium iodide, in the following manner. Add 33 ml. of concentrated sulphuric acid and a solution of 65 g. of sodium dichromate in 65 ml. of water. Allow the iodine to settle, wash it three times by decantation, filter, and allow to dry on a clock glass. The weight of crude iodine is about 50 g.

(2) Two extractions usually suffice, but if much organic material remains, a third extraction should be made. If the *p*-iodoaniline from the second and third extractions is coloured, it should be refluxed for a short period in light petroleum solution with a little decolourising carbon and filtered through a hot water funnel (*CAUTION:* inflammable).

Cognate Preparation

5-IODO-2-AMINOTOLUENE

A good yield of 5-iodo-2-aminotoluene may be obtained by intimately mixing *o*-toluidine hydrochloride, iodine and calcium carbonate, and then adding water to the mixture. The liberated hydriodic acid reacts at once with the calcium carbonate and the hydriodide of the base is not formed.



o-Toluidine hydrochloride — 5-Iodo 2-aminotoluene

Triturate 20 g. of dry *o*-toluidine hydrochloride and 35·5 g. of powdered iodine in a mortar and then grind in 17·5 g. of precipitated calcium carbonate. Transfer the mixture to a conical flask, and add 100 ml. of distilled water with vigorous shaking of the flask. Allow the mixture to stand for 45 minutes with occasional agitation, then heat gradually to 60–70° for 5 minutes, and cool. Transfer the contents of the flask to a separatory funnel, extract the base with three 80 ml. portions of ether, dry the extract with anhydrous calcium chloride or magnesium sulphate, and remove the excess of solvent. The crude 5-iodo-2-aminotoluene separates in dark crystals. The yield is 32 g. Recrystallise from 50 per cent. alcohol; nearly white crystals, m.p. 87°, are obtained.

IV,100. REACTIONS AND CHARACTERISATION OF AROMATIC AMINES

Those reactions which are common to both aliphatic and aromatic amines and have been described under *Aliphatic Amines* (Section **III,123**) will not be repeated in this Section except where differences in experimental technique occur.

PRIMARY AMINES

(i) **Carbylamine test.** See Section **III,123,**(iii). The following alternative technique may be employed. Add 1 drop of the liquid (or 0·02 g. of the solid) amine to 2 ml. of alcohol. Place 1 drop of the resulting *ca.* 1 per cent. solution in a small test-tube with 1 drop of chloroform and 4 ml. of 10 per cent. sodium hydroxide solution; heat the solution gently. The unpleasant odour of an *iso*-cyanide will be apparent with a primary amine.

(ii) **5-Nitrosalicylaldehyde reagent test.** A positive result is obtained in 2–3 minutes.

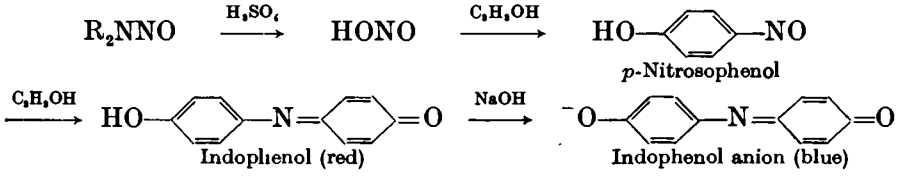
(iii) **Reaction with nitrous acid and the formation of an azo dye.** Dissolve 1·0 ml. (1·0 g.) of aniline (or the equivalent quantity of any other amine) in 3 ml. of concentrated hydrochloric acid and 5 ml. of water, and cool the solution to 0–5°. Add a cold solution of 1·0 g. of sodium nitrite in 5 ml. of water slowly (preferably by means of a dropper) and with stirring until, after standing for 3–4 minutes, an immediate positive test for nitrous acid is obtained. Remove 1 drop of the solution, dilute with 4–5 drops of water, and apply to potassium iodide-starch paper; an immediate blue colouration should be obtained. Divide the resulting diazonium solution into two parts. To one portion add a cold solution of 0·4 g. of β-naphthol in 4 ml. of 5 per cent. sodium hydroxide solution. A coloured (*e.g.*, orange-red) dye is formed; this may be filtered off and recrystallised from water, alcohol or acetic acid (for an explanation of the reaction involved, see Section **IV,76**). Warm the other half of the solution: nitrogen is evolved and a phenol is produced (see Section **IV,69**); note the odour.

Primary aromatic diamines cannot be diazotised (tetrazotised) and coupled normally. Thus *o*-phenylenediamine yields a triazole derivative and *m*-phenylenediamine gives an azo dye (Bismarck brown) by self-coupling.

SECONDARY AMINES

(iv) **Carbylamine test.** This is negative if the secondary amine is free from primary aromatic amine.

(v) **Reaction with nitrous acid.** Nitrosamines are formed (compare Section **IV,40**) ; these are usually yellow oils or low m.p. solids, and give the **Liebermann nitroso reaction.** The latter reaction consists in warming the nitrosamine with phenol and concentrated sulphuric acid. The sulphuric acid liberates nitrous acid from the nitrosamine, the nitrous acid reacts with the phenol to form *p*-nitrosophenol, which then combines with another molecule of phenol to give a red indophenol. In alkaline solution the red indophenol yields a blue indophenol anion :

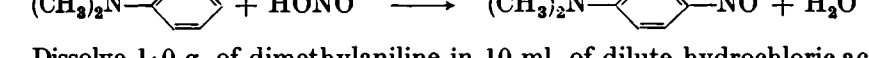


Dissolve 1 g. of the secondary amine in 3-5 ml. of dilute hydrochloric acid or of alcohol (in the latter case, add 1 ml. of concentrated hydrochloric acid). Cool to about 5° and add 4–5 ml. of 10 per cent. sodium nitrite solution, and allow to stand for 5 minutes. Add 10 ml. of water, transfer to a small separatory funnel and extract the oil with about 20 ml. of ether. Wash the ethereal extract successively with water, dilute sodium hydroxide solution and water. Remove the ether on a previously warmed water bath : no flames should be present in the vicinity. Apply Liebermann's nitroso reaction to the residual oil or solid thus. Place 1 drop or 0·01–0·02 g. of the nitroso compound in a dry test-tube, add 0·05 g. of phenol and warm together for 20 seconds ; cool, and add 1 ml. of concentrated sulphuric acid. An intense green (or greenish-blue) colouration will be developed, which changes to pale red upon pouring into 30–50 ml. of cold water ; the colour becomes deep blue or green upon adding excess of sodium hydroxide solution.

TERTIARY AMINES

(vi) **Carbylamine test.** This is negative for pure tertiary amines.

(vii) **Reaction with nitrous acid.** The dialkyl-anilines yield green solid *p*-nitroso compounds (compare Section **IV,42**). Thus dimethylaniline reacts with nitrous acid to yield *p*-nitrosodimethylaniline :



Dissolve 1·0 g. of dimethylaniline in 10 ml. of dilute hydrochloric acid (1 : 1), cool to 0–5°, and slowly add, with stirring, a solution of 0·70 g. of sodium nitrite in 4 ml. of water. After 20–30 minutes, filter off the precipitated yellow hydrochloride,* and wash it with a little dilute hydrochloric acid. Dissolve the precipitate in the minimum volume

* The hydrochloride may not separate with other dialkylanilines. Add a slight excess of sodium carbonate or sodium hydroxide to the solution, extract the free base with ether, etc.

of water, add a solution of sodium carbonate or sodium hydroxide to decompose the hydrochloride (*i.e.* until alkaline), and extract the free base with ether. Evaporate the ether, and recrystallise the residual green crystals of *p*-nitrosodimethylaniline from light petroleum (b.p. 60–80°) or from benzene. The pure compound has m.p. 85°.

The *p*-nitroso compounds do not give Liebermann's nitroso reaction.

(viii) **Separation of primary, secondary and tertiary amines (Hinsberg's method).** When a mixture of primary, secondary and tertiary amines is shaken with benzenesulphonyl chloride in the presence of dilute sodium hydroxide solution, the following reactions occur :—

primary amine : $C_6H_5SO_2Cl + H_2NR \xrightarrow{NaOH} C_6H_5SO_2N(Na)R$ (water-soluble) $\xrightarrow{HCl} C_6H_5SO_2NHR$ (water-insoluble)

secondary amine : $C_6H_5SO_2Cl + HNR'R'' \xrightarrow{NaOH} C_6H_5SO_2NR'R''$ (insoluble in alkali)

tertiary amine ; does not react, and may be removed by steam distillation or solvent extraction.

The benzenesulphonyl derivatives are crystalline solids and may be filtered off. They may be identified and separated from one another by taking advantage of the fact that the derivative from the primary amine is soluble in dilute sodium hydroxide solution (since it contains a hydrogen atom attached to nitrogen and activated by the strongly unsaturated sulphonyl group) whilst the derivative of the secondary amine is insoluble in dilute alkali (since it contains no corresponding hydrogen atom) :

$$C_6H_5SO_2NHR + NaOH \longrightarrow C_6H_5SO_2N(Na)R \text{ (soluble)}$$

Upon acidifying the solution of the sodium derivative with hydrochloric acid, the corresponding sulphonamide $C_6H_5SO_2NHR$ is precipitated. By boiling the sulphonamides with 10–12 times the weight of 25 per cent. hydrochloric acid or, better, with 80 per cent. sulphuric acid, rendering alkaline with sodium hydroxide and extracting with ether, the original primary and/or secondary amines may be recovered :

$$C_6H_5SO_2NHR + H_2O + HCl \longrightarrow C_6H_5SO_3H + \{RNH_3\}Cl$$
$$C_6H_5SO_2NR'R'' + H_2O + HCl \longrightarrow C_6H_5SO_3H + \{R'R''NH_2\}Cl$$

Certain primary amines yield disulphonyl derivatives, which are insoluble in alkali and therefore may be confused with the monosulphonyl derivatives of secondary amines.

$$RNH_2 + 2C_6H_5SO_2Cl \xrightarrow{-2HCl} RN(SO_2C_6H_5)_2$$

These may be hydrolysed to the monosulphonyl derivatives by boiling for 30 minutes with a 5 per cent. solution of sodium ethoxide in ethyl alcohol :

$$RN(SO_2C_6H_5)_2 + NaOC_2H_5 \longrightarrow RN(Na)SO_2C_6H_5 + C_2H_5OSO_2C_6H_5$$

There are complications in applying the Hinsberg test to certain amines containing hydroxyl, nitro and carboxyl groups, *e.g.*, *p*-*N*-methylaminobenzoic acid $\{CH_3NHC_6H_4COOH\ (1:4)\}$ may behave in this test as a primary amine (soluble in alkali) so that it is essential to consider the properties of the original compound in conjunction with the results of the test.

p-Toluenesulphonyl chloride may replace benzenesulphonyl chloride.

The following experimental details will illustrate how the Hinsberg separation of amines may be carried out in practice.

Method 1. Treat 2·0 g. of the mixture of amines with 40 ml. of 10 per cent. sodium hydroxide solution and add 4 g. (3 ml.) of benzenesulphonyl chloride (or 4 g. of *p*-toluenesulphonyl chloride) in small portions. Warm on a water bath to complete the reaction. Acidify the alkaline solution with dilute hydrochloric acid when the sulphonamides of the primary and secondary amines are precipitated. Filter off the solid and wash it with a little cold water; the tertiary amine will be present in the filtrate. To convert any disulphonamide that may have been formed from the primary amine into the sulphonamide, boil the solid under reflux with 2·0 g. of sodium dissolved in 40 ml. of absolute ethyl alcohol for 30 minutes. Dilute with a little water and distil off the alcohol: filter off the precipitate of the sulphonamide of the secondary amine. Acidify the filtrate with dilute hydrochloric acid to precipitate the derivative of the primary amine. Recrystallise the respective derivatives from alcohol or from dilute alcohol, and identify them *inter alia* by a determination of the m.p.

Method 2. Place a 3·0 g. sample of the mixture of amines in a flask, add 6 g. (4·5 ml.) of benzenesulphonyl chloride (or 6 g. of *p*-toluenesulphonyl chloride) and 100 ml. of a 5 per cent. solution of sodium hydroxide. Stopper the flask and shake vigorously until the odour of the acid chloride has disappeared: open the flask occasionally to release the pressure developed by the heat of the reaction. Allow the mixture to cool, and dissolve any insoluble material in 60–75 ml. of ether. If a solid insoluble in both the aqueous and ether layer appears at this point (it is probably the sparingly soluble salt of a primary amine, *e.g.*, a long chain compound of the type $C_6H_5(CH_2)_nNH_2$), add 25 ml. of water and shake; if it does not dissolve, filter it off. Separate the ether and aqueous layers. The ether layer will contain the unchanged tertiary amine and the sulphonamide of the secondary amine. Acidify the alkaline aqueous layer with dilute hydrochloric acid, filter off the sulphonamide of the primary amine, and recrystallise it from dilute alcohol. Extract the ether layer with sufficient 5 per cent. hydrochloric acid to remove all the tertiary amine present. Evaporate the ether to obtain the sulphonamide of the secondary amine: recrystallise it from alcohol or dilute alcohol. Finally, render the hydrochloric acid extract alkaline by the addition of dilute sodium hydroxide solution, and isolate the tertiary amine.

The above reactions will serve to place an amine into its class—primary, secondary or tertiary. For complete characterisation, a crystalline derivative should be prepared. A large number of derivatives of amines are available: the following will be found useful.

CRYSTALLINE DERIVATIVES OF PRIMARY AND SECONDARY AMINES

1. **Acetyl derivatives.** Primary and secondary amines are best acetylated with acetic anhydride :

$$RNH_2 + (CH_3CO)_2O \longrightarrow CH_3CONHR + CH_3COOH$$
$$R'R''NH + (CH_3CO)_2O \longrightarrow CH_3CONR'R'' + CH_3COOH$$

Acetyl chloride is not so satisfactory since an equivalent quantity of the amine hydrochloride is simultaneously produced :

$$2RNH_2 + CH_3COCl \longrightarrow CH_3CONHR + \{RNH_3\}Cl$$

Reflux gently in a test-tube under a short air condenser 1 g. of the base with 2·5 mols {or 3·0 g. (3·0 ml.) if the molecular weight is unknown} of redistilled acetic anhydride for 10–15 minutes. Cool the reaction mixture and pour it into 20 ml. of cold water (*CAUTION*). Boil to decompose the excess of acetic anhydride. When cold, filter the residual insoluble acetyl derivative and wash it with a little cold water. Recrystallise from water or from dilute alcohol.

Certain *ortho* substituted derivatives of aromatic amines are difficult to acetylate under the above conditions owing to steric hindrance. The process is facilitated by the addition of a few drops of concentrated sulphuric acid (compare Section IV,47), which acts as a catalyst, and the use of a large excess of acetic anhydride.

Excellent results may be obtained by conducting the acetylation in aqueous solution (*cf.* Section IV,45). Dissolve 0·5 g. of the amine in 2*N* hydrochloric acid, and add a little crushed ice. Introduce a solution of 5 g. of hydrated sodium acetate in 25 ml. of water, followed by 5 ml. of acetic anhydride. Shake the mixture in the cold until the smell of acetic anhydride disappears. Collect the solid acetyl derivative, and recrystallise it from water or dilute alcohol.

2. **Benzoyl derivatives.** Both primary and secondary amines form benzoyl derivatives under the conditions of the Schotten-Baumann reaction (see Section IV,52 and preceding discussion).

Suspend 1 g. (or 1 ml.) of the substance in 20 ml. of 5 per cent. sodium hydroxide solution * in a well-corked boiling tube or small conical flask, and add 2 ml. of redistilled benzoyl chloride, *ca.* 0·5 ml. at a time, with constant shaking, and cooling in water (if necessary). Shake vigorously for 5–10 minutes until the odour of the benzoyl chloride has disappeared. Make sure that the mixture has an alkaline reaction. Filter off the solid benzoyl derivative, wash it with a little cold water, and recrystallise it from alcohol or dilute alcohol.

If the benzoyl derivative is soluble in alkali, precipitate it together with the benzoic acid derived from the reagent by the addition of hydrochloric acid : filter and extract the product with cold ether or light petroleum (b.p. 40–60°) to remove the benzoic acid.

The following alternative procedure is sometimes useful. Heat the amine with the theoretical quantity of benzoyl chloride (if the molecular weight is unknown, use an equal weight of benzoyl chloride in the preliminary experiment) to 100° for 20–30 minutes. Allow to cool, add excess of 5 per cent. sodium hydroxide solution and shake, if necessary,

* Potassium hydroxide solution gives a slightly better yield of the benzoyl derivative.

until the odour of benzoyl chloride has disappeared. Filter off the precipitate, wash it with cold water, and recrystallise it from alcohol or dilute alcohol.

3. **Benzenesulphonyl or *p*-toluenesulphonyl derivatives.** The Hinsberg procedure for the separation of primary, secondary and tertiary amines is given under (viii) above, and this method may be used. The following experimental details may, however, be found useful for the preparation of derivatives of primary and secondary amines.

Treat 1 g. (1 ml.) of the amine with 4 mols of 10 per cent. sodium or potassium hydroxide solution (say, 20 ml.), and add 1·5 mols (or 3 g. if the molecular weight is unknown) of benzenesulphonyl or *p*-toluenesulphonyl chloride in small portions with constant shaking. To remove the excess of acid chloride, either shake vigorously or warm gently. Acidify with dilute hydrochloric acid and filter off the sulphonamide. Recrystallise it from alcohol or dilute alcohol.

If the presence of a disulphonyl derivative from a primary amine is suspected (*e.g.*, formation of a precipitate in alkaline solution even after dilution), reflux the precipitate, obtained after acidifying, with a solution of 1 g. of sodium in 20 ml. of rectified spirit for 15 minutes. Evaporate the alcohol, dilute with water, and filter if necessary; acidify with dilute hydrochloric acid. Collect the sulphonyl derivative and recrystallise it from alcohol or dilute alcohol.

It is generally more convenient to employ the solid *p*-toluenesulphonyl chloride (m.p. 69°) rather than the liquid benzenesulphonyl chloride. Moreover, the benzenesulphonamides of certain secondary amines are oils or low melting point solids that may be difficult to crystallise: the *p*-toluenesulphonamides usually have higher melting points and are more satisfactory as derivatives. **Technical *p*-toluenesulphonyl chloride may be purified** by dissolving it in benzene and precipitating with light petroleum (b.p. 40-60°).

Feebly basic amines, *e.g.*, the nitroanilines, generally react so slowly with benzenesulphonyl chloride that most of the acid chloride is hydrolysed by the aqueous alkali before a reasonable yield of the sulphonamide is produced; indeed, *o*-nitroaniline gives little or no sulphonamide under the conditions of the Hinsberg test. Excellent results are obtained by carrying out the reaction in *pyridine solution*:

$$o\text{-}NO_2C_6H_4NH_2 + C_6H_5SO_2Cl + C_5H_5N \longrightarrow o\text{-}NO_2C_6H_4NHSO_2C_6H_5 + C_5H_5N,HCl$$

Reflux a mixture of 1 g. (1 ml.) of the amine, 2-3 g. of benzenesulphonyl chloride and 6 ml. of pyridine for 30 minutes. Pour the reaction mixture into 10 ml. of cold water and stir until the product crystallises. Filter off the solid and recrystallise it from alcohol or dilute alcohol.

Most amines react so rapidly in pyridine solution that the reaction is usually complete after refluxing for 10-15 minutes.

4. **Benzal derivatives.** *Primary* aromatic amines generally condense directly with benzaldehyde to form benzal derivatives (**Schiff's bases** or **anils**):

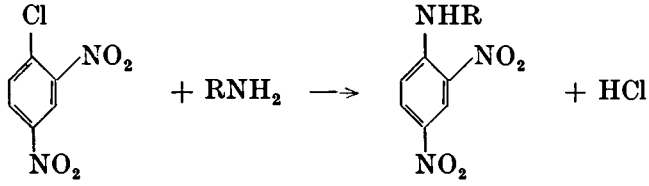
$$RNH_2 + OCHC_6H_5 \longrightarrow RN{=}CHC_6H_5 + H_2O$$

These are often crystalline and therefore useful for the characterisation of primary amines. Diamines may, of course, yield di-benzal derivatives.

Heat the amine with one or two mols of redistilled benzaldehyde (according as to whether the base is a monamine or diamine) to 100° for 10 minutes; if the molecular weight is unknown, use 1 g. of the base and 1 or 2 g. of benzaldehyde. Sometimes a solvent, such as alcohol (5 ml.) or acetic acid, may be used. Recrystallise from alcohol, dilute alcohol or benzene.

5. **Picrates.** Experimental details will be found under *Aliphatic Amines*, Section **III,123**, *3*.

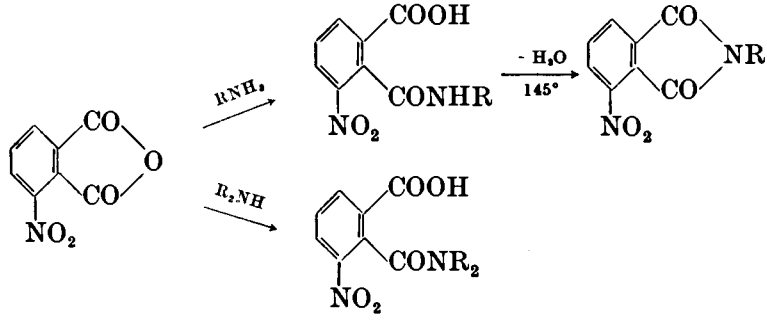
6. **2 : 4-Dinitrophenyl derivatives.** The halogen atom in 2 : 4-dinitrochlorobenzene is reactive and coloured crystalline compounds (usually yellow or red) are formed with primary and with secondary amines:



Dissolve 1·0 g. (or 1·0 ml.) of the amine and 1·0 g. of 2 : 4-dinitrochlorobenzene in 5–10 ml. of ethanol, add a slight excess of anhydrous potassium carbonate or of powdered fused sodium acetate, reflux the mixture on a water bath for 20–30 minutes, and then pour into water. Wash the precipitated solid with dilute sodium carbonate solution, followed by dilute hydrochloric acid. Recrystallise from ethanol, dilute alcohol or glacial acetic acid.

Note. Dinitrochlorobenzene must be handled with care: it is a skin irritant. If it touches the skin, wash it off immediately with methylated spirit.

7. **Derivatives with 3-nitrophthalic anhydride.** 3-Nitrophthalic anhydride reacts with primary and secondary amines to yield nitrophthalamic acids; it does not react with tertiary amines. The phthalamic acid derived from a primary amine undergoes dehydration when heated to 145° to give a neutral *N*-substituted 3-nitrophthalimide. The phthalamic acid from a secondary amine is stable to heat and is, of course, soluble in alkali. The reagent therefore provides a method for distinguishing and separating a mixture of primary and secondary amines.



Heat 0·5 g. (or 0·5 ml.) of the amine with 0·5 g. of pure 3-nitrophthalic anhydride (Section **VII,19**) in an oil bath at 145–150° for 10–20 minutes,

pour the reaction mixture into a small mortar or Pyrex dish, and allow it to solidify. Recrystallise from alcohol, aqueous alcohol or alcohol-acetone.

8. **Formyl derivatives.** Formic acid condenses with primary and secondary amines to yield formyl derivatives :

$$ArNHR + HCOOH \longrightarrow ArN(CHO)R + H_2O \ (R = H, \text{alkyl, etc.})$$

With *o*-phenylenediamine, benziminoazole is formed :

Reflux 0·5 g. of the amine with 5 ml. of 90 per cent. formic acid (CAUTION in handling) for 10 minutes, and dilute the hot solution with 10 ml. of cold water. Cool in ice and, in some cases, saturate with salt if the derivative does not separate immediately. Filter, wash with cold water, and recrystallise from water, alcohol or light petroleum (b.p. 60–80°).

9. **Phenylthioureas.** Experimental details are given under *Aliphatic Amines*, Section **III,123**, *2*.

The melting points of the derivatives of a number of selected primary and secondary aromatic amines are given in Tables **IV,100A** and **IV,100B** respectively.

TABLE IV,100A. PRIMARY AROMATIC AMINES

Amine	B.P.	M.P.	Acetamide	Benz-amide	Benzene-sulphon-amide	*p*-Tolu-enesul-phon-amide	Benzal Derivative	Picrate	3-Nitro-phthal-imide	2 : 4-Dinitro-phenyl Derivative	Formyl Derivative	Phenyl thio-urea
Aniline	183°	—	114°	163°	112°	103°	54°	—	138°	156°	47°	154°
o-Toluidine	200	—	112	144	124	110	—	213°	150	126	59	136
m-Toluidine	203	—	66	125	95	114	—	200	130	161	—	104
p-Toluidine	200	45°	154	158	120	118	—	181	156	137	53	141
vic.-m-Xylidine (1)	215	11	177	168	—	212	—	180	—	—	176	148
asym.-m-Xylidine (2)	216	—	130	192	130	181	—	209	—	156	114	152
sym.-m-Xylidine (3)	220	10	144	136	—	—	—	209	—	—	77	153
p-Xylidine (4)	214	15	142	140	—	232	—	—	—	150	—	—
Mesidine (5)	232	—	216	206	—	167	—	193	—	—	—	193
α-Naphthylamine	300	50	160	161	169	157	73	163	223	190	139	165
β-Naphthylamine	294	113	134	162	102	133	—	195	212	179	122	129
Benzylamine	185	—	60	106	88	116	—	199	143	—	—	156
β-Phenylethylamine	198	—	51	116	69	—	—	167	—	—	—	135
*cyclo*Hexylamine	134	—	104	149	—	—	—	—	—	—	—	—
o-Chloroaniline	209	—	88	99	130	105	34	134	136	150	77	156
m-Chloroaniline	230	—	79	122	121	138	—	177	172	184	58	124
p-Chloroaniline	232	71	179	193	122	95	62	178	199	167	102	152
o-Bromoaniline	229	32	99	116	—	90	—	129	—	161	—	146
m-Bromoaniline	251	18	88	120	—	—	—	180	187	—	—	143
p-Bromoaniline	—	66	167	204	134	101	67	180	202	158	—	148
o-Iodoaniline	—	60	110	139	—	—	—	112	—	—	—	—
m-Iodoaniline	—	25	119	151	—	128	—	—	—	—	—	—
p-Iodoaniline	—	63	184	222	—	—	86	—	—	—	109	153
o-Anisidine (6)	225	5	88	60	89	127	—	200	185	151	83	136
m-Anisidine	251	—	80	—	—	68	—	169	158	138	57	—
p-Anisidine	246	57	130	154	96	114	62	—	197	141	81	144
o-Phenetidine (7)	228	—	79	104	102	164	—	—	164	164	62	137
m-Phenetidine	248	—	96	103	—	157	—	158	—	—	52	138
p-Phenetidine	254	—	135	173	143	107	76	69	173	118	76	148

TABLE IV,100A. PRIMARY AROMATIC AMINES (*continued*)

Amine	B.P.	M.P.	Acetamide	Benzamide	Benzenesulphonamide	*p*-Toluenesulphonamide	Benzal Derivative	Picrate	3-Nitrophthalimide	2:4-Dinitrophenyl Derivative	Formyl Derivative	Phenyl thiourea
3-Bromo-4-aminotoluene	240°	26°	117°	149°	—	—	—	—	—	—	—	—
5-Bromo-2-aminotoluene	240	59	157	115	—	—	—	—	—	—	—	—
3-Nitro-4-aminotoluene	—	117	96	148	102°	146°	78°	—	—	—	—	—
4-Nitro-2-aminotoluene	—	107	151	186	172	—	116	—	—	—	179°	—
5-Nitro-2-aminotoluene	—	129	202	174	159	174	—	—	—	—	—	—
1-Nitro-2-naphthylamine	—	126	123	168	156	160	—	—	—	—	—	—
5-Nitro-1-naphthylamine	—	119	220	—	183	—	—	—	—	—	199	—
o-Aminodiphenyl	299	50	121	102	—	—	—	—	—	—	75	—
p-Aminodiphenyl (8)	302	51	171	230	—	255	—	—	—	—	172	—
2 : 4-Dichloroaniline	245	63	146	117	128	—	—	106°	—	116°	—	—
2 : 5-Dichloroaniline	251	50	132	120	—	—	—	—	—	—	—	166°
2 : 4-Dibromoaniline	—	79	146	134	—	—	—	124	—	—	146	171
2 : 4 : 6-Trichloroaniline	—	78	206	174	—	—	—	83	—	—	180	—
2 : 4 : 6-Tribromoaniline	—	120	—	232	198	—	95	—	—	—	222	—
o-Nitroaniline	—	71	94	98	104	110	—	73	171°	—	122	—
m-Nitroaniline	—	114	155	157	136	139	73	143	219	—	134	160
p-Nitroaniline	—	148	216	199	139	191	115	100	255	—	194	—
2 : 4-Dinitroaniline	—	180	121	220	—	219	—	—	—	—	—	—
2 : 6-Dinitroaniline	—	138	197	—	—	—	—	—	—	—	—	—
o-Phenylenediamine	257	102	186	301	186	202	106	208	—	—	170	—
m-Phenylenediamine	283	64	191	240	194	172	105	184	—	172	155	—
p-Phenylenediamine	267	141	304	>300	247	266	140	—	—	177	206	—
2 : 4-Diaminotoluene (9)	292	99	224	224	191	192	175	—	—	184	177	—
2 : 5-Diaminotoluene	273	64	220	307	—	—	—	—	—	—	—	—
Anthranilic acid	—	146	185	181	214	217	127	—	—	—	168	—
m-Aminobenzoic acid	—	174	250	—	—	—	119	—	—	—	225	—
p-Aminobenzoic acid	—	187	251	278	212	—	193	—	—	—	268	—
Benzidine	—	126	317	352	235	243	238	—	—	—	—	—
o-Tolidine (10)	—	129	314	265	—	—	152	185	—	—	254	—

TABLE IV,100A. **PRIMARY AROMATIC AMINES (*continued*)**

Amine	B.P.	M.P.	Acetamide	Benzamide	Benzenesulphonamide	*p*-Toluenesulphonamide	Benzal Derivative	Picrate	3-Nitrophthalimide	2 : 4-Dinitrophenyl Derivative	Formyl Derivative	Phenyl thiourea
p-Aminodimethylaniline	262°	41°	132°	228°	—	—	98°	188°	—	168°	108°	—
p-Aminodiethylaniline	261	—	104	172	—	—	—	—	—	—	—	—
p-Aminoazobenzene	—	126	145	211	—	—	130	—	—	—	162	—
Methyl anthranilate	255	24	101	100	—	—	—	106	—	—	58	—
Ethyl anthranilate	266	13	61	98	93°	112°	—	—	—	—	57	—
Ethyl *p*-aminobenzoate (11)	—	92	110	148	—	—	—	131	—	—	—	—
m-Aminoacetanilide	—	88	191	—	—	241	—	—	—	—	—	—
p-Aminoacetanilide	—	163	304	—	—	—	—	—	—	—	—	—
o-Aminophenol	—	174	124 (di)	184 (di)	141	139	89	—	—	199	129	146°
m-Aminophenol	—	123	101 (di)	153 (di)	—	—	—	—	—	—	—	156
p-Aminophenol	—	186	150 (di)	234 (di)	125	253	182	—	—	190	140	150
Picramic acid (12)	—	168	201 (N)	229 (N)	—	191 (N)	—	—	—	—	—	—
Phenylhydrazine	242	23	128	168	—	—	—	—	—	—	145	172
p-Nitrophenylhydrazine	—	157d	205	193	—	—	—	120	—	—	—	—
2:4-Dinitrophenylhydrazine	—	198d	198	207	—	—	—	—	—	—	—	—
Sulphanilamide	—	166	219	284	211	—	—	—	—	—	—	—

(1) 2-*m*-Xylidine or 2 : 6-dimethylaniline.
(2) 4-*m*-Xylidine or 2 : 4-dimethylaniline.
(3) 5-*m*-Xylidine or 3 : 5-dimethylaniline.
(4) 2-Amino-*p*-xylene or 2 : 5-dimethylaniline.
(5) 2 : 4 : 6-Trimethylaniline.
(6) *o*-Methoxyaniline.
(7) *o*-Ethoxyaniline.
(8) *p*-Xenylamine.
(9) *m*-Tolylenediamine.
(10) 4 : 4′-Diamino-3 : 3′-dimethyldiphenyl.
(11) Benzocaine.
(12) 4 : 6-Dinitro-2-aminophenol.

TABLE IV,100B. **SECONDARY AROMATIC AMINES**

Amine	B.P.	M.P.	Acetamide	Benzamide	Benzenesulphonamide	*p*-Toluenesulphonamide	Picrate	Formyl Derivative	Other Derivatives
Methylaniline	194°	—	103°	63°	79°	95°	145°	—	Phthalamic acid, 194°
Ethylaniline	205	—	55	60	—	88	138	—	Phthalamic acid, 204
n-Propylaniline	222	—	47	—	54	—	—	—	Phthalamic acid, 225
n-Butylaniline	240	—	—	56	—	56	—	—	Phthalamic acid, 204
Benzylaniline	306	38°	58	107	119	140	—	48°	*N*-Nitroso, 58
N-Methylbenzylamine	181	—	—	—	—	95	—	—	—
N-Ethylbenzylamine	199	—	—	—	—	50	118	—	Urea (with PhNCO), 81
N-Methyl *o*-toluidine	208	—	56	66	—	120	90	—	—
N-Methyl *m*-toluidine	206	—	66	—	—	—	—	—	—
N-Methyl *p*-toluidine	210	—	83	53	—	60	131	—	*N*-Nitroso, 52
N-Ethyl *o*-toluidine	214	—	—	72	—	75	—	—	—
N-Ethyl *m*-toluidine	221	—	—	72	—	—	—	—	—
N-Ethyl *p*-toluidine	217	—	—	39	—	71	—	—	—
N-Methyl α-naphthylamine	294	—	94	—	—	164	—	—	—
N-Methyl β-naphthylamine	317	—	51	84	—	78	145	—	*N*-Nitroso, 88
N-Phenyl-α-naphthylamine	335	62	115	152	—	—	—	—	—
N-Phenyl-β-naphthylamine	—	108	93	136	—	—	—	—	—
o-Nitromethylaniline	—	37	70	—	—	—	—	—	*N*-Nitroso, 36
m-Nitromethylaniline	—	68	95	155	83	—	—	—	*N*-Nitroso, 76
p-Nitromethylaniline	—	152	152	111	120	—	—	119	*N*-Nitroso, 104
m-Nitroethylaniline	—	60	89	—	—	—	—	—	—
p-Nitroethylaniline	—	96	119	—	—	—	—	—	*N*-Nitroso, 120
Diphenylamine	302	54	103	180	123	142	182	74	*N*-Nitroso, 67
Dibenzylamine	300d	—	—	112	68	—	—	52	—
Pyrrolidine	89	—	—	—	—	123	—	—	—
Piperidine	106	—	—	48	94	96	152	—	—
2-Methylpiperidine	117	—	—	45	—	55	134	—	—
3-Methylpiperidine	125	—	—	—	—	—	137	—	—
Tetrahydroquinoline	250	20	—	76	67	—	—	—	—
Tetrahydro-*iso*-quinoline	232	—	46	129	154	—	195	—	—
Indole	254	52	—	68	—	—	187	52	*N*-Nitroso, 171
Carbazole	355	246	69	98	—	137	185	—	—
Piperazine	140	104	—	196	282	—	280	—	*N*,*N*-Dinitroso, 158

CRYSTALLINE DERIVATIVES OF TERTIARY AROMATIC AMINES

1'. **Picrates.** Experimental details are given under *Aliphatic Amines*, Section **III,123**, *3*.

2'. **Methiodides.** Methyl iodide reacts with tertiary amines to form the crystalline quaternary ammonium iodide (methiodide) :

$$RR'R''N + CH_3I \longrightarrow \{RR'R''NCH_3\}^+I^-$$

Allow a mixture of 0·5 g. of the tertiary amine and 0·5 ml. of colourless methyl iodide * to stand for 5 minutes. If reaction has not occurred, warm under reflux for 5 minutes on a water bath and then cool in ice water. The mixture will generally set solid : if it does not, " scratch " the sides of the tube with a glass rod. Recrystallise the solid product from absolute alcohol, ethyl acetate, acetone, glacial acetic acid or alcohol-ether.

Alternatively, dissolve 0·5 g. of the tertiary amine and 0·5 ml. of methyl iodide in 5 ml. of dry ether or benzene, and allow the mixture to stand for several hours. The methiodide precipitates, usually in a fairly pure state. Filter, wash with a little of the solvent, and recrystallise as above.

The ethiodide is prepared similarly, using ethyl iodide.

3'. **Metho-*p*-toluenesulphonate.** Methyl *p*-toluenesulphonate combines with many tertiary amines to yield crystalline derivates :

$$RR'R''N + p\text{-}CH_3C_6H_4SO_3CH_3 \longrightarrow \{RR'R''NCH_3\}^+\{p\text{-}CH_3C_6H_4SO_3\}^-$$

Dissolve 2–3 g. of methyl *p*-toluenesulphonate in 10 ml. of dry benzene, add 1 g. of the amine, and boil the mixture for 20–30 minutes. Cool, and filter the precipitated quaternary salt. Recrystallise by dissolving the solid in the minimum volume of boiling ethyl alcohol and then adding ethyl acetate until crystallisation commences. Filter the cold mixture, dry rapidly on a porous plate, and determine the m.p. immediately.

The benzyl chloride quaternary salts $\{RR'R''NC_6H_5CH_2\}^+Cl^-$ are prepared similarly; 3 g. of redistilled benzyl chloride replaces the methyl *p*-toluenesulphonate.

4'. ***p*-Nitroso Derivatives.** Aromatic tertiary amines, such as dimethylaniline, react with nitrous acid to yield crystalline *p*-nitroso compounds. For further details, see (vii) above.

The melting points of the derivatives of a number of tertiary amines, both aliphatic and aromatic, are collected in Table **IV,100C**.

* Keep a coil of copper wire (prepared by winding copper wire round a glass tube) or a little silver powder in the bottle, which should be of brown or amber glass ; the methyl iodide will remain colourless indefinitely. Ethyl iodide may sometimes give more satisfactory results.

TABLE IV.100C. **TERTIARY AMINES**

Amine	B.P.	M.P.	Methiodide	Picrate	Methyl *p*-toluene-sulphonate	Other Derivatives
Trimethylamine	3°	—	230°	216°	—	—
Triethylamine	89	—	—	173	—	$d_{4°}^{20°}$ 0·728 ; $n_D^{20°}$ 1·401
Tri-*n*-propylamine	156	—	208	117	—	Ethiodide, 238° ; $d_{4°}^{20°}$ 0·756, $n_D^{20°}$ 1·417
Tri-*n*-butylamine	212	—	180	106	—	Benzyl chloride, 185 ; $d_{4°}^{20°}$ 0·778, $n_D^{20°}$ 1·430
Tri-*n*-amylamine	257	—	—	—	80°d	$d_{4°}^{20°}$ 0·791 ; $n_D^{20°}$ 1·437
Tri-iso-amylamine	245	—	—	125	—	$d_{4°}^{20°}$ 0·785 ; $n_D^{20°}$ 1·433
Dimethylaniline	193	—	228	164	161	*p*-Nitroso, 87 ; ethiodide, 136
Diethylaniline	215	—	102	142	—	*p*-Nitroso, 84 ; benzyl chloride, 104
Di-*n*-propylaniline	245	—	156	—	—	—
Di-*n*-butylaniline	271	—	—	125	180	—
Methylethylaniline	201	—	125	134	—	Ethiodide, 102 ; *p*-Nitroso, 66
Benzylmethylaniline	306	—	164	127	—	—
Benzylethylaniline	186°/22	—	161	121	—	—
Dibenzylaniline	300	70°	135	132	—	*p*-Nitroso, 91
Dimethyl-*o*-toluidine	185	—	210	122	—	—
Dimethyl-*m*-toluidine	212	—	177	131	—	—
Dimethyl-*p*-toluidine	211	—	220	130	85	Benzylchloride, 171
Diethyl-*o*-toluidine	210	—	224	180	—	—
Diethyl-*m*-toluidine	231	—	—	97	—	—
Diethyl-*p*-toluidine	229	—	184	110	—	—
Dimethyl-α-naphthylamine	273	—	—	145	—	—
Dimethyl-β-naphthylamine	305	47	—	206	—	—
p-Nitrosodimethylaniline	—	87	—	140	—	—
p-Nitrodimethylaniline	—	163	—	—	—	—

TABLE IV,100C. **TERTIARY AMINES (*continued*)**

Amine	B.P.	M.P.	Methiodide	Picrate	Methyl *p*-toluene-sulphonate	Other Derivatives
p-Bromodimethylaniline	264°	55°	—	—	—	—
p-Hydroxydimethylaniline	—	76	201°	—	—	*o*-Acetyl, 79°
Triphenylamine	365	127	—	—	—	—
Tribenzylamine	380	92	184	190°	—	Ethiodide, 190
Pyridine	115	—	118	167	139°	Ethiodide, 90
α-Picoline (1)	129	—	227	169	150	Ethiodide, 123; picolinic acid, 136
β-Picoline	144	—	92	150	—	Nicotinic acid, 228
γ-Picoline	143	—	152	167	—	*iso*-Nicotinic acid, 308
2 : 4-Lutidine (2)	157	—	113	183	—	—
2 : 6-Lutidine	142	—	238	163	—	Dipicolinic acid, 226
2 : 4 : 6-Trimethylpyridine (3)	172	—	—	156	—	—
2-Chloropyridine	170	—	—	—	120	—
3-Chloropyridine	149	—	—	135	—	—
2-Bromopyridine	194	—	—	—	127	—
3-Bromopyridine	170	—	165	—	156	—
2 : 6-Dibromopyridine	249	119	—	—	—	—
3 : 5-Dibromopyridine	222	112	274	—	219	—
Quinoline	238	—	72* (133)†	203	126	Ethiodide, 158
iso-Quinoline	242	24	159	223	163	Ethiodide, 148
Quinaldine (4)	247	—	195	195	161	Ethiodide, 234
Lepidine (5)	262	—	174	211	—	—
6-Methylquinoline	258	—	219	229	154	Benzyl chloride, 239
7-Methylquinoline	252	39	—	237	—	—
8-Methylquinoline	248	—	—	200	—	—
6-Hydroxyquinoline	—	193	—	236	—	—
8-Hydroxyquinoline	267	76	143	204	—	—
6-Methoxyquinoline	284	26	236	—	—	—
8-Methoxyquinoline	283	50	160	143	—	—

* Hydrated ($1H_2O$). † Anhydrous.

TABLE IV,100C. **TERTIARY AMINES** (*continued*)

Amine	B.P.	M.P.	Methiodide	Picrate	Methyl *p*-toluene-sulphonate	Other Derivatives
2-Chloroquinoline . .	267°	38°	—	122°	—	—
6-Chloroquinoline . .	262	41	248°	—	143°	Ethiodide, 169°
2-Bromoquinoline . .	—	49	210	—	—	—
6-Bromoquinoline . .	278	19	278	217	—	—
6-Nitroquinoline . . .	—	154	245	—	—	—
8-Nitroquinoline . . .	—	92	—	—	—	—
2 : 4-Dimethylquinoline .	264	—	264	194	—	Ethiodide, 214
2 : 6-Dimethylquinoline .	267	60	237	191	175	Ethiodide, 227
αα′-Dipyridyl . . .	273	70	—	158	—	—
Nicotine	246	—	—	218	—	Nicotinic acid, 228
Methyl nicotinate . .	204	38	—	—	—	—
Ethyl nicotinate . .	223	—	—	—	—	—
Acridine	—	111	224	208	—	Trinitrobenzene, 115
Hexamethylenetetramine .	—	Sub.	190	179	205	—

(1) 2-Methylpyridine.
(2) 2 : 4-Dimethylpyridine.
(3) γ-Collidine.
(4) 2-Methylquinoline.
(5) 4-Methylquinoline.

PHENOLS

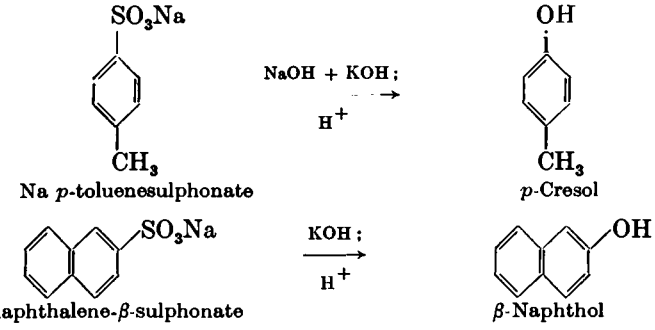
Phenols may be prepared in the laboratory :—

1. By hydrolysis of a diazonium salt, for example :

$$C_6H_5NH_2 \xrightarrow[NaNO_2]{H_2SO_4,} C_6H_5N_2{}^+OSO_3H^- \xrightarrow[50°]{H_2O,} C_6H_5OH + N_2 + H_2SO_4$$

(see Section **IV,69**).

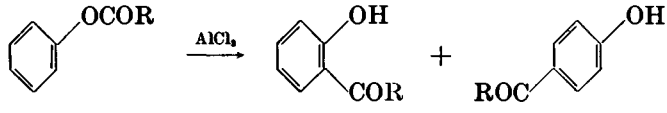
2. By alkali fusion of a sulphonate, for example :



Na *p*-toluenesulphonate — *p*-Cresol

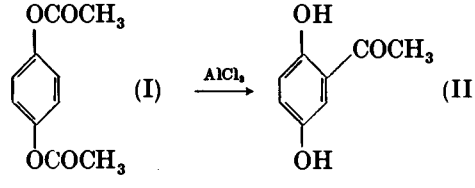
Na naphthalene-*β*-sulphonate — *β*-Naphthol

3. By the rearrangement of an ester of a phenol in the presence of aluminium chloride (**Fries reaction**), phenolic ketones are produced :



The ester and catalyst are usually employed in equimolecular amounts. With $R = C_2H_5$ (phenyl propionate), the products are ***o*- and *p*-propiophenol**; with $R = CH_3$ (phenyl acetate), ***o*- and *p*-hydroxyacetophenone** are formed. The nature of the product is influenced by the structure of the ester, by the temperature, the solvent and the amount of aluminium chloride used : generally, low reaction temperatures favour the formation of *p*-hydroxy ketones. It is usually possible to separate the two hydroxy ketones by fractional distillation under diminished pressure through an efficient fractionating column or by steam distillation ; the *ortho* compounds, being chelated, are more volatile in steam. It may be mentioned that Clemmensen reduction (compare Section **IV,6**) of the hydroxy ketones affords an excellent route to the substituted phenols.

2 : 5-Dihydroxyacetophenone (II) can be prepared in good yield by heating hydroquinone diacetate (I) in the presence of 3·3 mols of aluminium chloride, Hydroquinone cannot be acylated by the Friedel-Crafts method.



The *mechanism* of the Fries reaction is not known with certainty. One mechanism regards it as a true intramolecular rearrangement in which the acyl group migrates directly from the oxygen atom to the carbon atoms of the ring. Another scheme postulates that the ester is cleaved by the reagent

to the corresponding phenol complex and acid chloride and the latter recombines in the normal Friedel-Crafts manner :

$$C_6H_5.OCOR + AlCl_3 \longrightarrow C_6H_5.OAlCl_2 + RCOCl \longrightarrow$$
$$o\text{- and } p\text{-}RCO.C_6H_4.OAlCl_2 \longrightarrow o\text{- and } p\text{-}RCO.C_6H_4.OH$$

Crystalline derivatives, suitable for identification and characterisation are dealt with in Section **IV,114**, but the preparation of the following, largely liquid, derivatives will be described in the following Sections. When phenols are dissolved in aqueous sodium hydroxide solution and shaken with acetic anhydride, they undergo rapid and almost quantitative acetylation if the temperature is kept low throughout the reaction. This is because phenols form readily soluble sodium derivatives, which react with acetic anhydride before the latter undergoes appreciable hydrolysis, for example :

$$CH_3COOCOCH_3 + NaOC_6H_5 \longrightarrow \underset{\text{Phenyl acetate}}{CH_3COOC_6H_5} + CH_3COONa$$

$$CH_3COOCOCH_3 + NaOC_{10}H_7{}^{\beta} \longrightarrow \underset{\beta\text{-Naphthyl acetate}}{CH_3COOC_{10}H_7{}^{\beta}} + CH_3COONa$$

Salicylic acid, however, cannot be acetylated under these conditions.

Methyl and ethyl ethers of phenols are most conveniently prepared by alkylation with dimethyl sulphate and diethyl sulphate respectively in weakly alkaline solution, for example :

$$\underset{\text{Phenol}}{C_6H_5OH} + NaOH + (CH_3)_2SO_4 \longrightarrow \underset{\text{Anisole}}{C_6H_5OCH_3} + NaCH_3SO_4 + H_2O$$

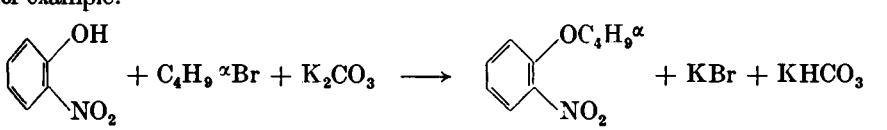
$$\underset{\beta\text{-Naphthol}}{C_{10}H_7{}^{\beta}OH} + NaOH + (CH_3)_2SO_4 \longrightarrow \underset{\beta\text{-Naphthyl methyl ether}}{C_{10}H_7{}^{\beta}OCH_3} + NaCH_3SO_4 + H_2O$$

$$C_6H_5OH + NaOH + (C_2H_5)_2SO_4 \longrightarrow \underset{\text{Phenetole}}{C_6H_5OC_2H_5} + NaC_2H_5SO_4 + H_2O$$

Higher alkyl ethers are prepared by treating the sodium derivative of the phenol (made by adding the phenol to a solution of sodium ethoxide in ethyl alcohol) with the alkyl iodide or bromide (**Williamson synthesis**), for example :

$$C_6H_5ONa + \underset{n\text{-Butyl iodide}}{C_4H_9{}^{\alpha}I} \longrightarrow \underset{\text{Phenyl } n\text{-butyl ether}}{C_6H_5OC_4H_9{}^{\alpha}} + NaI$$

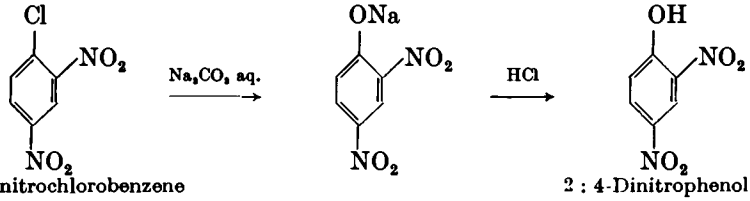
The preparation of the sodium derivative of the phenol may be avoided by heating the phenol and alkyl halide in the presence of potassium carbonate and acetone, for example:



o-Nitrophenol — *o*-*n*-Butoxynitrobenzene

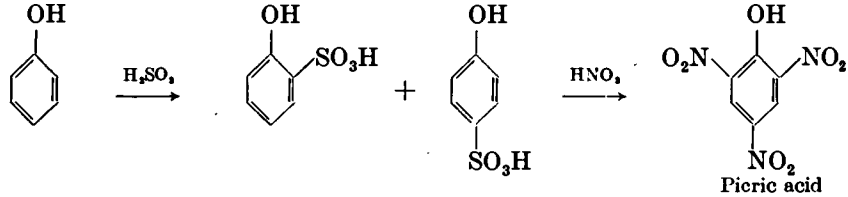
Phenol may be nitrated with *dilute* nitric acid to yield a mixture of ***o*- and *p*-nitrophenols**; the yield of *p*-nitrophenol is increased if a mixture of sodium nitrate and dilute sulphuric acid is employed. Upon steam distilling the mixture, the *ortho* isomer passes over in a substantially pure form ; the *para* isomer remains in the distillation flask, and can be readily isolated by extraction with hot 2 per cent. hydrochloric acid. The preparation of *m*-nitrophenol from *m*-nitroaniline by means of the diazo reaction is described in **Section IV,70.**

2:4-Dinitrophenol may be readily prepared by taking advantage of the great reactivity of the chlorine atom in 2 : 4-dinitro-1-chlorobenzene :



2 : 4-Dinitrochlorobenzene — 2 : 4-Dinitrophenol

Picric acid, the 2 : 4 : 6-trinitro derivative of phenol, cannot be prepared in good yield by the action of nitric acid upon phenol since much of the latter is destroyed by oxidation and resinous products are also formed. It is more convenient to heat the phenol with concentrated sulphuric acid whereby a mixture of *o*- and *p*-phenolsulphonic acids is obtained ; upon treatment of the mixture with concentrated nitric acid, nitration occurs at the two positions *meta* to the $-SO_3H$ group in each compound, and finally, since sulphonation is reversible, the acid groups are replaced by a third nitro group yielding picric acid in both cases :

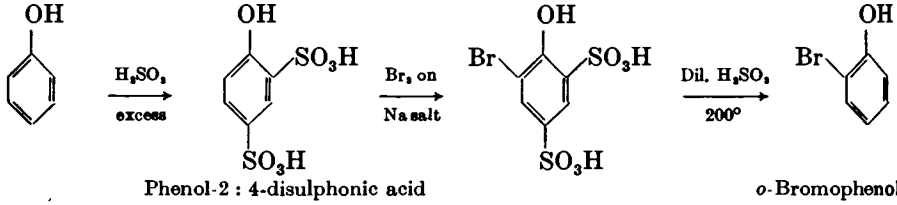


Picric acid

The mono-bromination of phenol at low temperatures in carbon disulphide or carbon tetrachloride solution results in almost exclusive *para* substitution :

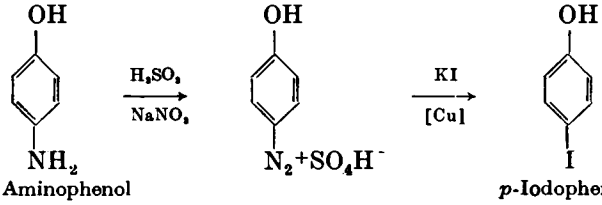
$$C_6H_5OH + Br_2 \longrightarrow \underset{p\text{-Bromophenol}}{p\text{-}BrC_6H_4OH} + HBr$$

***o*-Bromophenol** is conveniently prepared by first sulphonating with excess of concentrated sulphuric acid to yield phenol-2 : 4-disulphonic acid, neutralising with sodium hydroxide, heating the solution of the sodium salt with 1 mol of bromine, and then eliminating the sulphonate groups with dilute sulphuric acid at 200° :



Phenol-2 : 4-disulphonic acid — *o*-Bromophenol

***p*-Iodophenol** is readily obtained by diazotising *p*-aminophenol, and adding potassium iodide solution and a little copper bronze :



p-Aminophenol — *p*-Iodophenol

IV,101. *p*-CRESOL

Support a 250 ml. nickel or copper (better silver-plated copper) or iron crucible or beaker in a large circular hole in a sheet of asbestos board or uralite resting upon a tripod, and place in it 100 g. of sodium hydroxide pellets or sticks and 40 g. of potassium hydroxide pellets or sticks (1). Prepare a case of nickel or copper to surround the thermometer for about two-thirds of its length; this may be done either by cutting a suitable length of nickel or copper tube already closed at one end, or by hammering down the end of an open tube and folding over the flat part in a vice. Fit a large cork at the top of the tube; this will serve for handling the tube containing the thermometer when used for stirring the fused alkali. Since some spattering of the molten alkali cannot generally be avoided, the student should wear gloves, a well-fitting laboratory coat and, if possible, goggles (2). Heat the crucible, with stirring, until the alkali melts; then allow the temperature to fall to 230°, and stir in 15 g. of sodium *p*-toluenesulphonate (Section **IV,30**). Raise the temperature slowly so that it is about 270° in about 30 minutes. During this period add slowly 45 g. of sodium *p*-toluenesulphonate; it is best to make the additions whenever the melt becomes sufficiently thin to stir in the solid. Now raise the temperature to about 300° with occasional stirring: at this point there is a layer of froth on the surface of the melt. Stir the froth in, whilst raising the temperature slowly. At about 330°, the foaming (which has previously been considerable) suddenly disappears, the melt becomes dark and hydrogen is evolved. The mixture is now thin and of uniform consistency: do not allow it to solidify, but pour it at once into a shallow iron tray, and allow to cool.

Dissolve the solid in 700 ml. of water in a 1500 ml. round-bottomed flask, and add a solution of 88 ml. of concentrated sulphuric acid in about 200 ml. of water until the liquid has a distinct odour of sulphur dioxide; sufficient heat will be liberated in the neutralisation to cause the solution to boil. Immediately steam distil the liquid (Fig. *II*, *40*, 1; it is better to use the apparatus shown in Fig. *II*, *41*, 3) until a sample of the distillate gives only a slight precipitate with bromine water. About 700 ml. of distillate should be collected. Saturate the steam distillate with salt, extract the oil with ether, dry the extract with a little anhydrous magnesium or calcium sulphate, distil off the ether (compare Fig. *II*, *13*, 4, but with a 50 ml. Claisen flask replacing the distilling flask) and distil the residue under diminished pressure. Collect the *p*-cresol at 95–96°/15 mm.; the colourless liquid solidifies to a white crystalline solid, m.p. 31°. The yield is 24 g.

Notes.

(1) No cresol is obtained if sodium hydroxide alone is used, presumably because the fused sodium hydroxide has no solvent action upon the sodium *p*-toluenesulphonate. Potassium hydroxide alone gives excellent results, as do also mixtures of sodium and potassium hydroxide containing not less than 28 per cent. of potassium hydroxide. The experimental details utilise the minimum amount of potassium hydroxide for the sake of economy.

(2) It is recommended that the preparation be conducted in the fume cupboard (hood) with the window protecting the face.

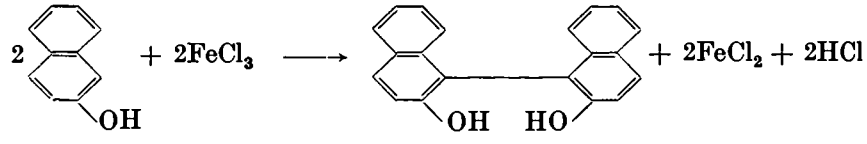
IV,102. β-NAPHTHOL

The apparatus required is similar to that detailed under p-*Cresol* (preceding Section). Place 120 g. of potassium hydroxide sticks or pellets (1) together with 5 ml. of water in the 250 ml. nickel crucible, and heat until it melts. When the temperature reaches about 250°, remove the flame, and quickly add with stirring 50 g. of finely-powdered sodium naphthalene-β-sulphonate (Section **IV,31**). Replace the flame, stir the stiff pasty mass, and continue the heating so that the temperature rises to 300° in 5–10 minutes. Stir the mixture continuously ; there is some frothing at first and at about 300° the mass suddenly becomes a clear, mobile, brown oil of the potassium salt of β-naphthol floating on a pasty mass of alkali. Raise the temperature during 5 minutes to 310°, remove the flame, push down the material from the side of the crucible, and reheat to 310° for about 2 minutes, and then allow the melt to cool. Do not permit the melt to solidify completely. When it becomes pasty, ladle it out in small portions (with a nickel spatula, " spoon " end) into a 1 litre beaker half-filled with crushed ice. Extract the residual material in the crucible with water and add it to the contents of the beaker. Precipitate the β-naphthol by adding concentrated hydrochloric acid slowly and with stirring. (*FUME CUPBOARD :* SO_2) ; if the β-naphthol separates in a finely-divided form, warm until the particles coagulate. Cool in ice, filter at the pump, make a hole in the filter paper and wash the precipitate into a beaker containing cold water. Add just sufficient 5 per cent. sodium hydroxide solution to dissolve the solid and also 1 g. of sodium hyposulphite $Na_2S_2O_4$ (to prevent oxidation), and filter from traces of insoluble matter. Precipitate the β-naphthol with acetic acid, warm to produce a more readily filterable form of the precipitate, cool in ice, and filter the product. Dry in the air upon filter paper. The yield is 25 g., m.p. 122°. If the m.p. is unsatisfactory, recrystallise from water, dilute alcohol or carbon tetrachloride.

Note.

(1) Sodium hydroxide may replace potassium hydroxide in this preparation; 150 g., together with 15 ml. of water, are required. The sulphonate is stirred in when the temperature reaches 280° and the reaction is completed at 310–320°.

Conversion of β-naphthol into di-β-naphthol. β-Naphthol is oxidised by aqueous ferric chloride solution into di-β-naphthol or 2 : 2′-dihydroxydinaphthyl :



In a 1 litre three-necked flask, provided with a dropping funnel, glycerine-sealed stirrer and reflux condenser, place 14·4 g. of β-naphthol and 600 ml. of water, and heat to the boiling point. To the boiling liquid containing liquid β-naphthol in suspension, add slowly through the dropping funnel and with vigorous stirring a solution of 28 g. of crystal-

lised ferric chloride in 60 ml. of water. The oily drops of β-naphthol will disappear and the di-β-naphthol separates out in flakes. Boil for 5–10 minutes, filter the hot suspension at the pump through a previously-warmed Buchner funnel, wash with boiling water, and dry in the air upon filter paper. The crude product weighs 18 g. Recrystallise from toluene or benzene (about 150 ml.); almost colourless crystals (15 g.), m.p. 218°, are obtained.

IV,103. PHENYL ACETATE

Dissolve 23·5 g. of phenol in 160 ml. of 10 per cent. sodium hydroxide solution contained in a 500 ml. reagent bottle, and add about 175 g. of crushed ice. Then add 32·5 g. (30 ml.) of acetic anhydride, cork the bottle and shake the contents vigorously for about 5 minutes. The reaction is then complete and an emulsion of phenyl acetate is produced. Pour the mixture into a separatory funnel, add about 10 ml. of carbon tetrachloride to facilitate the separation of the two layers, shake, and allow to stand. Run off the lower solution of phenyl acetate in carbon tetrachloride, and shake this with very dilute sodium carbonate solution or saturated sodium bicarbonate solution until effervescence ceases; release the pressure in the funnel from time to time. Run off the lower layer into a small conical flask, dry over anhydrous magnesium sulphate or calcium chloride, and filter through a small fluted filter paper into a 50 ml. distilling flask. Distil (Fig. *II*, *13*, 2) by *slowly* heating in an air bath (Fig. *II*, *5*, 3) or over an asbestos-centred wire gauze. The boiling point rises slowly to about 170° before all the carbon tetrachloride is removed and then rises rapidly to about 194°. Collect the phenyl acetate (a colourless liquid) at 194–197°. The yield is 42 g.

Cognate Preparation

β-Naphthyl acetate. Dissolve 5·0 g. of β-naphthol in 25 ml. of 10 per cent. sodium hydroxide solution in a 250 ml. reagent bottle, add 60 g. of crushed ice, and 5·7 g. (5·5 ml.) of acetic anhydride. Shake vigorously for 10-15 minutes: the β-naphthyl acetate separates as colourless crystals. Filter with suction, wash with water, drain and dry in the air. Recrystallise from light petroleum (b.p. 60–80°) or from dilute alcohol. The yield of pure product, m.p. 71°, is 6·5 g.

IV,104. ANISOLE

Equip a 500 ml. three-necked flask with a separatory funnel, a mercury-sealed mechanical stirrer and a reflux condenser. Place a solution of 21 g. of sodium hydroxide in 200 ml. of water and also 47 g. of pure phenol in the flask, and stir the mixture; cool the warm mixture to about 10° by immersing the flask in an ice bath. Place 63 g. (47 ml.) of dimethyl sulphate in the separatory funnel.

CAUTION. *Both the vapour and the liquid dimethyl sulphate are highly poisonous.* Inhalation of the vapour may lead to giddiness and even to more serious results. The cold liquid is easily absorbed through the skin, with toxic results. If the dimethyl sulphate is accidentally splashed upon the hands, wash immediately

with much concentrated ammonia solution in order to hydrolyse the compound before it can be absorbed through the skin ; then rub gently with a wad of cotton wool soaked in ammonia solution. All experiments involving dimethyl sulphate must therefore be carried out in the fume cupboard and under the supervision of the instructor.

Add the dimethyl sulphate dropwise during 1 hour whilst stirring the mixture vigorously. Then reflux for 2 hours, with stirring, in order to complete the methylation. Allow to cool, add water, transfer to a separatory funnel, remove the lower layer, and wash once with water, twice with dilute sulphuric acid, and then with water until the washings are neutral to litmus. Add some sodium chloride to each washing as this will facilitate the separation of the two layers ($d_{4^\circ}^{20^\circ}$ for anisole is 0·996). Dry over anhydrous calcium chloride or magnesium sulphate, and distil from an air bath. Collect the anisole at 151–154°. The yield is 40 g.

Cognate Preparations

β-Naphthyl methyl ether (nerolin). Use 36·0 g. of β-naphthol, 10·5 g. of sodium hydroxide in 150 ml. of water, and add 31·5 g. (23·5 ml.) of dimethyl sulphate whilst the mixture is cooled in ice. Warm for 1 hour at 70–80°, and allow to cool. Filter off the naphthyl methyl ether at the pump, wash with 10 per cent. sodium hydroxide solution, then liberally with water, and drain thoroughly. Recrystallise from benzene or methylated spirit. The yield is 33 g., m.p. 72°.

Phenetole. Proceed as for *Anisole* using the following quantities: 21 g. of sodium hydroxide in 200 ml. of water, 47 g. of pure phenol, and 77 g. (65·5 ml.) of diethyl sulphate (1).

CAUTION. Diethyl sulphate is poisonous, but to a less degree than dimethyl sulphate. Similar precautions should, however, be taken (see above).

After all the diethyl sulphate has been introduced, reflux the mixture gently for 2 hours with stirring. Transfer the diluted reaction mixture to a separatory funnel, run off the lower aqueous layer, wash successively with water, dilute sulphuric acid (twice), and with water until the washings are neutral to litmus. Dry over anhydrous calcium chloride or magnesium sulphate, and distil. Collect the phenyl ethyl ether (a colourless liquid) at 168–170°. The yield is 50 g.

Note.

(1) If the diethyl sulphate is dark in colour, it should be washed in the fume cupboard with ice water, then with sodium bicarbonate solution until all free acid is removed, and distilled under reduced pressure.

***o-n*-Butoxynitrobenzene.** Place a mixture of 28 g. of *o*-nitrophenol (Section **IV,108**), 28 g. of anhydrous potassium carbonate, 30 g. (23·5 ml.) of *n*-butyl bromide and 200 ml. of dry acetone in a 1-litre round-bottomed flask fitted with an efficient reflux condenser, and reflux on a steam bath for 48 hours. Distil off the acetone, add 200 ml. of water, and extract the product with two 100 ml. portions of benzene. Wash the combined benzene extracts with three 90 ml. portions of 10 per cent. sodium hydroxide solution, remove the benzene by distillation at atmospheric pressure, and distil the residue under reduced pressure. Collect the *o*-*n*-butoxynitrobenzene at 171–172°/19 mm. (or at 127–129°/2 mm.); the yield is 30 g.

IV,105. PHENYL *n*-BUTYL ETHER

Weigh out 11·5 g. of sodium (for experimental details, see Section **III,7,** *Note* 1) into a dry 1-litre round-bottomed flask, provided with a 25 cm. double surface condenser, and add 250 ml. of absolute ethyl alcohol. If the reaction becomes so vigorous that the alcohol cannot be held back by the condenser, direct a stream of cold water or place a wet towel on the outside of the flask until it is again under control: do not cool the alcohol unduly otherwise the last traces of sodium will take a considerable time to dissolve. Add a solution of 47 g. of pure phenol in 50 ml. of absolute alcohol and shake. Into a small separatory funnel, supported by a grooved cork in the top of the condenser, place 133 g (82·5 ml.) of *n*-butyl iodide (Section **III,40**) or an equivalent quantity of *n*-butyl bromide (Sections **III,35** and **III,37**) and add it, with shaking, during 15 minutes. Boil the solution gently for 3 hours. Fit a still-head (" knee tube ") to the flask (Fig. *II, 13,* 3) and distil off as much as possible of the alcohol on a water bath; this process is facilitated by wrapping the exposed part of the flask in a cloth. Add water to the residue in the flask, separate the organic layer and wash it twice with 25 ml. portions of 10 per cent. sodium hydroxide solution, then successively with water, dilute sulphuric acid and water: dry with anhydrous magnesium sulphate. Distil and collect the phenyl *n*-butyl ether at 207–208°. The yield is 60 g.

IV,106. REACTIONS AND CHARACTERISATION OF AROMATIC ETHERS

Purely aromatic ethers (*e.g.*, diphenyl ether), which are commonly encountered, are very limited in number. Most of the aromatic ethers are of the mixed aliphatic-aromatic type. They are not attacked by sodium nor by dilute acids or alkalis. When liquid, the physical properties (b.p., $d_4^{20°}$ and $n_D^{20°}$) are useful constants to assist in their identification. Three important procedures are available for the characterisation of aromatic ethers.

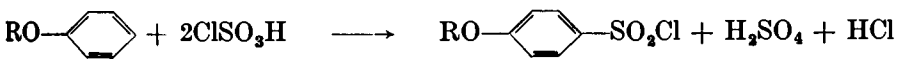
1. **Cleavage with hydriodic acid.** Aromatic ethers undergo fission when heated with constant boiling point hydriodic acid:

$$ArOR + HI \longrightarrow ArOH + RI$$

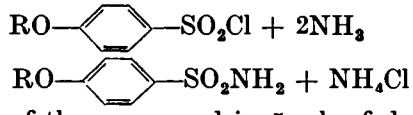
The cleavage products are a phenol and an alkyl iodide, which will serve to characterise the ether.

Experimental details can easily be adapted from those given under *Aliphatic Ethers*, Section **III,60,** *2.*

2. **Sulphonamides of aryl ethers.** Aromatic ethers react smoothly in chloroform solution with chlorosulphonic acid at 0° to give sulphonyl chlorides, for example:



The sulphonyl chlorides are treated with concentrated ammonia solution to produce sulphonamides, which usually possess sharp melting points and are therefore useful as derivatives, for example :



Dissolve 1·0 g. of the compound in 5 ml. of dry chloroform in a dry test-tube, cool to 0°, and add dropwise 5 g. (2·8 ml.) of redistilled chlorosulphonic acid. When the evolution of hydrogen chloride subsides, allow the reaction mixture to stand at room temperature for 20 minutes. Pour the contents of the test-tube cautiously on to 25 g. of crushed ice contained in a small beaker. Separate the chloroform layer and wash it with a little cold water. Add the chloroform layer, with stirring, to 10 ml. of concentrated ammonia solution. After 10 minutes, evaporate the chloroform on a water bath, cool the residue and treat it with 5 ml. of 10 per cent. sodium hydroxide solution ; the sulphonamide dissolves as the sodium derivative, $RO.C_6H_4.SO_2NHNa$. Filter the solution to remove any insoluble matter (sulphone, etc.), acidify the filtrate with dilute hydrochloric acid, and cool in ice water. Collect the sulphonamide and recrystallise it from dilute alcohol.

3. **Picrates of aromatic ethers.** Most phenolic ethers react with picric acid in chloroform or alcoholic solution to yield crystalline picrates (compare *Aromatic Hydrocarbons*, Section **IV,9,***1*).

Dissolve 0·01 mol of the phenolic ether in 10 ml. of warm chloroform, and also (separately) 0·01 mol of picric acid plus 5 per cent. excess (0·241 g.) in 10 ml. of chloroform. Stir the picric acid solution and pour in the solution of the phenolic ether. Set the mixture aside in a 100 ml. beaker and allow it to crystallise. Recrystallise the picrate from the minimum volume of chloroform. In most cases equally satisfactory results may be obtained by conducting the preparation in rectified spirit (95 per cent. C_2H_5OH). The m.p. should be determined immediately after recrystallisation. It must be pointed out, however, that the picrates of aromatic ethers suffer from the disadvantage of being comparatively unstable and may undergo decomposition during recrystallisation.

When aromatic ethers possess an aliphatic side chain, a satisfactory derivative may frequently be obtained by **oxidation of the side chain to carboxyl.** The general procedure may be illustrated by the oxidation of *p*-cresyl methyl ether *p*-$CH_3C_6H_4OCH_3$ to anisic acid *p*-$HOOCC_6H_4OCH_3$. Prepare a solution of 6 g. of potassium permanganate in a mixture of 20 ml. of 5 per cent. sodium hydroxide solution and 150 ml. of water, add 2 g. of *p*-cresyl methyl ether, and heat under reflux for 2–3 hours. If any permanganate remains at the end of this period, destroy it by the addition of a few drops of alcohol. Remove the precipitated manganese dioxide by filtration at the pump, evaporate the filtrate to a volume of 25–30 ml., and acidify it (to Congo red) with dilute sulphuric acid. Anisic acid, m.p. 183–184°, crystallises out on cooling.

Table **IV,106** contains data referring to a number of selected aromatic ethers.

TABLE IV,106. **AROMATIC ETHERS**

Ether	B.P.	M.P.	$d_{4^\circ}^{20^\circ}$	$n_D^{20^\circ}$	Sulphonamide	Picrate	Other Derivatives
Anisole	154°	—	0·996	1·518	111°	81°	Dinitro, 87°; 2:4-dibromo, 61°
Phenetole	170	—	0·965	1·507	150	92	*p*-Nitro, 58
Phenyl *n*-propyl ether	188	—	0·949	1·501	—	—	—
Phenyl *n*-butyl ether	208	—	0·934	1·497	—	112	—
o-Cresyl methyl ether (1)	171	—	0·985	1·505	137	119	*o*-Methoxybenzoic acid, 101
m-Cresyl methyl ether	177	—	0·972	1·513	130	114	*m*-Methoxybenzoic acid, 110
p-Cresyl methyl ether	175	—	0·970	1·512	182	89	Anisic acid, 184
o-Cresyl ethyl ether	184	—	0·953	1·505	149	118	*o*-Ethoxybenzoic acid, 25
m-Cresyl ethyl ether	191	—	0·949	1·506	111	115	*m*-Ethoxybenzoic acid, 137
p-Cresyl ethyl ether	190	—	0·949	1·505	138	111	*p*-Ethoxybenzoic acid, 196
Benzyl methyl ether	171	—	0·965	1·501	—	116	—
Benzyl ethyl ether	186	—	0·948	1·496	—	—	—
Methyl α-naphthyl ether	265	—	1·092	1·696	157	129	Dibromo, 55
Methyl β-naphthyl ether	274	72°	—	—	151	117	Bromo, 63
Ethyl α-naphthyl ether	280	5	1·060	1·597	165	119	4-Bromo, 48
Ethyl β-naphthyl ether	282	37	—	—	163	100	1-Bromo, 66
Benzyl α-naphthyl ether	—	77	—	—	—	—	—
Benzyl β-naphthyl ether	—	99	—	—	—	—	—
o-Methoxydiphenyl	274	29	—	—	—	—	Nitro, 95
p-Methoxydiphenyl	—	90	—	—	—	—	—
o-Chloroanisole	195	—	1·191	1·545	131	—	Nitro, 95
m-Chloroanisole	194	—	—	—	—	—	—
p-Chloroanisole	198	—	—	—	151	—	Nitro, 98
o-Bromoanisole	210	—	—	—	140	—	Nitro, 106
m-Bromoanisole	211	—	—	—	—	—	—
p-Bromoanisole	215	11	—	—	148	—	Nitro, 88
o-Iodoanisole	242	—	—	—	—	—	—
m-Iodoanisole	244	—	—	—	—	—	—
p-Iodoanisole	240	52	—	—	—	—	—
o-Nitroanisole	272	10	1·254	1·562	—	—	*o*-Anisidine

TABLE IV,106. **AROMATIC ETHERS** *(continued)*

Ether	B.P.	M.P.	$d_{4°}^{20°}$	$n_D^{20°}$	Sulphonamide	Picrate	Other Derivatives
m-Nitroanisole	258°	39°	—	—	—	—	*m*-Anisidine (Table IV,100A)
p-Nitroanisole	259	54	—	—	—	—	*p*-Anisidine (Table IV,100A)
2 : 4-Dinitroanisole	—	94	—	—	—	—	—
2 : 4 : 6-Trinitroanisole	—	68	—	—	—	—	—
2 : 4 : 6-Trichloroanisole	—	62	—	—	—	—	Dinitro, 95°
2 : 4 : 6-Tribromoanisole	—	88	—	—	—	—	—
o-Chlorophenetole	208	—	1·134	1·530	133°	—	Nitro, 82
m-Chlorophenetole	205	—	1·171	—	—	—	—
p-Chlorophenetole	212	21	1·121	1·522	134	—	Nitro, 61
o-Bromophenetole	218	—	—	—	135	—	Nitro, 98
p-Bromophenetole	233	4	—	—	145	—	Nitro, 47
o-Iodophenetole	246	—	—	—	—	—	Nitro, 96
m-Iodophenetole	134°/15	—	—	—	—	—	—
p-Iodophenetole	252	29	—	—	—	—	Nitro, 96
o-Nitrophenetole	267	—	—	—	—	—	*o*-Phenetidine (Table IV,100A)
m-Nitrophenetole	284	34	—	—	—	—	*m*-Phenetidine (Table IV,100A)
p-Nitrophenetole	283	60	—	—	—	—	*p*-Phenetidine (Table IV,100A)
2 : 4-Dinitrophenetole	—	87	—	—	—	—	—
2 : 4 : 6-Trinitrophenetole	—	78	—	—	—	—	—
2 : 4 : 6-Trichlorophenetole	246	44	—	—	—	—	Dinitro, 100
2 : 4 : 6-Tribromophenetole	—	73	—	—	—	—	Nitro, 79
Thymol methyl ether	212	—	—	—	—	—	Trinitro, 92
Safrole (2)	232	11	1·100	1·538	—	105°	Piperonylic acid, 228; pentabromo, 169
iso-Safrole (3)	248	7	1·122	1·578	—	75	Tribromo, 109; piperonylic acid, 228
Anethole (4)	235	22	0·989	1·558	—	70	Anisic acid, 184; tribromo, 108
Eugenol methyl ether (5)	244	—	1·050	1·532	—	—	Tribromo, 78; veratric acid, 179
Guaiacol (6)	205	28	1·129	1·544	—	88	Tribromo, 116

TABLE IV,106. **AROMATIC ETHERS (*continued*)**

Ether	B.P.	M.P.	$d_{4°}^{20°}$	$n_D^{20°}$	Sulphonamide	Picrate	Other Derivatives
iso-Eugenol methyl ether (7)	264°	—	1·053	1·569	—	—	—
Diphenyl ether	259	28°	—	—	159°	110°	Dibromo, 55°; dinitro, 144°
Dibenzyl ether	296	—	1·043	—	—	78	—
p-Bromodiphenyl ether	168°/15	—	—	—	131	—	—
Veratrole (8)	206	22	—	—	136	57	Dibromo, 93; nitro, 95
Resorcinol dimethyl ether	217	—	1·050	—	167	58	Dibromo, 140; trinitro, 124
Hydroquinone dimethyl ether	212	56	—	—	148	48	Nitro, 72; dibromo, 142
Catechol diethyl ether	217	43	—	—	162	71	Trinitro, 122
Resorcinol diethyl ether	235	12	—	—	184	109	—
Hydroquinone diethyl ether	—	72	—	—	155	—	Nitro, 49
Pyrogallol trimethyl ether	241	47	—	—	124	81	—
Pyrogallol triethyl ether	—	39	—	—	—	—	—

(1) Methyl *o*-tolyl ether; *o*-Methoxytoluene.
(2) 3 : 4-Methylenedioxy-1-allylbenzene.
(3) 3 : 4-Methylenedioxy-1-propenylbenzene.
(4) *p*-Propenylanisole.
(5) 3 : 4-Dimethoxy-1-allylbenzene.
(6) *o*-Methoxyphenol.
(7) 3 : 4-Dimethoxy-1-propenylbenzene.
(8) Catechol dimethyl ether.

IV,107. *o*-PROPIOPHENOL AND *p*-PROPIOPHENOL

Equip a 1 litre three-necked flask with a dropping funnel, a sturdy mechanical stirrer and a reflux condenser, and place 187 g. of anhydrous aluminium chloride and 200 ml. of carbon disulphide in it; attach a gas trap (Fig. *II*, *8*, 1) to the top of the condenser. Stir the suspension and add 188 g. (179 ml.) of phenyl propionate (1) slowly and at such a rate that the solvent boils vigorously (about 90 minutes). Much hydrogen chloride is evolved and is absorbed by the trap. When all the phenyl propionate has been introduced, gently reflux the reaction mixture on a water bath until the evolution of hydrogen chloride ceases (about 2 hours). Turn the reflux condenser downwards (compare Fig. *II*, *41*, 1), and distil off the solvent from the water bath. Then replace the latter by an oil bath maintained at 140–150°, and heat, with stirring, for 3 hours. During this period more hydrogen chloride is evolved, the mixture thickens, and finally becomes a brown resinous mass; continue the stirring as long as possible. Allow the reaction mixture to cool and decompose the aluminium chloride complex by *slowly* adding first 150 ml. of dilute hydrochloric acid (1 : 1) and then 250 ml. of water; much heat is evolved and a dark oil collects on the surface. Allow to stand overnight, when most of the *p*-propiophenol in the upper layer solidifies. Filter this off at the pump, and recrystallise it from 200 ml. of methyl alcohol; 74 g. of *p*-propiophenol (a pale yellow solid), m.p. 147°, are obtained.

Concentrate the mother liquors from this recrystallisation and combine with the oily filtrate: dissolve in 250 ml. of 10 per cent. sodium hydroxide solution, and extract with two 50 ml. portions of ether to remove non-phenolic products. Acidify the alkaline solution with hydrochloric acid, separate the oily layer, dry it over anhydrous magnesium sulphate, and distil under diminished pressure, preferably from a Claisen flask with fractionating side arm (Figs. *II*, *24*, 2–5). Collect the *o*-propiophenol (65 g.) at 110–115°/6 mm. and a further quantity (20 g.) of crude *p*-propiophenol at 140–150°/11 mm.

Note.

(1) The phenyl propionate may be prepared by slowly adding 196 g. (120 ml.) of redistilled thionyl chloride to a mixture of 150 g. of pure phenol and 132 g. (133 ml.) of propionic acid (compare Fig. *III*, *31*, 1), warming to drive all the sulphur dioxide and hydrogen chloride, and distilling; 190 g. of phenyl propionate, b.p. 202–212° (the pure substance boils at 211°) are obtained.

Cognate Preparations

o- and p-hydroxyacetophenone. Use 187 g. of anhydrous aluminium chloride, 200 ml. of carbon disulphide and 170 g. (158 ml.) of phenyl acetate (Section **IV,103**). After acidifying and leaving overnight, dilute the partly solidified oil with benzene, and extract the aqueous layer with benzene. Dry the benzene with anhydrous magnesium sulphate, distil off the benzene at atmospheric pressure, and then distil the residue under reduced pressure (15–20 mm.) until the *p*-isomer begins to collect in the condenser. Refractionate the distillate from a Widmer flask (Figs. *II*, *24*, 3–5) and collect the *o*-hydroxyacetophenone at 105–106°/20 mm. (or at 87–88°/7 mm.): the yield is 30 per cent. based on

the phenyl acetate. The *p*-hydroxyacetophenone remaining in the flask may be recrystallised from dilute alcohol or from benzene - light petroleum (b.p. 60–80°); it melts at 109°. Any residual *o*-hydroxyacetophenone may be removed by steam distillation; the *p*-isomer is non-volatile in steam.

2 : 5-Dihydroxyacetophenone. Finely powder a mixture of 40 g. of dry hydroquinone diacetate (1) and 87 g. of anhydrous aluminium chloride in a glass mortar and introduce it into a 500 ml. round-bottomed flask, fitted with an air condenser protected by a calcium chloride tube and connected to a gas absorption trap (Fig. *II*, *8*, 1). Immerse the flask in an oil bath and heat slowly so that the temperature reaches 110–120° at the end of about 30 minutes: the evolution of hydrogen chloride then begins. Raise the temperature slowly to 160–165° and maintain this temperature for 3 hours. Remove the flask from the oil bath and allow to cool. Add 280 g. of crushed ice followed by 20 ml. of concentrated hydrochloric acid in order to decompose the excess of aluminium chloride. Filter the resulting solid with suction and wash it with two 80 ml. portions of cold water. Recrystallise the crude product from 200 ml. of 95 per cent. ethanol. The yield of pure 2 : 5-dihydroxyacetophenone, m.p. 202–203°, is 23 g.

Note.

(1) Hydroquinone diacetate may be prepared as follows. Add 1 drop of concentrated sulphuric acid to a mixture of 55 g. of hydroquinone and 103 g. (95·5 ml.) of A.R. acetic anhydride in a 500 ml. conical flask. Stir the mixture gently by hand; it warms up rapidly and the hydroquinone dissolves. After 5 minutes, pour the clear solution on to 400 ml. of crushed ice, filter with suction and wash with 500 ml. of water. Recrystallise the solid from 50 cent. ethanol by weight (*ca.* 400 ml. are required). The yield of pure hydroquinone diacetate, m.p. 122°, is 89 g.

IV,108. *o*- AND *p*-NITROPHENOLS

Cautiously add 250 g. (136 ml.) of concentrated sulphuric acid in a thin stream and with stirring to 400 ml. of water contained in a 1 litre bolt-head or three-necked flask, and then dissolve 150 g. of sodium nitrate in the diluted acid. Cool in a bath of ice or iced water. Melt 94 g. of phenol with 20 ml. of water, and add this from a separatory funnel to the stirred mixture in the flask at such a rate that the temperature does not rise above 20°. Continue the stirring for a further 2 hours after all the phenol has been added. Pour off the mother liquid from the resinous mixture of nitro compounds. Melt the residue with 500 ml. of water, shake and allow the contents of the flask to settle. Pour off the wash liquor and repeat the washing at least two or three times to ensure the complete removal of any residual acid. Steam distil the mixture (Fig. *II*, *40*, 1 or Fig. *II*, *41*, 1) until no more *o*-nitrophenol passes over; if the latter tends to solidify in the condenser, turn off the cooling water temporarily. Collect the distillate in cold water, filter at the pump, and drain thoroughly. Dry upon filter paper in the air. The yield of *o*-nitrophenol, m.p. 46° (1), is 50 g.

Allow the residue in the flask to cool during 2 hours and then cool in ice for 15–30 minutes. Filter off the crude *p*-nitrophenol and boil it

with one litre of 2 per cent. hydrochloric acid (2) together with about 5 g. of decolourising charcoal for at least 10 minutes. Filter through a hot water funnel (or through a Buchner funnel, preheated by pouring boiling water through it): allow the filtrate to crystallise overnight. Filter off the almost colourless needles and dry them upon filter paper. The yield of *p*-nitrophenol, m.p. 112°, is 35 g. Further small quantities may be obtained by concentrating the mother liquor and also by repeating the extraction of the residue with 2 per cent. hydrochloric acid.

Notes.

(1) If the m.p. is not quite satisfactory, dissolve the *o*-nitrophenol in hot alcohol (or methylated spirit) under reflux, add hot water drop by drop until a cloudiness just appears, and allow to cool spontaneously. Filter off the bright yellow crystals and dry between filter paper.

(2) It is not advisable to treat the crude *p*-nitrophenol with sodium hydroxide solution in order to convert it into the sodium derivative: alkali causes extensive resinification.

IV,109. 2 : 4-DINITROPHENOL

In a 1 litre round-bottomed flask equipped with a reflux condenser place a solution of 62·5 g. of anhydrous sodium carbonate in 500 ml. of water and add 50 g. of commercial 2 : 4-dinitro-1-chlorobenzene. Reflux the mixture for 24 hours or until the oil passes into solution. Acidify the yellow solution with hydrochloric acid and, when cold, filter the crystalline dinitrophenol which has separated. Dry the product upon filter paper in the air. The yield is 46 g. If the m.p. differs appreciably from 114°, recrystallise from alcohol or from water.

IV,110. PICRIC ACID (2 : 4 : 6-TRINITROPHENOL)

Place 10 g. of phenol in a dry 750 ml. or 1 litre flat-bottomed flask and add 23 g. (12·5 ml.) of concentrated sulphuric acid, shake the mixture (which becomes warm) and heat it on a boiling water bath for 30 minutes to complete the formation of the *o*-and- *p*-phenolsulphonic acids, and then cool the flask thoroughly in an ice-water mixture. Place the flask on a non-conducting surface (*e.g.*, a wooden block or an asbestos board) in a fume cupboard, and, *whilst the phenolsulphonic acids are still a viscous syrup*, add 38 ml. of concentrated nitric acid and *immediately* mix the liquids by shaking for a few seconds. Allow the mixture to stand; generally within 1 minute a vigorous but harmless reaction takes place and copious red fumes are evolved. When the reaction subsides, heat the flask in a boiling water bath for 1·5–2 hours with occasional shaking; the heavy oil, initially present, will ultimately form a mass of crystals. Add 100 ml. of cold water, chill thoroughly in ice water, filter the crystals at the pump, wash well with water to remove all the nitric acid, and drain. Recrystallise from dilute alcohol (1 volume of alcohol : 2 volumes of water); about 110 ml. are required. Filter off the recrystallised material and dry between filter paper. The yield of picric acid (yellow crystals), m.p. 122°, is 16 g.

Note.

It is advisable to keep the picric acid in the moist condition (containing about 10 per cent. of water) in a bottle with a cork stopper. Small quantities may be

safely stored whilst dry, but this is not recommended in the interest of safety. Under no circumstances should glass stoppers be employed for potentially explosive substances, since on replacing the stopper some of the material may be ground between the stopper and the neck of the bottle and an explosion may result.

IV,111. *p*-BROMOPHENOL

Equip a 500 ml. three-necked flask with a reflux condenser, a mechanical stirrer and a separatory funnel ; use rubber stoppers throughout. Attach to the top of the condenser a calcium chloride (or cotton wool) tube leading by means of a glass tube to a funnel just immersed in a beaker holding about 150 ml. of water and crushed ice for the absorption of the hydrogen bromide (compare Fig. *II*, *13*, 8, *b*) (1). Place 100 g. of phenol dissolved in 100 ml. of dry carbon disulphide in the flask, set the stirrer in motion and cool the flask in a mixture of ice and salt. When the temperature falls below 5°, add slowly (during about 2 hours) from the separatory funnel a solution of 170 g. (54·5 ml.) of bromine in 50 ml. of carbon disulphide. Then arrange the flask for distillation (compare Fig. *II*, *41*, 1), attach a distilling flask as a receiver tightly to the lower end of the condenser and connect the side arm of the distilling flask to a device for absorbing the hydrogen bromide evolved (compare Fig. *II*, *8*, 1) (1). Distil off the carbon disulphide on a water bath (*CAUTION*), transfer the residue to a Claisen flask with fractionating side arm (Figs. *II*, *24*, 2-4) but with the upper side arm fused in as in Fig. *II*, *1*, 3, *d* so that any bromophenol which may come into contact with rubber is not carried over into the condenser ; if this precaution is not taken, a pinkish product will result. Distil under diminished pressure : the first fraction (25–35 g.) contains an inseparable mixture of *o*- and *p*-bromophenols, this is followed by fairly pure *p*-bromophenol at 145–150°/25–30 mm. (150–155 g.), and some high boiling material containing 2 : 4-dibromophenol. The *p*-bromophenol solidifies on cooling to a solid white mass, which usually contains traces of an oil ; this may be removed by spreading on a porous tile or by centrifuging. The dry crystals melt at 63°.

Note.

(1) A considerable quantity of constant boiling point hydrobromic acid may be obtained by distilling these solutions.

IV,112. *o*-BROMOPHENOL

In a 1-litre flask, equipped as in the preceding Section, place a mixture of 31 g. of phenol and 116 g. (63 ml.) of concentrated sulphuric acid, and heat in a boiling water bath for 3 hours with mechanical stirring. Cool to room temperature or below by immersing the flask in ice water, and then add slowly a solution of 95 g. of sodium hydroxide in 235 ml. of water : a solid salt may separate, but this will dissolve at a later stage. Replace the separatory funnel by a cork carrying a thermometer, which dips well into the liquid, and support a small dropping funnel by means of a grooved cork in the top of the condenser. Cool the alkaline solution to room temperature, and add 53 g. (17 ml.) of bromine from the dropping

funnel during 20–30 minutes whilst stirring constantly; permit the temperature to rise to 40–50°. Continue the stirring for 30 minutes after the bromine has been introduced: the reaction mixture should still be alkaline and contain only a small amount of suspended matter. The solution must now be evaporated. Arrange the flask assembly so that a rapid stream of air can be passed through the stirred reaction mixture, and heat the flask in an oil bath at 150–155°. After 30–40 minutes, a thick pasty mass remains. Allow to cool and then add 270 ml. of concentrated sulphuric acid (*FUME CUPBOARD*; much hydrogen bromide is evolved). Heat the flask in an oil bath at 195–205° and steam distil the mixture (compare Fig. *II*, *41*, 1); this results in the hydrolysis of the sulphonate groups and the bromophenol passes over as a heavy, colourless (or pale yellow) oil. When the distillate is clear, extract it with ether. Dry the ethereal extract with a little anhydrous magnesium sulphate, remove the ether on a water bath (Fig. *II*, *13*, 4) and distil the residue as rapidly as possible since the bromophenol is somewhat unstable and decomposes appreciably at the high temperature. Collect the fraction b.p. 195–200° (a colourless liquid with a characteristic odour), which is practically pure *o*-bromophenol. The yield is 25 g. The compound is somewhat unstable and decomposes on standing, becoming brown or red in colour.

IV,113. *p*-IODOPHENOL

Dissolve 54·5 g. of *p*-aminophenol (Section **IV,83**) in a mixture of 60 g. (32·5 ml.) of concentrated sulphuric acid, 250 ml. of water and 250 g. of crushed ice in a large beaker or bolt-head flask. Cool the solution in a freezing mixture, stir mechanically, and add during 1 hour a solution of 34·5 g. (1) of sodium nitrite in 75 ml. of water. Stir for a further 20 minutes, and then add 18·5 g. (10 ml.) of concentrated sulphuric acid. Pour the cold diazonium solution into an ice-cold solution of 100 g. of potassium iodide in 100 ml. of water contained in a beaker provided with a mechanical stirrer. After 5 minutes, add 1 g. of copper bronze (which has been washed with ether), with continued stirring, and warm the solution slowly on a water bath. Maintain the temperature at 75–80° until the evolution of nitrogen ceases; the iodophenol separates as a dark heavy oil. Cool to room temperature, extract the reaction mixture with three 80 ml. portions of chloroform, wash the combined extracts with dilute sodium bisulphite solution or sodium thiosulphate solution, and dry with anhydrous magnesium sulphate. Remove the solvent on a water bath (compare Fig. *II*, *13*, 4, but with a Claisen flask replacing the distilling flask) and distil the residue under diminished pressure. Collect the *p*-iodophenol at 138–140°/5 mm.; this solidifies on cooling. Recrystallise from about 1 litre of light petroleum (b.p. 80–100°). The yield of colourless product, m.p. 94°, is 78 g.

Note.

(1) This weight is for sodium nitrite of 100 per cent. purity; it should be adjusted according to the purity of the sodium nitrite employed.

IV,114. REACTIONS AND CHARACTERISATION OF PHENOLS

Most phenols are crystalline solids ; notable exceptions are *m*-cresol and *o*-bromophenol. The monohydric phenols generally have characteristic odours. The solubility in water increases with the number of hydroxl groups in the molecule.

(i) **Ferric chloride solution.** Dissolve about 0·05 g. of the compound in 5 ml. of water ; if the compound is sparingly soluble, prepare a hot, saturated aqueous solution, filter and use 1 ml. of the cold filtrate. Place the solution in a 75 × 10 mm. test-tube. Add 1 drop of " neutral " 1 per cent. ferric chloride solution and observe the colour ; add another drop after 2–3 seconds. If a transient or permanent colouration (usually purple, blue or green) other than yellow or orange-yellow is observed, the substance is probably a phenol (or an enol). If no colouration is obtained, repeat the test as above but substitute absolute ethanol or methanol for water as solvent.

(ii) **Sodium bicarbonate solution.** Phenols do not usually liberate carbon dioxide from 5 per cent. sodium bicarbonate solution {for details, see under *Aliphatic Carboxylic Acids*, Section **III,85**,(i)}. They will dissolve, however, in sodium hydroxide solution. Add 0·1 g. of the substance to 1 ml. of 5 per cent. sodium hydroxide solution and shake or stir. Observe whether the material dissolves and/or a colouration is produced (*e.g.*, a brown colouration from *o*- and *p*-polyhydric phenols) : if only partial solution takes place or another substance appears to form, dilute with 1 ml. of water and shake. The latter procedure is necessary for sparingly soluble sodium salts (*e.g.*, sodium methyl salicylate).

(iii) **Bromine water.** Many phenols (with the exception of those with strong reducing properties) yield crystalline bromination products ; these are often useful for purposes of characterisation. Dissolve or suspend 0·25 g. of the compound in 10 ml. of dilute hydrochloric acid or of water, and add bromine water dropwise until decolourisation is slow : a white precipitate of the bromophenol may form. Recrystallise and determine the m.p.

An alternative procedure, more suitable for the preparation of somewhat larger quantities of the bromo derivative, is the following. Dissolve 1·0 g. of the compound in 10–15 ml. of glacial acetic acid, cautiously add 3–4 ml. of liquid bromine, and allow the mixture to stand for 15–20 minutes. Pour into 50–100 ml. of water, filter off the bromo compound at the pump, and wash with a little cold water. Recrystallise from dilute alcohol.

(iv) **Phthalein test.** Many phenols yield phthaleins, which give characteristic colourations in alkaline solution, when fused with phthalic anhydride and a little concentrated sulphuric acid.

Place in a dry test-tube 0·5 g. of the compound and an equal bulk of pure phthalic anhydride, mix well together, and add 1 drop of concentrated sulphuric acid. Stand the tube for 3–4 minutes in a small beaker of concentrated sulphuric acid or oil previously heated to 160°. Remove from the bath, allow to cool, add 4 ml. of 5 per cent. sodium hydroxide solution and stir until the fused mass has dissolved. Dilute with an equal

volume of water, filter and examine the colour of the filtrate against a white back-ground : if the solution exhibits a fluorescence, observe the colour against a black back-ground.

Crystalline Derivatives of Phenols

1. **Acetates.** The acetates of monohydric phenols are usually liquids, but those of di- and tri-hydric phenols and also of many substituted phenols are frequently crystalline solids. They may be prepared with acetic anhydride as detailed under *Amines*, Section **IV,100,***1.*

Acetates may also be prepared by adding acetic anhydride to somewhat dilute solutions of compounds containing hydroxyl (or amino) groups in aqueous caustic alkalis. The amount of alkali used should suffice to leave the liquid slightly basic at the end of the operation, so much ice should be added that a little remains unmelted, and the acetic anhydride should be added quickly.

Dissolve 0·01 mol (or 1 g. if the molecular weight is unknown) of the compound in 5 ml. of 3*N* sodium hydroxide solution, add 10–20 g. of crushed ice followed by 1·5 g. (1·5 ml.) of acetic anhydride. Shake the mixture vigorously for 30–60 seconds. The acetate separates in a practically pure condition either at once or after acidification by the addition of a mineral acid. Collect the acetyl derivative, and recrystallise it from hot water or from dilute alcohol.

2. **Benzoates.** The benzoates of a few phenols (*e.g. o*-cresol) are liquids. Many phenols do, however, yield crystalline benzoyl derivatives : these are useful for purposes of characterisation.

The Schotten - Baumann method of benzoylation with benzoyl chloride in the presence of aqueous sodium hydroxide may be used. Full details are given under *Amines* ; Section **IV,100,** *2.*

3. ***p*-Nitrobenzoates and 3 : 5-dinitrobenzoates.** Both *p*-nitrobenzoyl chloride and 3 : 5-dinitrobenzoyl chloride react with phenols, best in pyridine solution, to yield crystalline *p*-nitrobenzoates and 3 : 5-dinitrobenzoates respectively :

$$p\text{-}NO_2C_6H_4COCl + ArOH \longrightarrow p\text{-}NO_2C_6H_4COOAr + HCl$$
$$3:5\text{-}(NO_2)_2C_6H_3COCl + ArOH \longrightarrow 3:5\text{-}(NO_2)_2C_6H_3COOAr + HCl$$

For properties of these reagents and their preparation from the corresponding acids, see under *Aliphatic Alcohols*, Section **III,27,** *1* and *2*.

Dissolve 0·5 g. of the phenol in 4–5 ml. of dry pyridine, add 1·3 g. of 3 : 5-dinitrobenzoyl chloride and reflux for 25–30 minutes. Pour the cold reaction mixture into 40 ml. of *ca.* 2*N* hydrochloric acid. Decant the supernatant aqueous liquid from the precipitated solid or oil and stir it vigorously with about 10 ml. of *N* sodium carbonate solution. Filter off the solid derivative and wash it with water. Recrystallise from alcohol, dilute alcohol, benzene - acetone or benzene - light petroleum (b.p. 60–80°).

4. **Aryloxyacetic acids.** Phenols, in the presence of alkali, react with chloroacetic acid to give aryloxyacetic acids :

$$ArONa + ClCH_2COONa \longrightarrow ArOCH_2COONa + NaCl$$
$$\xrightarrow{HCl} ArOCH_2COOH + 2NaCl$$

These are crystalline compounds with sharp melting points, and possess the further advantage that their equivalent weights may be determined by dissolving in dilute alcohol and titrating with standard alkali. Nitrophenols, however, give unsatisfactory derivatives.

To a mixture of 1·0 g. of the compound and 3·5 ml. of 33 per cent. sodium hydroxide solution in a test-tube, add 2·5 ml. of 50 per cent. chloroacetic acid solution. If necessary, add a little water to dissolve the sodium salt of the phenol. Stopper the test-tube loosely and heat on a gently-boiling water bath for an hour. After cooling, dilute with 10 ml. of water, acidify to Congo red with dilute hydrochloric acid, and extract with 30 ml. of ether. Wash the ethereal extract with 10 ml. of water, and extract the aryloxyacetic acid by shaking with 25 ml. of 5 per cent. sodium carbonate solution. Acidify the sodium carbonate extract (to Congo red) with dilute hydrochloric acid, collect the aryloxyacetic acid which separates, and recrystallise it from hot water.

5. **Diphenylurethanes.** Phenols react with diphenylcarbamyl chloride to yield diphenylurethanes (or aryl *N*,*N*-diphenylcarbamates):

$$(C_6H_5)_2NCOCl + HOAr \xrightarrow{C_5H_5N} (C_6H_5)_2NCOOAr + HCl$$

The reagent is unsuitable for a number of phenolic acids.

Dissolve 0·5 g. of the phenol in 2·5 ml. of pyridine, and add one equivalent of diphenylcarbamyl chloride (or 0·4–0·5 g. if the molecular weight is uncertain). Reflux the mixture for 30–60 minutes on a boiling water bath, and then pour into about 25 ml. of water. Filter the derivative, wash with a little sodium bicarbonate solution, and recrystallise from alcohol benzene, light petroleum (b.p. 60–80°) or carbon tetrachloride.

6. **α-Naphthylurethanes (α-naphthylcarbamates).** α-Naphthyl *iso*-cyanate reacts smoothly with monohydric, but not with polyhydric, phenols to give α-naphthylurethanes (or *N*-α-naphthylcarbamates):

$$C_{10}H_7{}^{\alpha}N{=}C{=}O + ArOH \longrightarrow C_{10}H_7{}^{\alpha}NHCOOAr$$

(compare *Aliphatic Alcohols*, Section **III,27**, *4*). Some phenols, *e.g.*, nitrophenols and halogeno-phenols, react with difficulty with the reagent alone; the addition of a few drops of pyridine or 1 drop of an ethereal solution of trimethylamine or triethylamine generally results in the rapid formation of the urethane.

Place 0·25 g. of the phenol together with an equal weight of α-naphthyl *iso*-cyanate in a *dry* test-tube closed with a stopper carrying a calcium chloride or cotton wool guard tube. If a spontaneous reaction does not occur, boil the mixture gently for 2–3 minutes, and cool; if the reaction mixture does not solidify, rub the walls of the tube vigorously with a glass rod. If no crystalline solid is obtained, add 2 drops of dry pyridine or 1 drop of an ethereal solution of triethylamine, and warm on a water bath for 5 minutes. Extract the contents of the tube with boiling light petroleum (b.p. 80–100° or 100–120°) to separate any insoluble di-α-naphthyl urea. Recrystallise the crystals which separate on cooling from the same solvent.

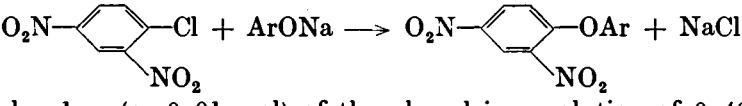
The following alternative method may be used. Dissolve 0·01 mol of the phenol and 0·01 mol of α-naphthyl *iso*-cyanate in 20 ml. of light petroleum (b.p. 60–80°), add 2 drops of triethylamine (or, less satisfactorily, 2 drops of pyridine), reflux for 5 minutes, and allow to crystallise. Filter off the crystalline solid through a sintered glass funnel.

7. **p-Toluenesulphonates.** *p*-Toluenesulphonyl chloride condenses readily with phenols to yield *p*-toluenesulphonates:

$$p\text{-}CH_3C_6H_4SO_2Cl + ArOH \longrightarrow p\text{-}CH_3C_6H_4SO_2OAr + HCl$$

Mix 1·0 g. of the phenol with 2·5 ml. of pyridine, add 2 g. of *p*-toluenesulphonyl chloride, and heat on a water bath for 15 minutes. Pour into 25 ml. of cold water and stir until the oil solidifies. Filter, wash with cold dilute hydrochloric acid (to remove pyridine), with cold dilute sodium hydroxide solution (to remove any phenol present), and then with cold water. Recrystallise from methyl or ethyl alcohol.

8. **2:4-Dinitrophenyl ethers.** 2:4-Dinitrochlorobenzene reacts with the sodium salts of phenols to yield crystalline 2:4-dinitrophenyl ethers:



Dissolve 1 g. (or 0·01 mol) of the phenol in a solution of 0·40 g. of sodium hydroxide in 5 ml. of water. Add the resulting solution to 2·0 g. of 2:4-dinitrochlorobenzene dissolved in 30 ml. of 95 per cent. ethanol; add more alcohol, if necessary, to effect solution. Heat the solution under reflux on a water bath until the colour (usually red) is discharged and a copious precipitate of sodium chloride appears (30–60 minutes). Dilute the reaction mixture with an equal volume of water, filter off the precipitated 2:4-dinitrophenyl ether, wash with water, and recrystallise from alcohol.

Note. The 2:4-dinitrochlorobenzene must be handled cautiously: it is a skin irritant. If any touches the skin, wash it immediately with methylated spirit.

9. **Pseudo-saccharin ethers.** When pseudo-saccharin chloride is heated with an excess of a phenol, *O*-aryl derivatives of saccharin are produced (compare Section **III,27,** 7).

Heat 0·5 g. of pseudo-saccharin chloride with an excess of the phenol to 125–140° for 15–20 minutes; hydrogen chloride is evolved. Wash the product with dilute sodium hydroxide solution and then with water. Recrystallise the derivative from ethanol.

The melting points of some *O*-aryl saccharin derivatives are: phenol, 182°; *o*-cresol, 163°; *m*-cresol, 146°; *p*-cresol, 172°; *o*-nitrophenol, 236°; *p*-nitrophenol, 192°.

The melting points of the derivatives of a number of selected phenols are collected in Table **IV,114.** The physical properties of a number of enols are given in Table **IV,114A.**

Heating of β-keto esters or of 1:3-diketones with an equivalent amount of phenylhydrazine often yields substituted pyrazolones or pyrazoles respectively. The latter may serve as *derivatives of enols.*

Heat a mixture of 0·5 g. of ethyl acetoacetate and an equivalent amount of phenylhydrazine in an oil bath at 100–110° for 2 hours. Water and alcohol vapours are evolved. Cool and recrystallise the product from alcohol. The resulting phenylmethylpyrazolone has m.p. 127°.

TABLE IV,114. **PHENOLS**

Phenol	B.P.	M.P.	Bromo Compound	Acetate	Benzoate	*p*-Nitrobenzoate	3 : 5-Dinitrobenzoate	Aryloxyacetic Acid	*NN*-Diphenylcarbamate	*N*-α-naphthylcarbamate	*p*-Toluenesulphonate	2 : 4-Dinitrophenyl Ether
Phenol	182°	43°	95°†	Liq.	69°	126°	146°	99°	105°	133°	96°	69°
o-Cresol	191	30	56*	Liq.	Liq.	94	138	152	73	142	55	90
m-Cresol	202	12	84†	Liq.	55	90	165	103	101	128	56	74
p-Cresol	202	36	49*	Liq.	71	98	189	136	94	146	70	94
o-Chlorophenol	176	9	—	Liq.	Liq.	115	143	145	—	120	74	99
m-Chlorophenol	214	33	—	Liq.	71	99	156	110	—	158	—	75
p-Chlorophenol	217	43	—	Liq.	86	168	186	156	97	166	71	126
o-Bromophenol	195	5	95†	Liq.	—	—	—	143	—	129	78	89
m-Bromophenol	236	33	—	Liq.	86	—	—	108	—	108	53	—
p-Bromophenol	235	64	95†	21°	102	180	191	159	99	169	94	141
o-Iodophenol	—	43	—	—	34	—	—	135	—	—	—	95
m-Iodophenol	—	40	—	38	—	133	183	115	—	—	61	—
p-Iodophenol	—	94	—	32	119	—	—	156	127	—	99	156
2 : 4-Dichlorophenol	210	45	68	—	96	—	—	140	—	—	125	119
2 : 4-Dibromophenol	239	40	—	36	98	184	—	153	—	—	120	135
2 : 4-Di-iodophenol	—	72	—	71	98	—	—	—	—	—	—	—
2 : 4 : 5-Trichlorophenol	249	68	—	—	93	—	—	157	—	—	—	—
2 : 4 : 6-Trichlorophenol	246	69	—	—	75	106	136	182	143	188	—	136
2 : 4 : 6-Tribromophenol	—	94	120‡	82	81	153	174	200	153	153	113	135
2 : 4 : 6-Tri-iodophenol	—	159	—	156	—	—	181	—	—	—	—	—
o-Nitrophenol	216	45	117*	41	59	141	155	158	114	113	83	142
m-Nitrophenol	—	97	91*	56	95	174	159	156	—	167	113	138
p-Nitrophenol	—	114	142*	83	142	159	186	187	112	151	97	120
2 : 4-Dinitrophenol	—	113	118	72	132	139	—	—	—	—	121	248
Picric acid	—	122	—	76	—	143	—	—	—	—	—	—
o-Methoxyphenol (1)	205	28	116†	Liq.	58	93	142	119	118	118	85	97
m-Methoxyphenol (2)	244	—	104†	Liq.	—	—	—	114	—	129	—	—
p-Methoxyphenol (3)	243	56	—	32	87	—	—	111	—	—	—	—
2 : 3-Dimethylphenol (4)	218	75	—	—	—	—	—	187	—	—	—	—
3 : 4-Dimethylphenol (5)	225	62	171†	—	58	—	181	163	—	142	—	—
2 : 4-Dimethylphenol (6)	211	28	179†	Liq.	38	105	164	142	—	135	—	—
3 : 5-Dimethylphenol (7)	219	68	166†	Liq.	24	109	195	86	—	—	—	—

TABLE IV,114. **PHENOLS (*continued*)**

Phenol	B.P.	M.P.	Bromo Compound	Acetate	Benzoate	*p*-Nitrobenzoate	3 : 5 Dinitrobenzoate	Aryloxyacetic Acid	*NN*-Diphenylcarbamate	*N*-α-naphthylcarbamate	*p*-Toluenesulphonate	2 : 4-Dinitrophenyl Ether
2 : 5-Dimethylphenol (8)	211°	75°	178°†	Liq.	61°	87°	137°	118°	—	173°	—	—
2 : 6-Dimethylphenol (9)	203	49	79	—	—	—	159	140	—	—	—	—
o-Ethylphenol	207	—	—	—	39	56	108	141	—	—	—	—
m-Ethylphenol	217	—	—	Liq.	52	68	—	75	—	—	—	—
p-Ethylphenol	219	47	—	Liq.	60	81	132	97	—	128	—	—
o-*cyclo*Hexylphenol	—	55	—	—	—	—	—	—	—	—	—	—
p-*cyclo*Hexylphenol	—	132	—	—	118	137	168	—	—	—	—	—
p-*n*-Butylphenol	248	22	—	—	127	68	—	81	—	—	—	—
p-*tert.*-Butylphenol	237	99	—	Liq.	82	—	—	86	—	110	—	—
p-*tert.*-Amylphenol	266	96	—	Liq.	61	—	—	—	—	—	54°	—
Eugenol (10)	254	—	118	30°	70	81	131	80	—	122	85	115°
iso-Eugenol (11)	266	—	—	80	106	109	—	94	—	150	—	130
Thymol (12)	233	51	55	Liq.	33	70	103	148	—	160	71	67
p-Chlorothymol	—	59	—	—	—	—	—	—	—	—	—	—
Vanillin (13)	—	81	160	102	78	—	—	189	—	—	115	131
Carvacrol (14)	238	—	46	Liq.	—	51	77	151	—	116	—	—
Salicylaldehyde (15)	197	—	—	39	—	128	—	132	—	—	64	—
m-Hydroxybenzaldehyde	240	108	—	Liq.	38	—	—	148	—	—	—	—
p-Hydroxybenzaldehyde	—	116	—	Liq.	90	—	—	198	—	—	—	—
Salicylic acid (16)	—	159	—	135	132	205	—	191	—	—	—	—
m-Hydroxybenzoic acid	—	200	—	131	—	—	—	206	—	—	—	—
p-Hydroxybenzoic acid	—	214	—	187	—	—	—	278	—	—	—	—
α-Naphthol	279	94	105*	49	56	143	217	192	—	152	88	128
β-Naphthol	285	123	84	72	107	169	210	154	141°	157	125	95
o-Hydroxydiphenyl (17)	275	58	—	63	76	—	—	—	—	—	65	—
p-Hydroxydiphenol	306	165	—	88	151	—	—	—	—	—	177	118
Catechol	240	105	192‡	65	84	169	152	—	—	175	—	—
Resorcinol	280	110	112*	Liq.	117	182	201	195	130	206	81	194
Hydroquinone	286	170	186*	124	199	250	317	250	230	247	159	—
Orcinol (18) (hydrate m.p. 58°)	289	108	104†	25	88	214	190	217	154	160	—	—
Pyrogallol	309	133	158*	173	90	230	205	198	212	—	—	—
Phloroglucinol	—	218	151†	104	174	283	162	—	—	—	—	—

TABLE IV,114. **PHENOLS (*continued*)**

Phenol	B.P.	M.P.	Bromo Compound	Acetate	Benzoate	*p*-Nitrobenzoate	3 : 5 Dinitrobenzoate	Aryloxyacetic Acid	*NN*-Diphenylcarbamate	*N*-α-naphthylcarbamate	*p*-Toluenesulphonate	2 : 4-Dinitrophenyl Ether
1 : 3-Dihydroxynaphthalene (19)	—	124°	—	56°	—	—	—	—	—	—	—	—
1 : 5-Dihydroxynaphthalene .	—	265	—	160	235°	—	—	—	—	—	—	—
1 : 8-Dihydroxynaphthalene .	—	142	—	155	175	—	—	—	—	220°	—	—
2 : 7-Dihydroxynaphthalene .	—	190	—	136	139	—	—	149°	176°	—	150°	—
2 : 2′-Dihydroxydiphenyl .	—	109	—	95	101	—	—	—	—	—	190	—
3 : 4-Dihydroxydiphenyl .	—	141	—	—	—	—	—	—	—	—	—	—
4 : 4′-Dihydroxydiphenyl .	—	274	—	161	241	—	—	274	—	—	—	—
Methyl salicylate . . .	223°	—	—	49	92	128°	—	—	—	—	—	—
Ethyl salicylate . . .	231	—	—	—	80	108	—	—	—	—	—	—
n-Propyl salicylate. . .	239	—	—	—	—	—	—	—	—	—	—	—
iso-Propyl salicylate . .	241	—	—	—	—	—	—	—	—	—	—	—
n-Butyl salicylate . . .	260	—	—	—	—	—	—	—	—	—	—	—
Salol (20)	—	43	—	98	81	111	—	—	144	—	—	—
β-Naphthyl salicylate . .	—	95	—	136	—	—	—	—	—	—	—	—
Methyl *p*-hydroxybenzoate .	—	131	—	85	135	—	—	—	—	—	—	—
Ethyl *p*-hydroxybenzoate .	—	116	—	—	94	—	—	—	—	—	—	—
Chlorohydroquinone . .	—	106	—	72	—	—	—	—	—	—	—	—
Bromohydroquinone . .	—	111	—	72	—	—	—	—	—	—	—	—
Hydroxyhydroquinone (21) .	—	140	—	97	120	—	—	—	—	—	—	—
n-Hexyl resorcinol . .	335	69	—	—	—	—	—	—	—	—	—	—
Saligenin (22) . . .	—	87	—	—	51	—	—	120	—	—	—	—

* Dibromo. † Tribromo. ‡ Tetrabromo.

(1) Guaiacol.
(2) Resorcinol monomethyl ether.
(3) Hydroquimone monomethyl ether.
(4) 1 : 2 : 3-Xylenol ; *o*-3-Xylenol.
(5) 1 : 2 : 4-Xylenol ; *o*-4-Xylenol.
(6) 1 : 3 : 4-Xylenol ; *m*-4-Xylenol.
(7) 1 : 3 : 5-Xylenol ; *m*-5-Xylenol.
(8) 1 : 4 : 5-Xylenol ; *p*-2-Xylenol.
(9) 1 : 3 : 2-Xylenol ; *m*-2-Xylenol.
(10) 2-Methoxy-4-allylphenol.
(11) 2-Methoxy-4-propenylphenol (*cis* and *trans*).
(12) 3-Hydroxy-4-*iso*propyltoluene.
(13) 4-Hydroxy-3-methoxybenzaldehyde.
(14) 2-Hydroxy-1-methyl-4-*iso*propylbenzene.
(15) *o*-Hydroxybenzaldehyde.
(16) *o*-Hydroxybenzoic acid.
(17) *o*-Phenylphenol.
(18) 3 : 4-Dihydroxytoluene.
(19) Naphthoresorcinol.
(20) Phenyl salicylate.
(21) 1 : 2 : 4-Trihydroxybenzene.
(22) *o*-Hydroxybenzyl alcohol.

TABLE IV,114A. ENOLS

Compound	B.P.	M.P.	$d_{4°}^{20°}$	$n_D^{20°}$	Semicarbazone	Pyrazolone
Acetylacetone	139°	—	0·977	1·452	—	100°*
Methyl acetoacetate	170	—	1·077	1·419	152°	127
Methyl methylacetoacetate	177	—	1·030	1·418	138	120
Ethyl acetoacetate	180	—	1·028	1·419	129d	127
Ethyl methylacetoacetate	181	—	1·006	1·419	86	120
Methyl ethylacetoacetate	189	—	0·989	—	98	108
Acetonylacetone	194	—	0·974	1·428	220	92
Ethyl ethylacetoacetate	198	—	0·972	1·422	154d	108
Ethyl acetonedicarboxylate	250d	—	1·113	—	95	85
Ethyl benzoylacetate	265d	—	1·117	—	125	63
Ethyl oxalacetate	131°/24	—	1·131	1·454	162	—
Benzoylacetone	261	61°	—	—	—	63
Dibenzoylmethane	—	78	—	—	—	137

* 1-(*p*-Nitrophenyl)-3 : 5-dimethylpyrazole : with aqueous solution of *p*-nitrophenylhydrazine hydrochloride. Phenylhydrazine yields a liquid pyrazole, b.p. 273°.

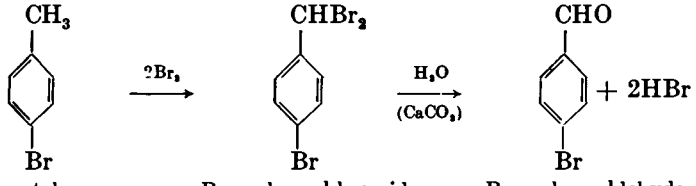
AROMATIC ALDEHYDES

Aromatic aldehydes may be prepared :—

1. By side-chain chlorination of the hydrocarbon (Section **IV,23**), followed by hydrolysis of the dichloro compound, say, with water at 95–100° in the presence of iron as a catalyst, for example :

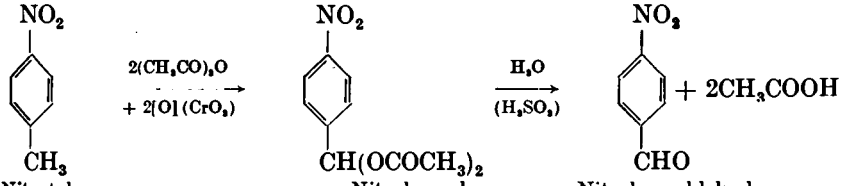
$$\underset{\text{Toluene}}{C_6H_5CH_3} \xrightarrow{2Cl_2} \underset{\text{Benzal chloride}}{C_6H_5CHCl_2} \xrightarrow{H_2O} \underset{\text{Benzaldehyde}}{C_6H_5CHO}$$

***p*-Bromobenzaldehyde** may be prepared by an analogous method :



p-Bromotoluene — *p*-Bromobenzal bromide — *p*-Bromobenzaldehyde

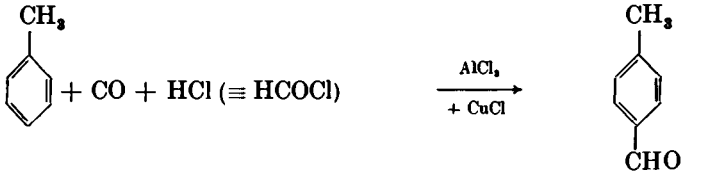
2. By oxidation of the methyl derivative of an aromatic hydrocarbon with a solution of chromic anhydride in acetic anhydride and acetic acid. The aldehyde formed is immediately converted into the *gem*-diacetate, which is stable to oxidation. The diacetate is collected and hydrolysed with sulphuric acid, for example :



p-Nitrotoluene — *p*-Nitrobenzal-diacetate — *p*-Nitrobenzaldehyde

Similarly, *p*- or *o*-bromotoluene —→ *p*- or *o*-bromobenzaldehyde diacetate —→ *p*- or *o*-bromobenzaldehyde.

3. By passing a mixture of carbon monoxide and hydrogen chloride into the aromatic hydrocarbon in the presence of a mixture of cuprous chloride and aluminium chloride which acts as a catalyst (**Gattermann - Koch reaction**). The mixture of gases probably reacts as the equivalent of the unisolated acid chloride of formic acid (formyl chloride) :



Toluene — *p*-Tolualdehyde

The Gattermann-Koch formylation was found unsuited to the preparation of aldehydes from phenols and phenol ethers : such aldehydes may be obtained by Gattermann's aldehyde reaction.

4. By interaction of hydrogen cyanide and hydrogen chloride with an aromatic compound (hydrocarbon, phenol or phenol ether) in the presence of aluminium chloride (or zinc chloride). This is known as the **Gattermann**

aldehyde reaction. The simplest (but not strictly accurate) formulation of the reaction is :

$$HCN + HCl \longrightarrow ClCH{=}NH \text{ (formimino chloride)}$$

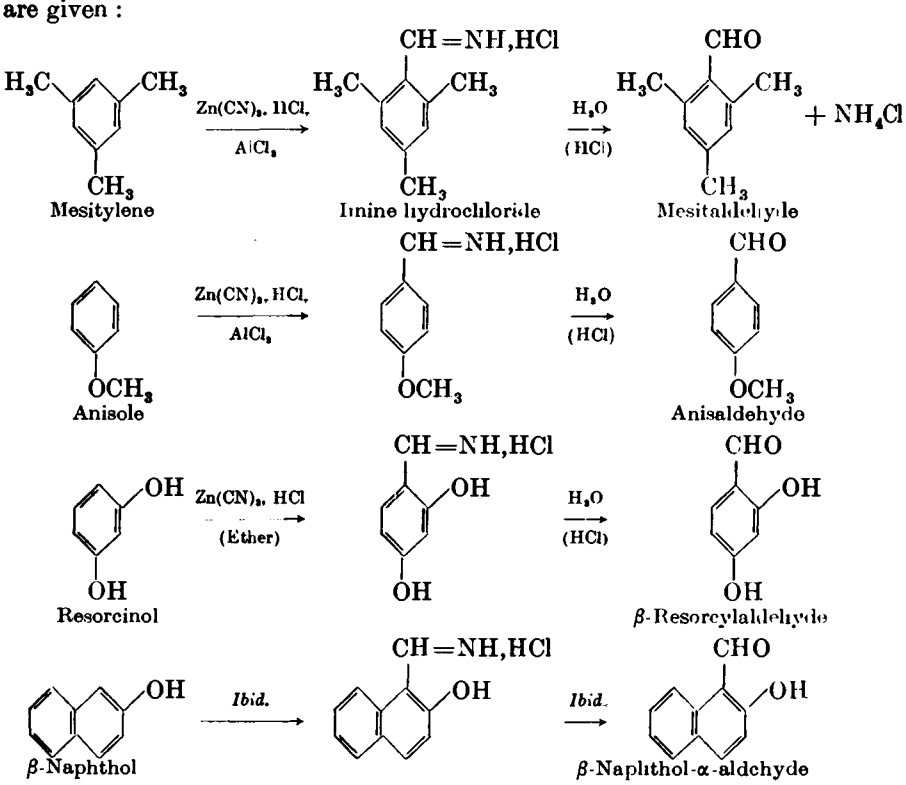
$$ArH + ClCH{=}NH \xrightarrow[ZnCl_2]{AlCl_3 \text{ or}} ArCH{=}NH,HCl \xrightarrow{H_2O} ArCHO + NH_4Cl$$

It is more likely that the HCN and HCl react to give chloromethyleneformamidine (I), which is the active intermediate :

$$2HCN + HCl \longrightarrow ClCH{=}N{-}CH{=}NH \text{ (I)}$$

$$ArH + \begin{matrix} ClCH{=}N \\ | \\ CH{=}NH \end{matrix} \xrightarrow{AlCl_3} \begin{matrix} ArCH{=}N \\ | \\ CH{=}NH,HCl \end{matrix} \xrightarrow{H_2O} \begin{matrix} ArCH{=}NH \\ + \\ HCOOH + NH_4Cl \end{matrix} \xrightarrow{H_2O} ArCHO$$

The use of the hazardous hydrogen cyanide may be avoided (R. Adams) by passing dry hydrogen chloride either into a mixture of zinc cyanide, aluminium chloride, the hydrocarbon or phenol ether and a solvent (such as tetrachloroethane or benzene), or into a mixture of zinc cyanide, the phenol and anhydrous ether or benzene. The zinc cyanide is converted by the hydrogen chloride into hydrogen cyanide (which reacts *in situ*) and zinc chloride (which is known to be an effective condensation reagent in this reaction). The following examples are given :



5. From acid chlorides by selective hydrogenation in the presence of a catalyst (palladium deposited upon a carrier, which is usually barium sulphate but is

occasionally charcoal). The reaction is known as the **Rosenmund reduction**, and has been widely applied in the aromatic and heterocyclic series :

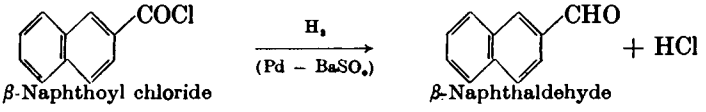
$$RCOCl + H_2 \xrightarrow{\text{Catalyst}} RCHO + HCl$$

The procedure is to pass purified hydrogen through a hot solution of the pure acid chloride in toluene or xylene in the presence of the catalyst ; the exit gases are bubbled through water to absorb the hydrogen chloride, and the solution is titrated with standard alkali from time to time so that the reduction may be stopped when the theoretical quantity of hydrogen chloride has been evolved. Further reduction would lead to the corresponding alcohol and hydrocarbon :

$$RCHO + H_2 \xrightarrow{\text{Catalyst}} RCH_2OH$$

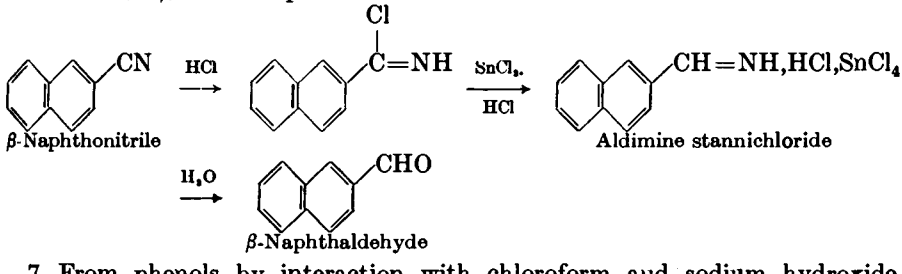
$$RCH_2OH + H_2 \xrightarrow{\text{Catalyst}} RCH_3 + H_2O$$

and to products produced by their interaction with acid chlorides. It is generally considered that the reduction of the aldehyde can be prevented by the use of an appropriate catalyst " poison " or " regulator ", which inactivates the catalyst towards the reduction of the aldehyde but not to the acid chloride. The " poison " usually contains sulphur, *e.g.*, " quinoline-sulphur " or thiourea. Such a regulator is not always necessary and it has been stated that the decisive factors are to keep the temperature near the lowest point at which hydrogen chloride is liberated and to arrest the reaction as soon as one mol of hydrogen chloride is evolved. The reduction is illustrated by :



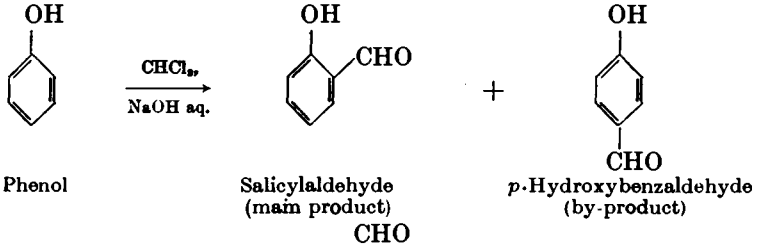
β-Naphthoyl chloride β-Naphthaldehyde

6. From nitriles by **Stephen's reaction** (see under *Aliphatic Aldehydes* and Section **III,64**), for example :

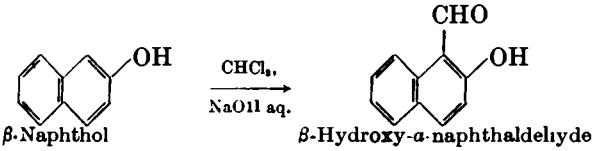


β-Naphthonitrile Aldimine stannichloride β-Naphthaldehyde

7. From phenols by interaction with chloroform and sodium hydroxide solution (**Reimer - Tiemann reaction**), for example :

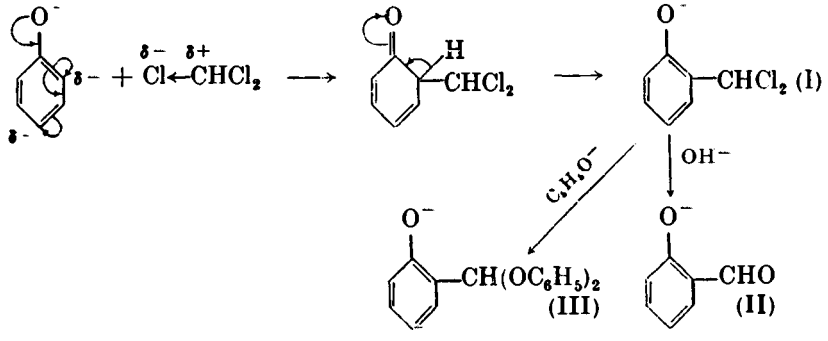


Phenol Salicylaldehyde (main product) *p*-Hydroxybenzaldehyde (by-product)



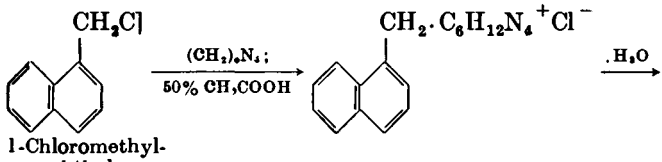
β-Naphthol β-Hydroxy-α-naphthaldehyde

This reaction, applicable only to the preparation of hydroxy-aldehydes, is alternative to the Gattermann aldehyde reaction (or the Adams modification of it) given under 4. The yields are usually smaller, but a large quantity of the phenol may be recovered. The following *mechanism* is consistent with the known facts :

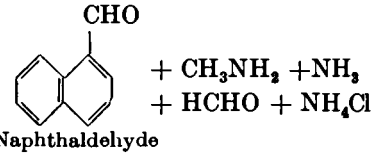


In the strongly basic medium, the reactant is the phenoxide ion ; high nucleophilic activity at the *ortho* and *para* positions is provided through the electromeric shifts indicated. The above scheme indicates the *ortho* substitution : the *para* substitution is similar. The intermediate *o*-hydroxybenzal chloride anion (I) may react either with a hydroxide ion or with water to give the anion of salicylaldehyde (II), or with phenoxide ion or with phenol to give the anion of the diphenylacetal of salicylaldehyde (III). Both these anions are stable in basic solution. Upon acidification (III) is hydrolysed to salicylaldehyde and phenol ; this probably accounts for the recovery of much unreacted phenol from the reaction.

8. From chloromethyl or bromomethyl aromatic compounds by heating with hexamethylenetetramine (hexamine) in aqueous alcohol or aqueous acetic acid. A quaternary ammonium compound is formed, which yields the aldehyde upon treatment with water in the presence of hexamine ; for example



1-Chloromethyl-naphthalene



α-Naphthaldehyde

The process whereby aldehydes are produced from arylmethyl (also alkyl and other) halides by the action of hexamine is known as the **Sommelet reaction.** The reaction is essentially the conversion of an amine into an aldehyde ; the hexamine serves the dual role of converting the halide into the amine and the amine into the aldehyde, but its function is different in the two steps. When starting from a halide, the reaction proceeds in three stages :—

(1) The formation of a hexamine salt :

$$RCH_2X + C_6H_{12}N_4 \longrightarrow [RCH_2 \cdot C_6H_{12}N_4]^+X^-$$

(ii) Hydrolysis of this salt to an amine and its methylene derivative :

$$[RCH_2 \cdot C_6H_{12}N_4]^+X^- + H_2O \longrightarrow RCH_2NH_2 + CH_2O \rightleftharpoons RCH_2N{=}CH_2$$

(Strong acids produce salts of the primary amines ; alkalis or ammonia give the corresponding methyleneamines.)

(iii) Formation of the aldehyde (the Sommelet reaction proper), best at *p*H 3·0–6·5 :

$$RCH_2NH_2 \longrightarrow RCHO$$

(A *p*H of 6·0–6·5 is generally ensured by the buffering action of the ammonia produced by hydrolysis upon the hexamine salt.)

Frequently the three steps can be combined without isolation of the intermediates.

Evidence which suggests a possible *mechanism* of the reaction is provided by a study of the formation of benzaldehyde in poor yield from methylenebenzylamine : benzaldehyde and ammonia (in equivalent amounts) and methylbenzylamine are isolated :

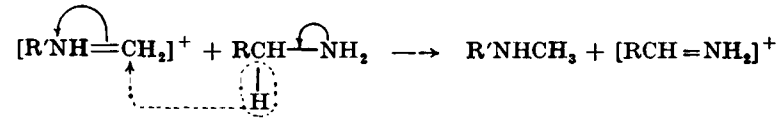
$$C_6H_5CH_2NH_2 + C_6H_5CH_2N{=}CH_2 + H_2O \longrightarrow C_6H_5CHO + NH_3 + C_6H_5CH_2NHCH_3 \quad (1)$$

Evidently this is a hydrogenation and the source of the hydrogen is benzylamine as indicated by the production of benzaldehyde and ammonia in equivalent amounts ; presumably the benzylamine is dehydrogenated to the imine $C_6H_5CH{=}NH$, which is then hydrolysed. In the absence of hexamine, the maximum yield of benzaldehyde is 50 per cent. When hexamine is added to the reaction mixture, the yield of aldehyde is increased and that of methylbenzylamine is decreased, and methylamine is present at the end of the reaction. Hexamine reacts as the methylene derivative of ammonia, $CH_2{=}NH$, which is hydrogenated to methylamine. The fundamental stage of the Sommelet reaction may be written as :

$$C_6H_5CH_2NH_2 + CH_2{=}NH + H_2O \longrightarrow C_6H_5CHO + NH_3 + CH_3NH_2 \quad (2)$$

The methylation of benzylamine (1) and of ammonia (2) are competitive processes ; by increasing the proportion of hexamine, the source of ammonia, the yield of benzaldehyde is increased and that of methylbenzylamine is decreased.

It has been suggested that the Sommelet reaction proceeds by a hydride ion transfer, the acceptor being the conjugate acid of a Schiff base :



IV,115. BENZALDEHYDE

Place 45 g. (43 ml.) of benzal chloride (Section IV,22), 250 ml. of water and 75 g. of precipitated calcium carbonate (1) in a 500 ml. round-bottomed flask fitted with a reflux condenser, and heat the mixture for 4 hours in an oil bath maintained at 130°. It is advantageous to pass a current of carbon dioxide through the apparatus. Filter off the calcium salts, and distil the filtrate in steam (Fig. *II*, *40*, 1) until no more oil passes over (2). Separate the benzaldehyde from the steam distillate by two extractions with small volumes of ether, distil off most of the ether on a water bath, and transfer the residual benzaldehyde to a wide-mouthed bottle or flask. Add excess of a concentrated solution of sodium bisulphite in portions with stirring or shaking : stopper the vessel and shake vigorously until the odour of benzaldehyde can no longer be detected. Filter the paste of the benzaldehyde bisulphite compound at the pump

and wash it with a little ether. Immediately transfer the bisulphite compound to a separatory funnel and decompose it with a slight excess of sodium carbonate solution. Extract the liberated benzaldehyde with ether, wash the ethereal extract successively with sodium carbonate solution and water, dry with anhydrous magnesium sulphate or calcium chloride. Remove the ether on a water bath using the apparatus shown in Fig. *II, 13,* 4, and distil the residue. Collect the benzaldehyde at 178–180°. The yield is 25 g.

Notes.

(1) A little iron powder or ferric benzoate can be used as a catalyst.

(2) If the clear filtrate in the flask is strongly acidified with concentrated hydrochloric acid and then allowed to cool, benzoic acid (a by-product of the reaction) separates in glistening plates. Filter at the pump, and recrystallise from hot water; m.p. 121°.

ALTERNATIVE PREPARATION

Purification of commercial benzaldehyde.* Wash 50 g. (48 ml.) of technical benzaldehyde in a separatory funnel with 20 ml. portions of 10 per cent. sodium carbonate solution until no further carbon dioxide is evolved, then with water, and dry over 5 g. of anhydrous magnesium sulphate or calcium chloride. Add 0·5 g. of hydroquinone or catechol (1) during the drying operation. Decant through a small fluted filter paper (or through a *small* plug of cotton wool) into a 100 ml. Claisen flask, and distil under reduced pressure (Fig. *II, 19,* 1) (2). Collect the benzaldehyde over a 2° range, *i.e.*, 1° on either side of the true b.p. The correct b.p. under the diminished pressure obtained in the apparatus may be interpolated from the following boiling point data : 79°/25 mm. ; 69°/15 mm. ; 62°/10 mm. Place about 0·05 g. of hydroquinone or catechol in the product (1).

Notes.

(1) Benzaldehyde is easily oxidised by atmospheric oxygen giving, ultimately, benzoic acid. This auto-oxidation is considerably influenced by catalysts ; these are considered to react with the unstable " peroxide " complexes which are the initial products of the oxidation. Catalysts which inhibit or retard auto-oxidation are termed anti-oxidants, and those that accelerate auto-oxidation are called pro-oxidants. Anti-oxidants find important applications in preserving many organic compounds, *e.g.*, acrolein. For benzaldehyde, hydroquinone or catechol (considerably less than 0·1 per cent. is sufficient) are excellent anti-oxidants.

(2) A very fine capillary tube should be used. It is better to conduct the distillation in a stream of an inert gas, such as hydrogen or nitrogen.

IV,116. *p*-BROMOBENZALDEHYDE

Equip a 1 litre three-necked flask with a reflux condenser, a mechanical stirrer, and a cork carrying a dropping funnel and a thermometer which reaches nearly to the bottom of the flask ; connect the upper end of the condenser to an absorption trap (Fig. *II,* 8, 1). Place 100 g. of *p*-bromotoluene (Section **IV,62**) in the flask and immerse the latter in an oil bath (colourless oil in a large beaker). Heat the bath until the temperature of the stirred *p*-bromotoluene reaches 105°. Illuminate the liquid with

* This provides an excellent exercise in distillation under diminished pressure.

an unfrosted 150-watt tungsten lamp, and add 197 g. (63 ml.) of bromine slowly from the dropping funnel : do not allow a large excess of bromine to accumulate in the reaction mixture. Add about one half of the bromine during 1 hour while the temperature is kept at 105–110°, and add the remainder during 2 hours while the temperature is slowly raised to 135°. Raise the temperature slowly to 150° when all the bromine has been introduced. Transfer the crude *p*-bromobenzal bromide (1) to a 2-litre flask, mix it intimately with 200 g. of precipitated calcium carbonate, and then add about 300 ml. of water. Attach a reflux condenser to the flask, heat the mixture first on a water bath and then on a wire gauze over a free flame with continuous shaking until the liquid boils (2) ; reflux the mixture for 15 hours to complete the hydrolysis. Steam distil the reaction mixture rapidly (3) ; collect the first one litre of distillate separately, filter off the product, and dry in a vacuum desiccator. 60 G. of pure *p*-bromobenzaldehyde, m.p. 56–57°, are thus obtained. Collect a further 2 litres of distillate (4) ; this yields about 15 g. of a less pure product, m.p. 52–56°. Purify this by trituration with saturated sodium bisulphite solution (2 ml. per gram) and, after about 3 hours, filter off the pasty mixture at the pump, wash it with alcohol, and then with ether. Transfer the bisulphite compound to a flask fitted for steam distillation (Fig. *II*, *40*, 1), add excess of sodium carbonate solution, and isolate the aldehyde by steam distillation ; 13 g. of *p*-bromobenzaldehyde, m.p. 56–57°, are thus collected.

Notes.

(1) This compound is a lachrymator and also produces a burning sensation on the skin ; the latter is relieved by washing the affected parts with alcohol.

(2) This gradual heating reduces the risk of breaking the flask.

(3) The best results are obtained by conducting the steam distillation in a large three-necked flask (compare Fig. *II*, *41*, 1) provided with a glycerine-sealed mechanical stirrer in the central aperture ; the aldehyde distils slowly unless the mixture is well stirred.

(4) If the solution in the flask is acidified with hydrochloric acid, about 8 g. of crude *p*-bromobenzoic acid may be isolated.

IV,117. *p*-NITROBENZALDEHYDE

Equip a 1 litre three-necked flask with a mechanical stirrer and a thermometer, and immerse the flask in a bath of ice and salt. Place 306 g. (283 ml.) of acetic anhydride, 300 g. (285 ml.) of glacial acetic acid and 25 g. of *p*-nitrotoluene in the flask, and add slowly, with stirring, 42·5 ml. of concentrated sulphuric acid. When the temperature has fallen to 5°, introduce 50 g. of A.R. chromic anhydride in small portions at such a rate that the temperature does not rise above 10° ; continue the stirring for 10 minutes after all the chromium trioxide has been added. Pour the contents of the flask into a 3 litre beaker two-thirds filled with crushed ice and almost fill the beaker with cold water. Filter the solid at the pump and wash it with cold water until the washings are colourless. Suspend the product in 250 ml. of cold 2 per cent. sodium carbonate solution and stir mechanically for 10–15 minutes ; filter (1), wash with cold water, and finally with 10 ml. of alcohol. Dry in a vacuum desiccator ; the yield of crude *p*-nitrobenzal diacetate is 25 g. (2).

Reflux a mixture of 22·5 g. of crude *p*-nitrobenzal diacetate, 50 ml. of alcohol, 50 ml. of water and 5 ml. of concentrated sulphuric acid for 30 minutes, filter through a fluted paper, and cool the filtrate in ice. Collect the crystals by suction filtration, wash with cold water, and dry in a vacuum desiccator. The yield of *p*-nitrobenzaldehyde, m.p. 106° is 12 g. (3).

Notes.

(1) Upon acidification of the sodium carbonate washings, 4–5 g. of *p*-nitro benzoic acid, m.p. 242-243°, are recovered.

(2) The pure diacetate may be isolated by dissolving in 75 ml. of hot alcohol, filtering from any insoluble impurities and allowing to cool: 23 g., m.p. 125–126°, are obtained.

(3) By diluting the filtrate with 150 ml. of water, a further 1 g. of the aldehyde may be isolated.

Cognate Preparations

o-Nitrobenzaldehyde. Use 25 g. of *o*-nitrotoluene and the same quantities of the other reactants as for *p*-nitrobenzaldehyde. During the addition of the chromium trioxide (1–2 hours), do not allow the temperature to rise above 10°: at higher temperatures, the reaction may become violent. Continue the stirring for a further 5 hours; a powerful stirrer should be used since a hard, tarry mass is formed in the oxidation. Pour the reaction mixture into a 3-litre beaker two-thirds full of crushed ice. Add 500 g. of crushed ice and 50 ml. of water to the reaction flask, break up the mass with a spatula, and add the suspension to the contents of the 3-litre beaker. Stir the mixture in the beaker vigorously until all the oily layer has solidified. Filter the somewhat oily solid at the pump, wash well with cold water, suspend the solid in 250 ml. of cold 2 per cent. sodium carbonate solution, and stir mechanically; filter again, wash with cold water, and dry in the air. To remove any unchanged *o*-nitrotoluene, digest the crude substance with 75 ml. of light petroleum (b.p. 60-80°) for 30 minutes, cool and filter. Dry in a vacuum desiccator. The yield of *o*-nitrobenzal diacetate, m.p. 87–88°, is 11 g.

Heat a suspension of 22 g. of the diacetate in a mixture of 120 ml. of concentrated hydrochloric acid, 190 ml. of water and 35 ml. of alcohol under reflux for 45 minutes. Cool the mixture to 0°, filter the solid with suction, and wash with water. Purify the crude aldehyde by rapid steam distillation (Fig. *II*, *41*, 3); collect about 1500 ml. of distillate during 15 minutes, cool, filter, and dry in a vacuum desiccator over calcium chloride. The yield of pure *o*-nitrobenzaldehyde, m.p. 44–45°, is 10 g. The crude solid may also be purified after drying either by distillation under reduced pressure (the distillate of rather wide b.p., *e.g.*, 120–144°/3–6 mm., is quite pure) or by dissolution in toluene (2–2·5 ml. per gram) and precipitation with light petroleum, b.p. 40°–60° (7 ml. per ml. of solution).

***p*-Bromobenzaldehyde.** Use 31 g. of *p*-bromotoluene (Section IV,62) and proceed exactly as for *p*-nitrobenzaldehyde. The yield of crude *p*-bromobenzal diacetate, m.p. 90–92°, is 30 g.; upon recrystallisation from 75 ml. of hot alcohol, 24·5 g. of the pure diacetate, m.p. 95°, are obtained. Hydrolyse the crude product (22·5 g.) with 75 ml. of alcohol,

50 ml. of water and 5 ml. of concentrated sulphuric acid, filter the hot solution through a fluted filter paper, cool, collect the crystals and dry in a vacuum desiccator. The yield of *p*-bromobenzaldehyde, m.p. 56–57°, is 18 g.

IV,118. *p*-TOLUALDEHYDE *

Set up the apparatus depicted in Fig. *IV*, *118*, 1 in a fume cupboard. The narrow wide-mouthed reaction vessel *A* has a capacity of about 250 ml. and is equipped with a rubber stopper carrying a mercury-sealed

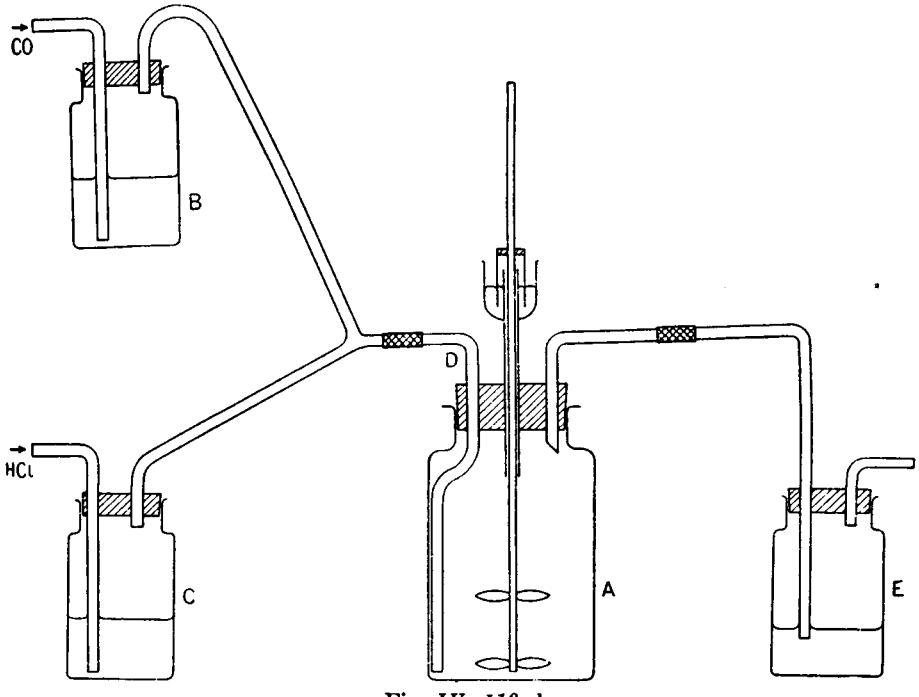


Fig. *IV*, *118* 1.

stirrer, an inlet tube for admitting a mixture of gases, and an outlet tube connected to the wash bottle *E* containing concentrated sulphuric acid. Place 100 g. (115·5 ml.) of pure toluene, 15 g. of dry cuprous chloride (Section **II,50,***l*) and 133·5 g. of finely-powdered anhydrous aluminium chloride in the bottle *A*, and stir the mixture vigorously. Immerse the bottle in a water bath at 20°. Pass a mixture of carbon monoxide (Section **II,48,***g*) and hydrogen chloride (Section **II,48,***l*) into the bottom of the reaction vessel through the tube *D* at a not too rapid but uniform rate (1) during 7 hours : adjust the rates of flow so that the volume of carbon monoxide is about twice that of the hydrogen chloride by observing the bubbling in the wash bottles *B* and *C*. The rate of absorption can be estimated from the bubbling in *E*. The carbon monoxide is absorbed almost quantitatively at the commencement, but as the mixture

* Also termed *p*-tolylaldehyde.

becomes viscous the absorption is less complete. Transfer the very viscid product gradually and with shaking to a 1500 ml. round-bottomed flask containing 750 g. of crushed ice. Steam distil the resulting mixture until all the aldehyde and unchanged toluene have been driven over. Add 25 ml. of ether to the distillate, and separate the two layers ; extract the aqueous layer with 75 ml. of ether. Dry the combined extracts over anhydrous magnesium sulphate or calcium chloride, remove the ether slowly (Fig. *II*, *13*, 4, but with a Claisen flask replacing the distilling flask) and then distil the residue from an air bath. Collect the *p*-tolualdehyde (an almost colourless liquid) at 203–205°. The yield is 65 g. Place a few small crystals of hydroquinone in the product to improve its keeping qualities.

Note.

(1) About 1–2 litres of carbon monoxide should be passed in the course of an hour.

IV,119. β-NAPHTHALDEHYDE

Method 1—*from* β-*Naphthonitrile*

Fit a 1 litre three-necked flask with a wide inlet tube reaching nearly to the bottom of the flask, a mechanical stirrer, and a reflux condenser carrying a drying tube. Place 38 g. of anhydrous stannous chloride (Section **II,50,***II*) and 200 ml. of sodium-dried ether in the flask. Saturate the mixture with dry hydrogen chloride (Section **II,48,***I*) while it is slowly stirred ; this operation requires about 2·5 hours during which time the stannous chloride forms a viscous lower layer. Replace the gas-inlet tube by a dropping funnel, and by means of it add a solution of 15·3 g. of β-naphthonitrile, m.p. 61–62° (1) in 100 ml. of anhydrous ether rapidly. Remove the dropping funnel and again pass hydrogen chloride into the mixture until it is saturated ; continue to stir rapidly for 1 hour, and allow to stand overnight.

Decant the ethereal solution from the yellow aldimine stannichloride which has separated, rinse the solid with two 50 ml. portions of ether, and transfer the solid to a 2·5 litre flask fitted for steam distillation and immersed in an oil bath at 110–120°. Pass steam through a trap (compare Fig. *II*, *40*, 1, *b*) to remove condensed water, then through a superheater heated to 260° (Fig. *I*, *7*, 2), and finally into the mixture (2). Continue the passage of dry steam until the aldehyde is completely removed (4–5 litres ; 8–10 hours). Filter the white solid at the pump, and dry in the air. The resulting β-naphthaldehyde, m.p. 53–54°, weighs 12 g. It may be further purified by distillation under diminished pressure (Fig. *II*, *19*, 1) ; pour the colourless distillate, b.p. 156–158°/15 mm., while hot into a mortar and powder it when cold. The m.p. is 57–58°, and the recovery is over 90 per cent.

Notes.

(1) The substance may be obtained from β-naphthylamine (Section IV,38) by the procedure described under *p-Tolunitrile* (Section IV,66).

(2) The use of dry, superheated steam, although not essential, considerably reduces the time of distillation.

Method 2—from β-Naphthoyl Chloride

Fit a 250 ml. three-necked flask, equipped with ground glass joints (Fig. *II*, *56*, 14), with a reflux condenser, a high-speed mercury-sealed stirrer (1), and a gas inlet tube extending to a point just above the bottom of the stirrer. Place 28·5 g. of β-naphthoyl chloride (2), 100 ml. of sodium-dried xylene, 3 g. of palladium - barium sulphate catalyst (3), and 0·3 ml. of the stock poison solution (4) in the flask. Connect the top of the condenser by a rubber tube to a 6 mm. glass tube extending to the bottom of a 250 ml. conical flask containing 200 ml. of distilled water and a few drops of phenolphthalein indicator ; arrange a burette charged with *ca. N* sodium hydroxide solution (prepared from the A.R. solid) for delivery into the flask. Place the flask at least 2–3 feet away from any flame for the sake of safety.

Displace the air in the reaction flask with hydrogen, heat the flask in an oil bath at 140–150° and stir the mixture vigorously. Follow the course of the reaction by the rate of hydrogen chloride evolution. The first 25 ml. of alkali should be neutralised in 12–15 minutes, and the reaction should be complete in about 2 hours. About 92 per cent. of the theoretical amount of hydrogen chloride (≡ 142·5 ml. of *N*-NaOH solution) is recovered ; the end of the reaction is indicated by a rather abrupt cessation of hydrogen chloride evolution. Cool the flask, add 1 g. of decolourising carbon with stirring, and filter the solution with suction through a hardened filter paper in order to recover the palladium (5). Distil off the xylene using a 50–75 ml. Claisen flask with fractionating side arm (for general form of apparatus, see Fig. *II*, *13*, 4) and an air bath. (Fig. *II*, *5*, 3). Then distil under reduced pressure (Fig. *II*, *19*, 1) with the aid of an oil bath : a small fraction, consisting largely of naphthalene, passes over first, followed by β-naphthaldehyde at 147–149°/11 mm. (temperature of bath, 170–180°). This (19 g.) solidifies on cooling to a white solid, m.p. 59–60° (compare preceding Section).

Notes.

(1) Rapid stirring is desirable in order to obtain the maximum reaction rate ; absorption of hydrogen occurs chiefly at the rapidly agitated surface. The vigorous stirring may cause spraying of fine droplets of mercury from the seal ; this can be prevented either by covering the mercury with a layer of paraffin oil or by using the seal shown in Fig *II*,*7*, 9, *c*.

(2) **β-Naphthoyl chloride may be prepared from** β-naphthoic acid (Section IV,164) in the following manner. Warm a mixture of 57·4 g. of acid and 69 g. of phosphorus pentachloride in a 250 ml. Claisen flask with fractionating side arm (Figs. *II*, *24*, 2-3) on a water bath in the fume cupboard. As soon as the vigorous reaction commences, remove the flask from the water bath until the rapid evolution of hydrogen chloride subsides, then heat on a water bath for 30 minutes. Distil under reduced pressure using a water pump to remove the phosphorus oxychloride ; an oil pump may then be substituted. Collect the fraction, b.p. 160–162°/11 mm. ; this solidifies on cooling to a colourless solid, m.p. 51–52.° The yield of β-naphthoyl chloride is 60 g.

(3) **The palladium - barium sulphate catalyst is prepared** by treating a suspension of 20 g. of barium sulphate (which has been precipitated in hot solution) in 400 ml. of hot water with a solution of 1·7 g. of palladium chloride (equivalent to 1·0 g. of palladium) in 50 ml. of water and with 1·5 ml. of 40 per cent. formaldehyde solution. The mixture is rendered faintly alkaline to litmus by the addition of sodium hydroxide solution and then boiled for a short time. When the supernatant liquid is clear, the grey precipitate is filtered off, and washed with hot water until the

washings are neutral in reaction. The catalyst is then dried in a vacuum desiccator over solid sodium or potassium hydroxide, then finely ground in a glass mortar, and preserved in a well-stoppered bottle.

(4) The stock solution of quinoline-sulphur poison is prepared by refluxing 1 g. of sulphur with 6 g. of quinoline for 5 hours and diluting the resulting brown liquid to 70 ml. with xylene which has been purified by distilling over anhydrous aluminium chloride. The addition of the quinoline-sulphur poison ensures that the reduction does not proceed beyond the aldehyde stage; it merely slows up the reaction and has no harmful effects.

It has been stated that thiourea (about 20 per cent. of the weight of the palladium-barium sulphate) may also be used as a catalyst poison.

(5) The palladium may be recovered by heating the spent catalyst to redness in order to remove organic impurities; this treatment may reduce some of the barium sulphate to barium sulphide, which acts as a catalytic poison. The palladium is then dissolved out with *aqua regia* and the solution evaporated; the residue is dissolved in hot water and hydrochloric acid to form palladium chloride.

IV,120 α-NAPHTHALDEHYDE (*Sommelet Reaction*)

In a 500 ml. flask, fitted with a reflux condenser, place 53 g. of 1-chloromethylnaphthalene (Section **IV,23**), 84 g. of hexamethylenetetramine and 250 ml. of 1 : 1 acetic acid [*CAUTION:* 1-Chloromethylnaphthalene and, to a lesser degree, α-naphthaldehyde have lachrymatory and vesicant properties; adequate precautions should therefore be taken to avoid contact with these substances.] Heat the mixture under reflux for 2 hours; it becomes homogeneous after about 15 minutes and then an oil commences to separate. Add 100 ml. of concentrated hydrochloric acid and reflux for a further 15 minutes; this will hydrolyse any Schiff's bases which may be formed from amine and aldehyde present and will also convert any amines into the ether-insoluble hydrochlorides. Cool, and extract the mixture with 150 ml. of ether. Wash the ether layer with three 50 ml. portions of water, then cautiously with 50 ml. of 10 per cent. sodium carbonate solution, followed by 50 ml. of water. Dry the ethereal solution with anhydrous magnesium sulphate, remove the ether by distillation on a steam bath, and distil the residue under reduced pressure. Collect the α-naphthaldehyde at 160–162°/18 mm.; the yield is 38 g.

Cognate Preparations

***p*-Nitrobenzaldehyde.** This preparation is an example of the Sommelet reaction in which the hexaminium salt is isolated. Dissolve 11 g. of hexamine in 70 ml. of chloroform and add 11·4 g. of *p*-nitrobenzyl chloride or 14·4 g. of *p*-nitrobenzyl bromide (Section **VII,13**). Heat the mixture under reflux on a steam bath for 4 hours; a precipitate gradually separates. Replace the reflux condenser by a condenser set for distillation and distil off about 35 ml. of solvent. Add 35 ml. of acetone, cool in ice, collect the precipitate by suction filtration, and dry it in the air. Heat the hexaminium salt thus obtained under reflux for 1 hour with 100 ml. of 50 per cent. acetic acid; then add 100 ml. of water and 25 ml. of concentrated hydrochloric acid and continue the refluxing for 5–10 minutes. Cool the solution in ice, collect, the crystals of *p*-nitrobenzaldehyde and dry them in a vacuum desiccator. The yield is 6·4 g., m.p. 106°.

β-Naphthaldehyde. This preparation illustrates the use of *N*-bromosuccinimide (Section **VI,26**) in the conversion of the readily available β-methylnaphthalene into 2-bromomethylnaphthalene and of the latter into β-naphthaldehyde by the Sommelet reaction.

Dissolve 71 g. of β-methylnaphthalene in 450 g. (283 ml.) of A.R. carbon tetrachloride and place the solution in a 1-litre three-necked flask equipped with a mechanical stirrer and reflux condenser. Introduce 89 g. of *N*-bromosuccinimide through the third neck, close the latter with a stopper, and reflux the mixture with stirring for 16 hours. Filter off the succinimide and remove the solvent under reduced pressure on a water bath. Dissolve the residual brown oil (largely 2-bromomethylnaphthalene) in 300 ml. of A.R. chloroform, and add it to a rapidly stirred solution of 84 g. of hexamine in 150 ml. of A.R. chloroform contained in a 2-litre three-necked flask, fitted with a reflux condenser, mechanical stirrer and dropping funnel: maintain the rate of addition so that the mixture refluxes vigorously. A white solid separates almost immediately. Heat the mixture to reflux for 30 minutes, cool and filter. Wash the crystalline hexaminium bromide with two 100 ml. portions of light petroleum, b.p. 40–60°, and dry; the yield of solid, m.p. 175–176°, is 147 g. Reflux the hexaminium salt for 2 hours with 750 ml. of 50 per cent. acetic acid, add 150 ml. of concentrated hydrochloric acid, continue the refluxing for 5 minutes more, and cool. Extract the aldehyde from the solution with ether, evaporate the ether, and recrystallise the residue from hot *n*-hexane. The yield of β-naphthaldehyde, m.p. 59–60°, is 50 g.

IV,121. MESITALDEHYDE

Equip a 500 ml. three-necked flask with a reflux condenser, an efficient stirrer, and a gas-inlet tube and a thermometer. The last-named is fitted into one neck of the flask by a device similar to that shown in Fig. *II*, 7, 12, *b*; the thermometer in the gas-inlet tube should have the bulb well immersed in the liquid, but the inlet tube need extend only just below the surface. Set up the apparatus in the fume cupboard because both hydrogen cyanide and tetrachloroethane are toxic. Place 51 g. (59 ml.) of redistilled mesitylene (b.p. 163–166°), 73·5 g. of zinc cyanide (1) and 200 ml. of tetrachloroethane in the flask, and stir the mixture while a rapid stream of dry hydrogen chloride (Section **II,48,***l*) is passed through it until the zinc cyanide is decomposed (about 3 hours). Immerse the flask in a bath of crushed ice, remove the inlet tube and replace it by means of the arrangement depicted in Fig. *II*, 7, 12, *c* (or *d*), having previously charged the conical flask with 197 g. of finely-ground, anhydrous aluminium chloride. Stir the mixture *very vigorously* and add the aluminium chloride over a period of 10 minutes. Remove the ice bath, and resume the passage of hydrogen chloride gas for 3·5 hours; the heat of reaction will raise the temperature to about 70° at the end of an hour. Maintain the temperature at 67-72° for the remainder of the reaction period. Cool, and pour the reaction mixture, with hand stirring, into a 2 litre beaker about half-full of crushed ice to which 50 ml. of concentrated hydrochloric acid has been added. Allow to stand overnight, transfer to a 1·5 litre round-bottomed flask, fit a condenser and

reflux for 3 hours. Allow to cool, separate the organic layer, and extract the aqueous layer once with 25 ml. of tetrachloroethane. Wash the combined tetrachloroethane solutions with 75 ml. of 10 per cent. sodium carbonate solution, and steam distil (Fig. *II*, *40*, 1). Set the first 400–450 ml. of distillate aside for the recovery of the solvent (2), and collect the second portion (about 4·5 litres) as long as oily drops pass over. Extract the distillate with 250 ml. of benzene, dry the extract with a little anhydrous magnesium sulphate, and remove the solvent on a water bath. Distil the residue from a 150 ml. Claisen flask with fractionating side arm (Fig. *II*, *24*, 2-5), and collect the mesitaldehyde at 118–121°/16 mm.; the yield is 50 g. (3).

Notes.

(1) Commercial zinc cyanide is quite satisfactory. It may be prepared as described in Section II,50,*18*. If the zinc cyanide is too highly purified, it does not react well.

(2) The first portion of the steam distillate consists almost entirely of tetrachloroethane and water. The solvent is recovered by separating the organic layer, drying with anhydrous calcium chloride or magnesium sulphate and distilling.

(3) The following procedure is more convenient and less time-consuming, but the yield is lower (about 40 g.). Mix the powdered aluminium chloride and zinc cyanide by shaking, add the mesitylene, and immerse the flask in an oil bath at 100°. Stir the mixture and pass in a fairly rapid stream of dry hydrogen chloride for 4 hours; continue the heating and stirring for a further 2 hours, but discontinue the passage of the gas. Decompose the reaction mixture, and complete the preparation as above.

Cognate Preparations

β-Resorcylaldehyde (2 : 4-dihydroxybenzaldehyde). Equip a 500 ml. three-necked flask (or wide-mouthed bottle) with a reflux condenser, a mercury-sealed stirrer, and a wide inlet tube (to prevent clogging by the precipitate) extending nearly to the bottom of the vessel. Attach the inlet tube to an empty (safety) wash bottle and to this a generator producing hydrogen chloride (Section II,48,*1*); connect the top of the condenser by means of a tube to a wash bottle containing concentrated sulphuric acid, then to an empty bottle, and finally to the surface of sodium hydroxide solution (Fig. *II*, *8*, 1, *a*). Place 20 g. of resorcinol, 175 ml. of sodium-dried ether, and 40 g. of powdered anhydrous zinc cyanide (Section II,50,*18*) in the flask, start the stirrer and pass in a rapid stream of hydrogen chloride. The zinc cyanide gradually disappears with the formation of a cloudy solution; further passage of hydrogen chloride results in the separation of the imide hydrochloride condensation product as a thick oil which solidifies after 10–30 minutes. When the ether is saturated with hydrogen chloride (after about 1·5 hours), pass the gas more slowly and continue the stirring for a further half an hour to ensure the completeness of the reaction. Decant the ether from the solid material, add 100 ml. of water to the latter, heat to the boiling point, filter the hot solution through a hot water funnel, and allow the filtrate to cool. Filter the resorcylaldehyde (12 g.) which separates as soon as the mixture is cold; allow the filtrate to stand for 15 hours when a further 11·5 g. of the aldehyde is obtained. The β-resorcylaldehyde, after drying, has m.p. 135–136° and is very faintly coloured. The colour may be removed by recrystallisation from hot water with the addition of a little decolourising carbon.

β-Naphthol-α-aldehyde (β-hydroxy-α-naphthaldehyde). Proceed as for β-resorcylaldehyde except that 20 g. of β-naphthol replaces the resorcinol. Recrystallise the crude product (20 g.) from water with the addition of a little decolourising carbon ; the pure aldehyde has m.p. 80–81°.

Anisaldehyde (*p*-methoxybenzaldehyde). Use the apparatus described for β-resorcylaldehyde. Place 30 g. (27 ml.) of anisole (Section **IV,104**), 75 ml. of sodium-dried A.R. benzene, and 52 g. of powdered zinc cyanide in the flask. Cool the mixture in a bath of cold water, start the stirrer, and pass in a rapid stream of hydrogen chloride for 1 hour. Remove the condenser, and without stopping the stirrer, add 45 g. of finely-powdered anhydrous aluminium chloride slowly, replace the condenser, etc. Pass in a slow steam of hydrogen chloride whilst heating the mixture at 40–45° for 3-4 hours. Allow to cool somewhat and pour the reaction mixture with stirring into excess of dilute hydrochloric acid ; the imide hydrochloride separates as a heavy precipitate. Reflux the mixture for half an hour in order to decompose the imide hydrochloride and steam distil. Separate the organic layer in the distillate, dry with a little anhydrous magnesium sulphate, and distil off the benzene. Treat the residue, which consists of anisaldehyde together with traces of anisole, with excess of sodium bisulphite solution and extract any unchanged anisole with ether. Decompose the bisulphite compound with sodium hydroxide solution (compare cyclo*Hexanone*, Section **III,74,A**), extract the anisaldehyde with ether, dry and distil. Collect the anisaldehyde at 246–248° ; the b.p. under diminished pressure is 134–135°/12 mm. The yield is 35 g.

IV,122. SALICYLALDEHYDE

Equip a 1 litre three-necked flask with an efficient (double surface) reflux condenser, a mechanical stirrer, and a thermometer, the bulb of which is within 2 cm. of the bottom of the flask. Place a warm solution of 80 g. of sodium hydroxide in 80 ml. of water in the flask, add a solution of 25 g. of phenol in 25 ml. of water, and stir. Adjust the temperature inside the flask to 60–65° (by warming on a water bath or by cooling, as may be found necessary) ; do not allow the crystalline sodium phenoxide to separate out. Introduce 60 g. (40·5 ml.) of chloroform in three portions at intervals of 15 minutes by means of a dropping funnel fitted into the top of the condenser with a grooved cork (1). Maintain the temperature of the well-stirred mixture at 65–70° during the addition by immersing the flask in hot or cold water as may be required. Finally heat on a boiling water bath for 1 hour to complete the reaction. Remove the excess of chloroform from the alkaline solution by steam distillation (Fig. *II*, *41*, 1). Allow to cool, acidify the orange-coloured liquid cautiously with dilute sulphuric acid, and again steam distil the almost colourless liquid until no more oily drops are collected. Set aside the residue in the flask for the isolation of *p*-hydroxybenzaldehyde. Extract the distillate at once with ether, remove most of the ether from the extract on a water bath (compare Fig. *II*, *13*, 4). Transfer the residue, which contains phenol as well as salicylaldehyde, to a separatory funnel

or small glass-stoppered bottle, add about twice the volume of saturated sodium bisulphite solution, and shake vigorously (preferably mechanically) for at least half an hour, and allow to stand for 1 hour. Filter the paste of bisulphite compound at the pump, wash it with a little alcohol, and finally with a little ether (to remove the phenol). Decompose the bisulphite compound by warming in a round-bottomed flask on a water bath with dilute sulphuric acid, allow to cool, extract the salicylaldehyde with ether, and dry the extract with anhydrous magnesium sulphate. Remove the ether (Fig. *II*, *13*, 4) and distil the residue from an air bath. Collect the salicylaldehyde (a colourless liquid) at 195-197°. The yield is 12 g.

To isolate the ***p*-hydroxybenzaldehyde**, filter the residue from the steam distillation while hot through a fluted filter paper in order to remove resinous matter, and extract the cold filtrate with ether. Distil off the ether, and recrystallise the yellow solid from hot water to which some aqueous sulphurous acid is added. The yield of *p*-hydroxybenzaldehyde (colourless crystals), m.p. 116°, is 2–3 g.

Note.

(1) If preferred, the chloroform may be added slowly during 30–40 minutes whilst the mixture is stirred and the temperature is maintained at 65–70°.

Purification of commercial salicylaldehyde. When comparatively large quantities of salicylaldehyde are required, it is more economical to purify the relatively inexpensive commercial product. This may be done either through the bisulphite compound (compare Section **III,74,A**) or by the following method. Add the commercial salicylaldehyde to a large excess of a luke-warm solution of copper acetate (previously saturated near the boiling point), shake well, and allow to stand several hours in ice. Filter, wash the precipitate thoroughly first with alcohol and then with ether. Decompose the solid with dilute (10 per cent.) sulphuric acid, extract the aldehyde with ether, dry (anhydrous magnesium sulphate), and distil. The yield from a good commercial sample may be as high as 80 per cent.

Cognate Preparation

β-Hydroxy-α-naphthaldehyde. Equip a 1 litre three-necked flask with a separatory funnel, a mercury-sealed mechanical stirrer, and a long (double surface) reflux condenser. Place 50 g. of β-naphthol and 150 ml. of rectified spirit in the flask, start the stirrer, and rapidly add a solution of 100 g. of sodium hydroxide in 210 ml. of water. Heat the resulting solution to 70–80° on a water bath, and place 62 g. (42 ml.) of pure chloroform in the separatory funnel. Introduce the chloroform dropwise until reaction commences (indicated by the formation of a deep blue colour), remove the water bath, and continue the addition of the chloroform at such a rate that the mixture refluxes gently (about 1·5 hours). The sodium salt of the phenolic aldehyde separates near the end of the addition. Continue the stirring for a further 1 hour. Distil off the excess of chloroform and alcohol on a water bath ; use the apparatus shown in Fig. *II*, *41*, 1, but retain the stirrer in the central aperture. Treat the residue, with stirring, dropwise with concentrated hydrochloric acid until

the contents of the flask are acid to Congo red paper (about 88 ml. are required); a dark oil, accompanied by a considerable amount of sodium chloride, separates. Add sufficient water to dissolve the salt, extract the oil with ether, wash the ethereal solution with water, dry with anhydrous magnesium sulphate, and remove the solvent. Distil the residue under reduced pressure and collect the slightly coloured aldehyde at 163-166°/8 mm. (or at 177-180°/20 mm.); it solidifies on cooling. Recrystallise the solid from 38 ml. of alcohol. The yield of β-hydroxy-α-naphthaldehyde, m.p. 80°, is 28 g.

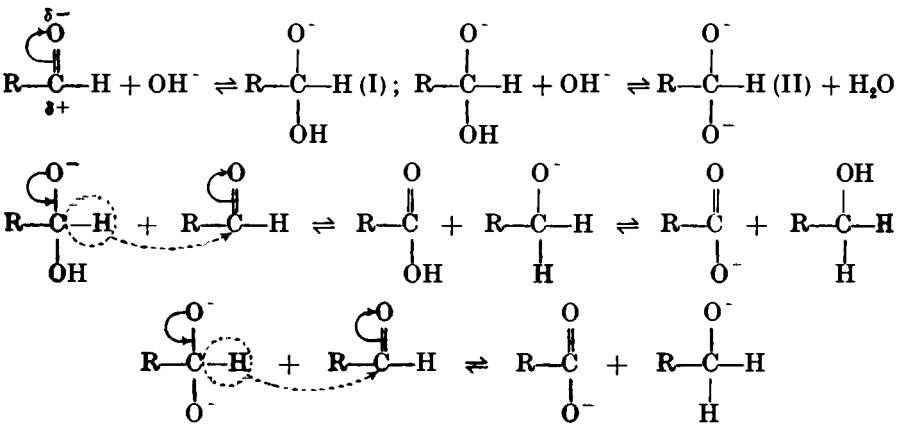
CONDENSATION REACTIONS OF AROMATIC ALDEHYDES

1. **Cannizzaro reaction.** Aromatic aldehydes (and other aldehydes in which α-hydrogen atoms are absent, *e.g.*, formaldehyde, trimethylacetaldehyde, and α-hydroxy-*iso*-butyraldehyde) under the influence of strong aqueous or alcoholic alkali undergo simultaneous oxidation and reduction yielding the alcohol and corresponding acid. Thus :—

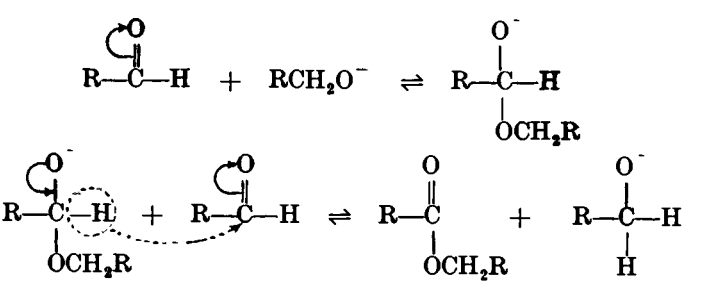
$$\underset{\text{Benzaldehyde}}{C_6H_5CHO} + C_6H_5CHO \xrightarrow{KOH} \underset{\text{Benzyl alcohol}}{C_6H_5CH_2OH} + \underset{\text{Potassium benzoate}}{C_6H_5COOK}$$

This dismutation or disproportionation reaction is known as the **Cannizzaro reaction.**

The *mechanism* of the reaction probably involves the production, by interaction of the aldehyde with hydroxide ions, of two reducing anions, the first (I) more easily than the second (II). Either of these anions may transfer a hydride ion to a carbonyl carbon atom in another aldehyde molecule :



The production of benzyl benzoate from benzaldehyde, which may be isolated under special conditions (low temperature and absence of excess of alkali), is explained by assuming that when some benzyloxide ions ($C_6H_5—CH_2O^- \equiv RCH_2O^-$) are formed in the alkaline solution, these can replace hydroxide ions thus :



The analogous dismutation of furfural is described in Section V,8. For " crossed Cannizzaro reaction ", see discussion following Section IV,199.

2. **Perkin reaction.** The condensation of an aromatic aldehyde with an acid anhydride in the presence of the sodium or potassium salt of the acid

corresponding to the anhydride to yield an αβ-unsaturated acid is known as the **Perkin reaction.** Thus benzaldehyde when heated with a mixture of acetic anhydride and potassium acetate gives rise to cinnamic acid :

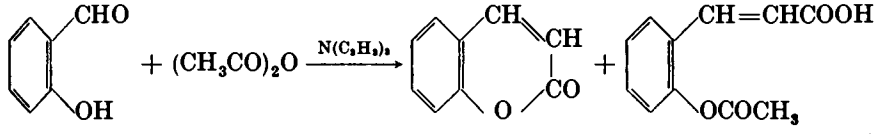
$$C_6H_5CHO + (CH_3CO)_2O \xrightarrow[170\text{–}180°]{CH_3COOK,} C_6H_5CH{=}CHCOOH + CH_3COOH$$

Benzaldehyde Acetic anhydride Cinnamic acid Acetic acid

It is interesting to note that although *cis-trans* isomerism about the double bond is theoretically possible in cinnamic acid, the Perkin reaction gives rise only to the *trans* form, m.p. 133°, the *cis* form, m.p. 68° (termed *allo*-cinnamic acid) being unstable and easily converted into the *trans* acid.

Allo-cinnamic acid (*cis*) Cinnamic acid (*trans*).

Basic catalysts other than alkali acetates have been employed in the Perkin reaction : thus salicylaldehyde condenses with acetic anhydride in the presence of triethylamine to yield **coumarin** (the lactone of the *cis* form of *o*-hydroxycinnamic acid) together with some of the acetyl derivative of the *trans* form (*o*-acetoxycoumaric acid) :



Salicylaldehyde Coumarin *o*-Acetoxycoumaric acid

The *mechanism* of the reaction, which is of the aldol type, involves the carbonyl group of the aldehyde and an active methylene group of the anhydride : the function of the basic catalyst B (acetate ion CH_3COO^- or triethylamine $N(C_2H_5)_3$) is to form the anion of the active hydrogen component, *i.e.*, by the extraction of a proton from the anhydride :

$$CH_3CO{-}O{-}COCH_3 + B \rightleftharpoons \bar{C}H_2CO{-}O{-}COCH_3 + BH^+$$

$$ArCH{=}O + \bar{C}H_2CO{-}O{-}COCH_3 \rightleftharpoons ArCH(O^-){-}CH_2CO{-}O{-}COCH_3$$

$$ArCH(O^-){-}CH_2CO{-}O{-}COCH_3 + BH^+ \rightleftharpoons ArCH(OH){-}CH_2CO{-}O{-}COCH_3 + B \longrightarrow$$

$$ArCH{=}CHCO{-}O{-}COCH_3 + H_2O \xrightarrow[HCl]{Na_2CO_3\ aq.;} ArCH{=}CHCOOH + CH_3COOH$$

The production of α-phenylcinnamic acid by heating benzaldehyde with acetic anhydride and sodium phenylacetate :

$$C_6H_5CHO \xrightarrow[(CH_3CO)_2O]{C_6H_5CH_2COONa,} C_6H_5CH{=}C(C_6H_5){-}COOH$$

at first sight suggests that condensation occurs between the aldehyde and the sodium salt. The correct interpretation is, however, that at temperatures

above 100° there is a mobile equilibrium between the anhydride and the sodium salt derived from the other acid as follows :

$$(CH_3CO)_2O + 2C_6H_5CH_2COONa \rightleftharpoons (C_6H_5CH_2CO)_2O + 2CH_3COONa$$

Here the phenylacetic anhydride, possessing more reactive α-hydrogen atoms, condenses with benzaldehyde to give α-phenylcinnamic acid. The preparation of the latter is an example of the **Oglialoro modification** of the Perkin reaction.

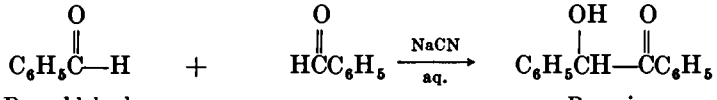
The preparation of **α-phenylcinnamic acid** from benzaldehyde, phenylacetic acid, acetic anhydride and triethylamine is described. Presumably equilibria are set up between phenylacetic acid and acetic anhydride to form phenylacetic anhydride, a mixed anhydride or both :

$$C_6H_5CH_2COOH + (CH_3CO)_2O \rightleftharpoons C_6H_5CH_2COOCOCH_3 + CH_3COOH$$

The α-carbon atom of the phenylacetyl group is more susceptible to attack by the basic catalyst (triethylamine) than the acetyl group ; hence α-phenylcinnamic acid, but no cinnamic acid, is obtained.

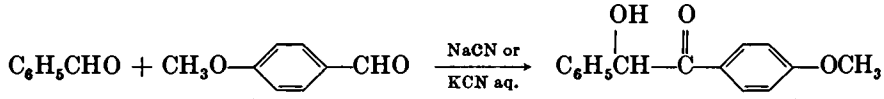
Phthalic anhydride may be used as the carbonyl compound in the Perkin reaction : see the preparation of phthalylacetic acid under *Ninhydrin* (Section **VIII,14**).

3. **Benzoin condensation.** Aromatic aldehydes when treated with an alkali cyanide, usually in aqueous solution, undergo condensation to the α-hydroxyketone or benzoin. The best known example is the conversion of benzaldehyde to **benzoin** :



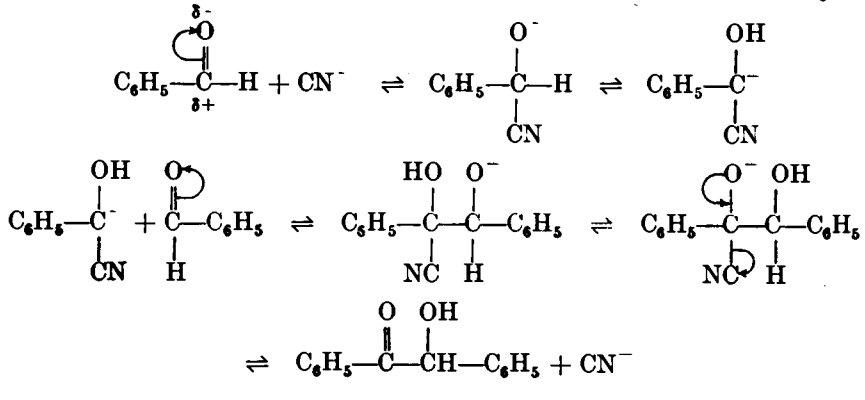
Benzaldehyde — Benzoin

By the use of 1 mol each of two different aldehydes, an unsymmetrical or mixed benzoin is obtained, for example :



Benzaldehyde — Anisaldehyde — 4-Methoxybenzoin

The reaction depends upon the catalytic influence of the cyanide ion, the *mechanism* being probably as follows :



Oxidation of benzoin with concentrated nitric acid or by catalytic amounts of cupric salts in acetic acid solution, which are regenerated continuously by ammonium nitrate, yields the diketone **benzil**:

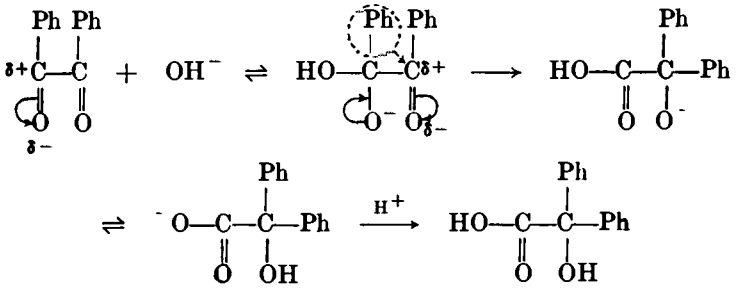
$$\underset{\text{Benzoin}}{C_6H_5CH(OH)COC_6H_5} + (O) \longrightarrow \underset{\text{Benzil}}{C_6H_5COCOC_6H_5} + H_2O$$

The latter procedure gives a purer product; it is difficult to remove the last traces of benzoin from the benzil obtained by the nitric acid method.

Benzil (and other α-diketones Ar—CO—CO—Ar) upon refluxing with aqueous-alcoholic potassium hydroxide undergo the **benzilic acid rearrangement.** Thus benzil is converted into a salt of **benzilic acid**:

$$C_6H_5COCOC_6H_5 + KOH \longrightarrow (C_6H_5)_2C(OH)COOK$$

A probable *mechanism* for this rearrangement postulates the intermediate formation of a hydroxide-ion addition complex, followed by the migration of a phenyl group as an anion:



Benzilic acid may be obtained in a high state of purity by the action of an alkaline bromate solution upon benzoin at 85–90°:

$$3C_6H_5CH(OH)COC_6H_5 + NaBrO_3 + 3NaOH \longrightarrow 3(C_6H_5)_2C(OH)COONa + NaBr + 3H_2O$$

4. **Claisen-Schmidt reaction.** Aromatic aldehydes condense with aliphatic or mixed alkyl-aryl ketones in the presence of aqueous alkali to form αβ-unsaturated ketones:

$$\underset{\text{Benzaldehyde}}{C_6H_5CHO} + \underset{\text{Acetone}}{CH_3COCH_3}\ (\text{excess}) \xrightarrow{-H_2O} \underset{\text{Benzalacetone}}{C_6H_5CH{=}CHCOCH_3}$$

$$2C_6H_5CHO + CH_3COCH_3 \xrightarrow{-2H_2O} \underset{\text{Dibenzalacetone}}{C_6H_5CH{=}CHCOCH{=}CHC_6H_5}$$

$$\underset{\text{Acetophenone}}{C_6H_5CHO + CH_3COC_6H_5} \xrightarrow{-H_2O} \underset{\text{Benzalacetophenone}}{C_6H_5CH{=}CHCOC_6H_5}$$

The above are examples of the **Claisen - Schmidt reaction.** The formation of β-nitrostyrenes by reaction of nitroalkanes with aromatic aldehydes in the presence of aqueous alkali may be included under the Claisen-Schmidt condensation:

$$\underset{\text{Nitromethane}}{C_6H_5CHO + CH_3NO_2} \xrightarrow{-H_2O} \underset{\text{β-Nitrostyrene}}{C_6H_5CH{=}CHNO_2}$$

It is of interest to note that reduction of β-nitrostyrene with lithium aluminium hydride (compare Section **VI,10**) gives β-phenylethylamine $C_6H_5CH_2CH_2NH_2$.

The *mechanism* of this base-catalysed reaction probably involves the intermediate formation of an aldol:

$$CH_3COCH_3 + \bar{O}H \rightleftharpoons \bar{C}H_2COCH_3 + H_2O$$

$$C_6H_5{-}\overset{\delta-}{\overset{\curvearrowright}{O}}{=}\overset{\delta+}{C}{-}H + \bar{C}H_2COCH_3 \rightleftharpoons C_6H_5{-}\overset{O^-}{\overset{|}{C}}{-}CH_2COCH_3 \xrightleftharpoons{H_2O}$$

$$C_6H_5{-}\overset{HO}{\overset{|}{C}}{-}\overset{H}{\overset{|}{C}}HCOCH_3 + \bar{O}H \xrightarrow[(H^+)]{-H_2O} C_6H_5CH{=}CHCOCH_3$$

5. **Claisen aldol condensation.** This consists in the condensation of an aromatic aldehyde and an ester $R{-}CH_2COOC_2H_5$ in the presence of finely divided sodium and a trace of alcohol at a low temperature. The catalyst is the alkoxide ion; aqueous alkalis cannot be employed since they will hydrolyse the resulting ester. The product is an $\alpha\beta$-unsaturated ester, for example:

$$\underset{\text{Benzaldehyde}}{C_6H_5CHO} + \underset{\text{Ethyl acetate}}{CH_3COOC_2H_5} \xrightarrow[C_2H_5ONa]{\text{Na or}} \underset{\text{Ethyl cinnamate}}{C_6H_5CH{=}CHCOOC_2H_5}$$

The *mechanism* of the reaction between aromatic aldehydes and esters probably involves the intermediate formation of an aldol (hence the name—Claisen aldol condensation):

$$CH_3COOC_2H_5 + \bar{O}C_2H_5 \rightleftharpoons \bar{C}H_2COOC_2H_5 + HOC_2H_5$$

$$C_6H_5{-}\overset{\delta-}{\overset{\curvearrowright}{O}}{=}\overset{\delta+}{C}{-}H + \bar{C}H_2COOC_2H_5 \rightleftharpoons C_6H_5{-}\overset{O^-}{\overset{|}{C}}{-}CH_2COOC_2H_5 \xrightarrow{H^+}$$

$$C_6H_5{-}\overset{OH}{\overset{|}{C}}{-}CH_2COOC_2H_5 \xrightarrow{-H_2O} C_6H_5CH{=}CHCOOC_2H_5$$

This reaction must be distinguished from the Claisen condensation, which is an acylation process (see discussion before Section III,151).

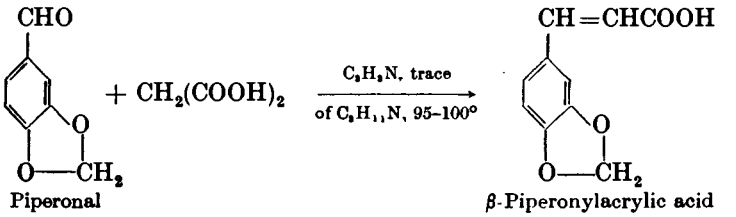
6. **Knoevenagel reaction.** The condensation of an aldehyde with an active methylene compound (usually malonic acid or its derivatives) in the presence of a base is generally called the **Knoevenagel reaction.** Knoevenagel found that condensations between aldehydes and malonic acid are effectively catalysed by ammonia and by primary and secondary amines in alcoholic solution; of the organic amines piperidine was regarded as the best catalyst.

$$RCHO + H_2C(COOH)_2 \xrightarrow[-H_2O)]{C_5H_{11}N} RCH{=}C(COOH)_2 \xrightarrow{-CO_2} RCH{=}CHCOOH$$

The **Doebner condensation** (or **reaction**)* is a slight modification of the Knoevenagel reaction and consists in warming a solution of the aldehyde and

* Priority for the use of pyridine as a catalyst should be assigned to Verley; Doebner subsequently extended its use.

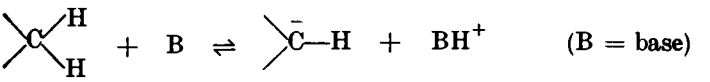
malonic acid in pyridine (sometimes in the presence of a little piperidine) on a steam bath for a few hours. The modification is very convenient, gives excellent results, and is particularly useful when the Perkin reaction gives poor yields, for example :

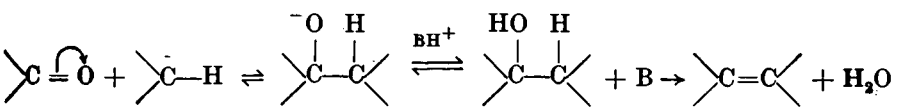


Piperonal — β-Piperonylacrylic acid

Examples of the Knoevenagel reaction with aldehydes are given under crotonic acid (**III,145**), β-*n*-hexylacrylic acid (**III,144**), sorbic acid (**III,145**) and furylacrylic acid (**V,10**).

A probable *mechanism* of these base-catalysed aldol reactions may be written in general terms as follows :

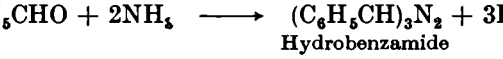




Benzaldehyde reacts with hydroxylamine in the presence of excess of sodium hydroxide to yield an oxime of low m.p. (**α- or *syn*-benzaldoxime**) which is stable to alkali, but is rapidly rearranged by acids to give an isomeric oxime of higher m.p. (**β- or *anti*-benzaldoxime**) :

α- or *syn*-Benzaldoxime (m.p. 35°) — β- or *anti*-Benzaldoxime (m.p. 130°)

Unlike aliphatic aldehydes (with the exception of formaldehyde which yields hexamethylenetetramine, Section **III,67**) benzaldehyde yields **hydrobenzamide** (and not an aldehyde ammonia) with ammonia :



Hydrobenzamide

IV,123. BENZYL ALCOHOL AND BENZOIC ACID
(*Cannizzaro Reaction*)

Dissolve 27 g. of potassium hydroxide in 25 ml. of water contained in a beaker or conical flask, and cool the solution to about 20° in ice water. Pour the solution into a 250 ml. reagent bottle, and add 30 g. (29 ml.) of pure benzaldehyde (1) ; *cork* the bottle securely and shake the mixture vigorously until it has been converted into a thick emulsion. Allow the mixture to stand overnight or for 24 hours in the stoppered bottle. Add *just sufficient water* (about 105 ml.) to dissolve the potassium benzoate. Pour the liquid into a separatory funnel, rinse out the bottle with about 30 ml. of ether and add this ether to the solution in the funnel. Shake the

solution in order to thoroughly extract the benzyl alcohol with the ether, separate the lower aqueous solution, and carry out two further extractions each with about 25 ml. of ether. *Save the aqueous solution.* Combine the ether extracts and distil the ether from a water bath (*CAUTION :* see Section **II,14**) until the volume is about 25 ml. Cool and shake the ether solution twice with 5 ml. portions of saturated sodium bisulphite solution in order to remove any benzaldehyde which may be present. Separate the ethereal solution, wash it with 10 ml. of 10 per cent. sodium carbonate solution (to ensure complete removal of the bisulphite), then with 10 ml. of water, and dry with anhydrous magnesium sulphate or anhydrous potassium carbonate. Remove the ether (Fig. *II, 13,* 4 ; 50 ml. distilling flask) on a water bath, and distil the residual liquid over a wire gauze or, better, from an air bath (Fig. *II, 5,* 3) ; replace the water condenser by an air condenser or empty the water completely from the condenser jacket. Collect the benzyl alcohol at 204–207° (the pure compound boils at 205·5°). The yield is 13 g.

Pour the aqueous solution remaining from the ether extraction with stirring into a mixture of 80 ml. of concentrated hydrochloric acid, 80 ml. of water and about 100 g. of crushed ice. Filter the precipitated benzoic acid at the pump, wash it with a little cold water, drain, and recrystallise from boiling water. The yield of benzoic acid (colourless crystals), m.p. 121°, is 18 g.

Note.

(1) The benzaldehyde should be free from benzoic acid ; it may be purified as described in Section **IV,115.**

IV,124. CINNAMIC ACID

Place 21 g. (20 ml.) of pure benzaldehyde (1), 30 g. (28 ml.) of acetic anhydride and 12 g. of freshly fused and finely-powdered potassium acetate (2) in a dry, 250 ml. round-bottomed flask fitted with an air condenser carrying a calcium chloride (or cotton wool) guard tube. Mix well and heat the reaction mixture in an oil bath at 160° for 1 hour and at 170–180° for 3 hours. Pour the mixture while still hot (80–100°) into about 100 ml. of water contained in a 1-litre round-bottomed flask which has previously been fitted for steam distillation (Fig. *II, 40,* 1) ; rinse the reaction flask with a little hot water. Now add with vigorous shaking a saturated aqueous solution of sodium carbonate (3) until a drop of the liquid withdrawn on the end of a glass rod turns red litmus a distinct blue. Steam distil the solution until all the unchanged benzaldehyde is removed and the distillate is clear. Cool the residual solution and filter at the pump from resinous by-products. Acidify the filtrate by adding concentrated hydrochloric acid slowly and with vigorous stirring until the evolution of carbon dioxide ceases. When cold, filter the cinnamic acid at the pump, wash with cold water, and drain well. Recrystallise either from hot water or from a mixture of 3 volumes of water and 1 volume of alcohol (or methylated spirit). The yield of dry cinnamic acid (colourless crystals), m.p. 133°, is 18 g.

Notes.

(1) The benzaldehyde must be free from benzoic acid ; it may be purified as detailed in Section **IV,115.**

(2) An equivalent quantity of freshly fused sodium acetate (Section II,50,9) may also be used, but the reaction is slower and a further 3–4 hours heating is necessary. Fused potassium acetate is prepared by melting the potassium acetate of commerce in a porcelain dish and heating gently, with occasional stirring, until no more vapour is evolved and the salt is completely fluid. When cold, the solid is finely ground in a mortar and preserved in a tightly-stoppered bottle until required.

(3) Sodium hydroxide solution cannot be used at this stage since it may produce benzoic acid by the Cannizzaro reaction (Section IV,123) from any unchanged benzaldehyde. If, however, the reaction mixture is diluted with 3–4 volumes of water, steam distilled to remove the unreacted benzaldehyde, the residue may then be rendered alkaline with sodium hydroxide solution. A few grams of decolourising carbon are added, the mixture boiled for several minutes, and filtered through a fluted filter paper. Upon acidifying carefully with concentrated hydrochloric acid, cinnamic acid is precipitated. This is collected, washed and purified as above.

Cognate Preparations

Coumarin. In a 250 ml. round-bottomed flask, provided with a small reflux condenser and a calcium chloride drying tube at the top, place 2·1 g. of salicylaldehyde, 2·0 ml. of anhydrous triethylamine and 5·0 ml. of acetic anhydride, and reflux the mixture gently for 12 hours. Steam distil the mixture from the reaction flask and discard the distillate. Render the residue in the flask basic to litmus with solid sodium bicarbonate, cool, filter the precipitated crude coumarin at the pump and wash it with a little cold water. Acidify the filtrate to Congo red with 1 : 1-hydrochloric acid, collect the precipitated *o*-acetoxycoumaric acid and recrystallise it from 70 per cent. *iso*propyl alcohol; the yield is 0·40 g., m.p. 153–154°.

Boil the crude coumarin with 200 ml. of water to which 0·2 g. of decolourising carbon is added, filter the hot solution, and concentrate it to a volume of 80 ml. Cool, collect the coumarin which separates, and recrystallise it from 40 per cent. aqueous methanol. The yield of coumarin, m.p. 68–69°, is 1·0 g.

α-Phenylcinnamic acid. Place 42·5 g. (40·5 ml.) of purified benzaldehyde (Section IV,115), 54·5 g. of phenylacetic acid, 80 ml. of redistilled A.R. acetic anhydride and 40 ml. of anydrous triethylamine in a 500 ml. round-bottomed flask fitted with a reflux condenser and drying tube. Boil the mixture gently for 5 hours. Steam distil the mixture directly from the reaction flask until the distillate passing over is no longer cloudy, and collect a further 50 ml. of distillate: discard the distillate. Cool the residue in the flask and decant the solution from the solid; make up the volume of the solution to 500 ml. with water (*A*). Dissolve the solid in 500 ml. of hot 95 per cent. ethanol, add the solution (*A*) followed by 2 g. of decolourising carbon; heat the mixture to boiling, filter and acidify the filtrate immediately to Congo red with 1 : 1-hydrochloric acid. Cool. Collect the separated crystals by suction filtration and recrystallise from 60 per cent. ethanol. The yield of α-phenylcinnamic acid (1), m.p. 172–173°, is 55 g.

Note.

(1) The product is the isomer with the two phenyl groups *cis* to each other, since decarboxylation with quinoline-copper chromium oxide at 210–220° yields *cis*-stilbene.

IV,125. BENZOIN

In a 500 ml. round-bottomed flask place 65 ml. of rectified spirit, 50 g. (47·5 ml.) of pure benzaldehyde (1) and a solution of 5 g. of sodium cyanide (96–98 per cent.) (*CAUTION*) in 50 ml. of water. Attach a reflux condenser (preferably of the double surface type) and boil the mixture gently for half an hour (2). Cool the contents of the flask (preferably in an ice bath). Filter the crude benzoin, wash it with cold water, drain well (3) and dry. The yield of crude benzoin, which is white or pale yellow in colour, is 45 g.

Recrystallise 5·0 g. from about 40 ml. of hot rectified (or methylated) spirit; upon cooling, 4·5 g. of pure benzoin (a white, crystalline solid, m.p. 137°) separate. Reserve the remainder of the preparation for benzil and benzilic acid (Sections **IV,126** and **IV,127** respectively).

Notes.

(1) For the purification of commercial benzaldehyde, see Section **IV,115.**

(2) The reaction sometimes takes place with considerable violence and material may be lost through the condenser unless a large flask (*e.g.*, at least of the size given) is employed.

(3) The filtrate contains sodium cyanide, and should be washed down the sink with a liberal quantity of water.

Cognate Preparation

4-Methoxybenzoin. Dissolve 25 g. of potassium cyanide in 175 ml. of water in a 1500 ml. round-bottomed flask, and add 136 g. (121·5 ml.) of redistilled 4-methoxybenzaldehyde (anisaldehyde), 108 g. (103 ml.) of redistilled benzaldehyde and 350 ml. of 95 per cent. ethanol. Reflux the mixture (which becomes homogeneous at the boiling temperature) for 90 minutes. Remove all the unreacted aldehydes and the ethanol by steam distillation. Decant the water from the residue and set it aside to crystallise. Press the product as free as possible from oily material on a suction funnel and wash it with a little ethanol. Recrystallise the crude product (*ca.* 125 g.) by dissolving it in hot ethyl alcohol and allowing to crystallise slowly. The *p*-methoxybenzoin separates out first in large clumps of long needles, whilst the little benzoin present crystallises in small compact balls of needles. With a little experience it is possible to filter off a good yield of the former before the appearance of the benzoin. The yield of 4-methoxybenzoin is about 55 g. Recrystallise it again until the m.p. is 105–106°.

IV,126. BENZIL

Method 1. Place 20 g. of crude benzoin (preceding Section) and 100 ml. of concentrated nitric acid in a 250 ml. round-bottomed flask. Heat on a boiling water bath (in the fume cupboard) with occasional shaking until the evolution of oxides of nitrogen has ceased (about 1·5 hours). Pour the reaction mixture into 300–400 ml. of cold water contained in a beaker, stir well until the oil crystallises completely as a yellow solid. Filter the crude benzil at the pump, and wash it thoroughly with water to remove the nitric acid. Recrystallise from alcohol or methylated spirit (about 2·5 ml. per gram). The yield of pure benzil, m.p. 94–96°, is 19 g.

Method 2. Place 0·2 g. of cupric acetate, 10 g. of ammonium nitrate, 21·2 g. of benzoin and 70 ml. of an 80 per cent. by volume acetic acid - water solution in a 250 ml. flask fitted with a reflux condenser. Heat the mixture with occasional shaking (1). When solution occurs, a vigorous evolution of nitrogen is observed. Reflux for 90 minutes, cool the solution, seed the solution with a crystal of benzil (2), and allow to stand for 1 hour. Filter at the pump and keep the mother liquor (3) : wash well with water and dry (preferably in an oven at 60°). The resulting benzil has m.p. 94–95° and the m.p. is unaffected by recrystallisation from alcohol or from carbon tetrachloride (2 ml. per gram). Dilution of the mother liquor with the aqueous washings gives a further 1·0 g. of benzil (4).

Notes.

(1) For large scale preparations use a three-necked flask equipped with two reflux condensers and an oil-sealed stirrer.

(2) Stirring or vigorous shaking also induces crystallisation.

(3) The mother liquor should not be concentrated as an explosion may result.

(4) The above appears to be a general reaction for converting α-hydroxy ketones into diketones in excellent yield : thus furoin and anisoin give furil and anisil respectively. The reaction is probably :

$$RCH(OH)COR + 2Cu(OAc)_2 \longrightarrow RCOCOR + 2CuOAc + 2AcOH$$

$$2CuOAc + NH_4NO_3 + 2AcOH \longrightarrow 2Cu(OAc)_2 + NH_4NO_2 + H_2O$$

$$NH_4NO_2 \xrightarrow[(HOAc)]{H+} N_2 + 2H_2O$$

IV,127. BENZILIC ACID

Method 1. In a 500 ml. round-bottomed flask, place a solution of 35 g. of potassium hydroxide in 70 ml. of water, then add 70 g. (87 ml.) of rectified spirit and 35 g. of recrystallised benzil (preceding Section). A deep bluish-black solution is produced. Fit a reflux condenser to the flask and boil the mixture on a water bath for 10–15 minutes. Pour the contents of the flask into a porcelain dish and allow to cool, preferably overnight. The potassium salt of benzilic acid crystallises out. Filter off the crystals at the pump and wash with a little ice-cold alcohol. Dissolve the potassium salt in about 350 ml. of water, and add 1 ml. of concentrated hydrochloric acid from a burette slowly and with stirring. The precipitate thus produced is coloured red-brown and is somewhat sticky. Filter this off ; the filtrate should be nearly colourless. Continue the addition of hydrochloric acid with stirring until the solution is acid to Congo red paper. Filter off the benzilic acid with suction, wash it thoroughly with cold water until free from chlorides, and allow to dry. The yield of crude benzilic acid, which is usually light pink or yellow in colour, is 30 g. Purify the product either by recrystallisation from hot benzene (about 6 ml. per gram) or from hot water with the use of a little decolourising carbon. The coloured and sticky material obtained by the first precipitation may be recrystallised from hot water with the addition of a little decolourising carbon, and a further 1–2 g. obtained. Pure benzilic acid has m.p. 150°.

Method 2. Prepare a solution of 50 g. of sodium hydroxide and 11·5 g. of sodium bromate (or 12·5 g. of potassium bromate) in 90 ml. of water

in an evaporating dish or casserole. Add 44 g. of benzil (1) in portions to this solution whilst stirring (preferably with a mechanical stirrer) and heating on a water bath at 85–90° (2). Add small quantities of water from time to time to prevent the mixture becoming too thick; about 80 ml. of water are required. Continue the heating and stirring until a test portion is completely or almost completely soluble in water; this usually requires 3–4 hours. Dilute the mixture with 400 ml. of water and allow to stand, preferably overnight. Filter off the solid or oily impurity (benzhydrol). Set aside 5 ml. of the filtrate (3) and add dilute sulphuric acid (1 : 3 by volume) slowly and with stirring to a point just short of the liberation of bromine; about 130 ml. are required. If the end point is overstepped, add the 5 ml. of the filtrate which was set aside and then sufficient sulphuric acid to the end point. Filter off the product at the pump, wash it well with water and dry. The benzilic acid weighs 46 g. and has a m.p. of 149–150°, *i.e.*, is practically pure. If desired, it may be recrystallised from benzene.

Notes.

(1) Moist and/or crude benzil (see Section IV,126) gives equally satisfactory results.

(2) The reaction mixture should not be heated to boiling since this leads to the formation of much benzhydrol. The temperature attained by heating on a boiling water bath is 85–90°.

(3) This precaution is generally unnecessary if the addition of sulphuric acid is made carefully.

IV,128. BENZALACETONE

Place 42 g. (40 ml.) of pure benzaldehyde (Section IV,115) and 63·5 g. (80 ml.) of pure acetone in a 250 ml. wide-mouthed bottle or bolt-head flask equipped with a mechanical stirrer. Immerse the reaction vessel in a bath of cold water and add slowly (during about 30 minutes) from a dropping funnel 10 ml. of 10 per cent. sodium hydroxide solution: adjust the rate of addition so that the temperature remains between 25° and 30°. Stir the mixture at room temperature for a further 2 hours; alternatively, securely stopper the bottle and shake mechanically for the same period. Render the mixture just acid to litmus paper by the addition of dilute hydrochloric acid. Transfer to a separatory funnel. Remove the upper organic layer, extract the lower aqueous layer with 20 ml. of benzene and add the extract to the yellow upper layer. Wash the latter with 20 ml. of water, and dry with a little anhydrous magnesium sulphate. Remove the benzene on a water bath with the aid of the apparatus illustrated in Fig. *II*, *13*, 4 but with the distilling flask replaced either by a Claisen flask or, better, a Claisen flask with fractionating side arm (Figs. *II*, *24*, 2–5), and distil the residue under diminished pressure (Fig. *II*, *20*, 1). The benzalacetone distils at 133–143°/16 mm. (or at 120–130°/7 mm. or at 150–160°/25 mm.), and solidifies to a crystalline mass on standing, m.p. 38–39°; the yield is 45 g. This is pure enough for most practical purposes, but may be further purified by redistillation (b.p. 137–142°/16 mm.) or by recrystallisation from light petroleum (b.p. 40–60°): the pure benzalacetone melts at 42°. The residue in the distilling flask contains some dibenzalacetone, which may be prepared in the pure state by employing the theoretical quantities of benzaldehyde and acetone.

DIBENZALACETONE

In a 500 ml. wide-mouthed reagent bottle place a cold solution of 25 g. of sodium hydroxide in 250 ml. of water and 200 ml. of alcohol (1); equip the bottle with a mechanical stirrer and surround it with a bath of water. Maintain the temperature of the solution at 20–25°, stir vigorously and add one-half of a previously prepared mixture of 26·5 g. (25·5 ml.) of pure benzaldehyde (Section **IV,115**) and 7·3 g. (9·3 ml.) of A.R. acetone. A flocculent precipitate forms in 2–3 minutes. After 15 minutes add the remainder of the benzaldehyde - acetone mixture. Continue the stirring for a further 30 minutes. Filter at the pump and wash with cold water to eliminate the alkali as completely as possible. Dry the solid at room temperature upon filter paper to constant weight; 27 g. of crude dibenzalacetone, m.p. 105–107°, are obtained. Recrystallise from hot ethyl acetate (2·5 ml. per gram) or from hot rectified spirit. The recovery of pure dibenzalacetone, m.p. 112°, is about 80 per cent.

Note.

(1) Sufficient alcohol is employed to dissolve the benzaldehyde and to retain the initially-formed benzalacetone in solution until it has had time to react with the second molecule of benzaldehyde.

IV,129 β-NITROSTYRENE

Equip a 1500 ml. three-necked flask with a thermometer, mechanical stirrer and a dropping funnel. Place 61 g. (54 ml.) of nitromethane (Section **III,55**), 106 g (101 ml.) of purified benzaldehyde (Section **IV,115**) and 200 ml. of methanol in the flask and cool it with a mixture of ice and salt to about −10°. Dissolve 42 g. of sodium hydroxide in 40–50 ml. of water, cool and dilute to 100 ml. with ice and water; place this cold solution in the dropping funnel. Add the sodium hydroxide solution, with vigorous stirring, to the nitromethane mixture at such a rate that the temperature is held at 10–15°. Introduce the first few ml. cautiously since, after a short induction period, the temperature may rise to 30° or higher; check the rise in temperature, if necessary, by adding a little crushed ice to the reaction mixture. A bulky white precipitate forms; if the mixture becomes so thick that stirring is difficult, add about 10 ml. of methanol. After standing for about 15 minutes, add 700 ml. of ice water containing crushed ice; the temperature should be below 5°. Run the resulting cold solution immediately from a dropping funnel and with stirring into 500 ml. of 2 : 3-hydrochloric acid contained in a 3-litre flask or jar; adjust the rate of addition so that the stream just fails to break into drops. A pale yellow crystalline precipitate separates almost as soon as the alkaline solution mixes with the acid. The solid settles to the bottom of the vessel when the stirrer is stopped. Decant most of the cloudy liquid layer, filter the residue by suction and wash it with water until free from chlorides. Transfer the solid to a beaker immersed in hot water; two layers form and on cooling again, the lower layer of nitrostyrene solidifies; pour off the upper water layer. Dissolve the crude nitrostyrene in 85 ml. of hot ethanol (*FUME CUPBOARD:* nitrostyrene vapours are irritating to the nose and eyes, and the skin of the face is sensitive to the solid), filter through a hot water funnel and cool until

crystallisation is complete. The yield of pure β-nitrostyrene, m.p. 57–58° is 125 g.

IV,130. BENZALACETOPHENONE (CHALCONE)

Place a solution of 22 g. of sodium hydroxide in 200 ml. of water and 100 g. (122·5 ml.) of rectified spirit in a 500 ml. bolt-head flask provided with a mechanical stirrer. Immerse the flask in a bath of crushed ice, pour in 52 g. of freshly-distilled acetophenone (Section **IV,136**), start the stirrer, and then add 46 g. (44 ml.) of pure benzaldehyde (Section **IV,115**). Keep the temperature of the mixture at about 25° (the limits are 15–30°) and stir vigorously until the mixture is so thick that stirring is no longer effective (2–3 hours). Remove the stirrer and leave the reaction mixture in an ice chest or refrigerator overnight. Filter the product with suction on a Buchner funnel or a sintered glass funnel, wash with cold water until the washings are neutral to litmus, and then with 20 ml. of ice-cold rectified spirit. The crude chalcone, after drying in the air, weighs 88 g. and melts at 50–54°. Recrystallise from rectified spirit warmed to 50° (about 5 ml. per gram). The yield of pure benzalacetophenone (a pale yellow solid), m.p. 56–57°, is 77 g. This substance should be handled with great care since it acts as a skin irritant.

IV,131 ETHYL CINNAMATE

Prepare powdered (or "molecular") sodium from 14·5 g. of clean sodium and 150–200 ml. of sodium-dried xylene contained in a 1-litre three-necked flask (Section **II,50,***6*) fitted with a mechanical stirrer and a reflux condenser. When cold, pour off the xylene as completely as possible, and then add 230 ml. of absolute ethyl acetate (Section **II,47,***19*) containing 2 ml. of absolute ethyl alcohol (1). Cool the flask rapidly to 0°, and add 53 g. (51 ml.) of pure benzaldehyde (Section **IV,115**) slowly (during 90 minutes) from a dropping funnel whilst the mixture is stirred. Keep the temperature between 0° and 5°; do not allow it to rise above 10° otherwise a poor yield will be obtained. The reaction commences as soon as the benzaldehyde is added, as is indicated by the production of a reddish substance on the particles of sodium. Continue the stirring until practically all the sodium has reacted (about 1 hour after all the benzaldehyde has been introduced). Then add 45 ml. of glacial acetic acid, followed by an equal volume of water (*CAUTION*: some sodium may be present). Separate the layer of ester, extract the aqueous layer with 25 ml. of ethyl acetate, wash the combined organic layers with 150 ml. of 1 : 1 hydrochloric acid, and dry with anhydrous magnesium or sodium sulphate. Distil off the ethyl acetate on a water bath (Fig. *II*, *13*, 4 but with a Claisen flask replacing the distilling flask). Distil the residue under diminished pressure (Fig. *II*, *20*, 1). Collect the ethyl cinnamate (a colourless liquid) at 126–131°/6 mm.; the yield is 65 g. (2).

Notes.

(1) A little alcohol (*ca.* 1 per cent.) is required to start the reaction; the yield is consistently lower in its absence.

(2) Ethyl cinnamate may also be prepared by the esterification of cinnamic acid. The pure compound boils at 127°/6 mm.

IV,132. β-PIPERONYLACRYLIC ACID (3 : 4-METHYLENE-DIOXYCINNAMIC ACID)

Dissolve 50 g. of piperonal and 75 g. of malonic acid in a mixture of 150 ml. of pyridine and 2·5 ml. of piperidine contained in a 500 ml. round-bottomed flask, and heat under reflux for 1 hour on a water bath. A rapid evolution of carbon dioxide takes place. Complete the reaction by boiling the solution for 5 minutes. Cool, pour into excess of water containing enough hydrochloric acid to combine with the pyridine, filter off the piperonylacrylic acid, wash with a little water, and dry. The yield is almost quantitative and the acid is practically pure. It may be recrystallised from glacial acetic acid ; m.p. 238°.

Cognate Preparations

***p*-Methylcinnamic acid.** From *p*-tolualdehyde ; heat for 6 hours. Recrystallise from glacial acetic acid ; m.p. 198°. Yield : 87 per cent.

***m*-Nitrocinnamic acid.** From *m*-nitrobenzaldehyde. Recrystallise from alcohol ; m.p. 197°. Yield : 80 per cent.

***p*-Methoxycinnamic acid.** From anisaldehyde. Recrystallise from alcohol ; m.p. 172°. Yield : 80 per cent.

IV,133. α- AND β-BENZALDOXIMES

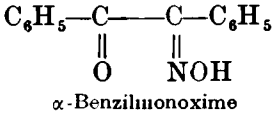
In a 250 ml. conical flask mix a solution of 14 g. of sodium hydroxide in 40 ml. of water and 21 g. (20 ml.) of pure benzaldehyde (Section **IV,115**). Add 15 g. of hydroxylamine hydrochloride in small portions, and shake the mixture continually (mechanical stirring may be employed with advantage). Some heat is developed and the benzaldehyde eventually disappears. Upon cooling, a crystalline mass of the sodium derivative separates out. Add sufficient water to form a clear solution, and pass carbon dioxide into the solution until saturated. A colourless emulsion of the α- or *syn*-aldoxime separates. Extract the oxime with ether, dry the extract over anhydrous magnesium or sodium sulphate, and remove the ether on a water bath. Distil the residue under diminished pressure (Fig. *II*, *20*, 1). Collect the pure *syn*-benzaldoxime (α-benzaldoxime) at 122–124°/12 mm. ; this gradually solidifies on cooling in ice and melts at 35°. The yield is 12 g.

To prepare the β-benzaldoxime, dissolve 10 g. of α-benzaldoxime in 50 ml. of pure anhydrous ether and pass dry hydrogen chloride (Section **II,48**,*1*) through a *wide* delivery tube into the solution with constant shaking. Colourless crystals of the hydrochloride of the β-aldoxime separate. Filter these at the pump through a sintered glass funnel, wash with dry ether, transfer to a separatory funnel and cover with a layer of ether. Add a concentrated solution of sodium carbonate gradually and with constant shaking until effervescence ceases. Separate the ethereal layer, which contains the β-oxime, dry over anhydrous magnesium or sodium sulphate, and remove the ether by evaporation in a vacuum desiccator. The residue crystallises ; remove the small amount of oily matter by pressing on a porous tile. Recrystallise by dissolving it in the minimum volume of ether and then adding light petroleum (b.p. 60–80°). The yield of β-benzaldoxime (*anti*-benzaldoxime), m.p. 130°, is 7–8 g.

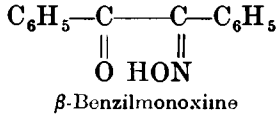
COGNATE PREPARATION

α-Benzilmonoxime. Grind 43 g. of pure benzil (Section **IV,126**) to a thin paste with a little alcohol, and add a concentrated aqueous solution of 17·5 g. of hydroxylamine hydrochloride. Cool to − 5° (*e.g.*, with crushed ice and concentrated hydrochloric acid) and add 30 g. of sodium hydroxide in 20 per cent. aqueous solution dropwise with rapid mechanical stirring: do not allow the temperature to rise above 0°. After 90 minutes dilute the mixture with water and filter off the small quantity of unchanged benzil on a sintered glass funnel. Just acidify the filtrate with glacial acetic acid, allow to stand for 30 minutes, filter off the crude pinkish α-monoxime, and recrystallise it from aqueous alcohol (60 vol. % alcohol); the resulting oxime weighs 37 g. and melts at 137°. To obtain the pure α-benzilmonoxime, recrystallise twice from benzene; the final yield is 28 g. of the pure product, m.p. 140°. Animal charcoal must not be used in the recrystallisation (see below).

β-Benzilmonoxime. Boil 10 g. of the pure α-monoxime for 15 minutes with 1 g. of dried animal charcoal in a quantity of pure benzene just sufficient to dissolve the α-monoxime at the boiling point. Filter off the charcoal and allow the filtrate to stand. The β-monoxime + 0·5 C_6H_6 crystallises slowly on cooling: a further crop can be obtained by evaporation of the mother liquid. An excellent yield of the β-monoxime, m.p. 112°, is obtained. The pure β-oxime causes no colour change with aqueous-alcoholic copper acetate solution; if it is contaminated with the α-oxime, a greenish colour is produced.



α-Benzilmonoxime



β-Benzilmonoxime

IV,134. HYDROBENZAMIDE

Place 10 ml. of pure benzaldehyde (Section **IV,115**) and 100 ml. of concentrated ammonia solution (sp. gr. 0·88) in a 250 ml. wide-mouthed reagent bottle. Cork the bottle securely, shake vigorously for 10 minutes and allow to stand with occasional shaking for 24 hours. By this time the benzaldehyde should be converted into a hard mass of hydrobenzamide. Break up the solid mass with a spatula or a thick glass rod, filter with suction, wash with water, and drain thoroughly. Recrystallise from absolute alcohol (or absolute methylated spirit). The yield of hydrobenzamide (colourless crystals), m.p. 101°, is 7 g. It is easily hydrolysed by cold dilute acids.

IV,135. REACTIONS AND CHARACTERISATION OF AROMATIC ALDEHYDES

Aromatic aldehydes usually have relatively high boiling points, but distil with little or no decomposition. The vapours burn with a smoky flame. They are easily oxidised on standing in the air into the corresponding acids; the odours are often pleasant and characteristic. Aromatic aldehydes, by virtue of their high molecular weight, yield

crystalline derivatives with phenylhydrazine and hydroxylamine—these reagents are not generally recommended for aliphatic aldehydes since they give derivatives which are either liquids or solids of low m.p.

Aromatic aldehydes react with the dimedone reagent (Section **III,70,** *2*). All aromatic aldehydes (i) reduce ammoniacal silver nitrate solution and (ii) restore the colour of Schiff's reagent; many react with sodium bisulphite solution. They do not, in general, reduce Fehling's solution or Benedict's solution. Unlike aliphatic aldehydes, they usually undergo the Cannizzaro reaction (see Section **IV,123**) under the influence of sodium hydroxide solution. For full experimental details of the above tests, see under *Aliphatic Aldehydes*, Section **III,70**. They are easily oxidised by dilute alkaline permanganate solution at the ordinary temperature: after removal of the manganese dioxide by sulphur dioxide or by sodium bisulphite, the acid can be obtained by acidification of the solution.

Crystalline Derivatives

1. **Dimedone derivatives.** For experimental details, see under *Aliphatic Aldehydes*, Section **III,70,***2*.

2. **2 : 4-Dinitrophenylhydrazones.** For experimental details, see under *Aliphatic ketones*, Section **III,74,***1*.

3. **Semicarbazones.** See Section **III,74,***2*.

4. **Oximes** (compare Section **III,74,B**). The following procedure has wide application. Dissolve 0·5 g. of hydroxylamine hydrochloride in 2 ml. of water, add 2 ml. of 10 per cent. sodium hydroxide solution and 0·2 g. of the aldehyde (or ketone). If the latter is insoluble, add just sufficient alcohol to the mixture to give a clear solution. Heat the mixture under reflux for 10–15 minutes, and then cool in ice. If crystals separate, filter these off, and recrystallise from alcohol, dilute alcohol, benzene or light petroleum (b.p. 60–80°). If no solid separates on cooling, dilute with 2–3 volumes of water, filter the precipitated solid, and recrystallise.

5. **Phenylhydrazones** (compare Section **III,74,C**). Dissolve 0·5 g. of *colourless* phenylhydrazine hydrochloride and 0·8 g. of sodium acetate in 5 ml. of water, and add a solution of 0·2–0·4 g. of the aldehyde (or ketone) in a little alcohol (free from aldehydes and ketones). Shake the mixture until a clear solution is obtained and add a little more alcohol, if necessary. Warm on a water bath for 10–15 minutes and cool. Filter off the crystalline derivative, and recrystallise it from dilute alcohol or water; sometimes benzene or light petroleum (b.p. 60–80°) may be used.

The use of liquid phenylhydrazine in the preparation of phenylhydrazones is not recommended for beginners because of the highly poisonous character of the liquid (see Section IV,89). A phenylhydrazine reagent may, however, be used.

The phenylhydrazine reagent may be prepared by either of two methods.

Method A. Dissolve 25 ml. of light-coloured phenylhydrazine (redistil, if necessary) in 250 ml. of 10 per cent. acetic acid, add 0·5 g. of decolourising carbon, shake and filter into a dark bottle.

Method B. Dissolve 25 g. of colourless phenylhydrazine hydrochloride (recrystallise, if necessary) in 250 ml. of water; warming may be required. Add 45 g. of crystallised sodium acetate to the cold solution and shake until dissolved. Add 0·5 g. of decolourising carbon, shake, and filter into a dark bottle. The reagent should not be kept for longer than 1 month.

6. ***p*-Nitrophenylhydrazones** (compare Section **III,74,*1***). Reflux a mixture of 0·5 g. of *p*-nitrophenylhydrazine, 0·5 g. of the aldehyde (or ketone), 10–15 ml. of alcohol and 2 drops of glacial acetic acid for 10 minutes. Add more alcohol if the boiling solution is not homogeneous. Cool the clear solution, filter off the *p*-nitrophenylhydrazone, and recrystallise it from alcohol or acetic acid.

Alternatively, dissolve approximately equivalent amounts of the aldehyde (or ketone) and the solid reagent in the minimum volume of cold glacial acetic acid, and reflux for 15 minutes. The *p*-nitrophenylhydrazone separates on cooling or upon careful dilution with water.

Note.

All aldehydes, and also those ketones which have two different groups attached to the carbonyl grouping, are capable of yielding two stereoisomeric oximes, hydrazones or semicarbazones. As a general rule, however, one of the stereoisomerides is formed in much greater amount than the other, and no doubt therefore arises as to the purity of the ketonic compound under investigation; occasionally a mixture of stereoisomerides is obtained, which may be difficult to separate by recrystallisation. The formation, therefore, of one of the above derivatives of indefinite melting point and obvious heterogeneity does not necessarily imply the presence of an impure ketonic substance.

7. **2 : 4-Dinitrophenylhydrazones.** The following procedure for the preparation of 2 : 4-dinitrophenylhydrazones is alternative to those given in Section **III,74,*1***.

To the clear solution obtained by warming 0·5 g. of 2 : 4-dinitrophenylhydrazine, 1 ml. of concentrated hydrochloric acid and 8–10 ml. of ethanol, add 0·25 g. of the aldehyde and heat just to boiling. Allow to cool to room temperature, filter off the 2 : 4-dinitrophenylhydrazone and recrystallise it from ethanol or glacial acetic acid.

8. **Azines.** Aldehydes react with hydrazine to yield azines: the reaction cannot usually be arrested at the hydrazone stage. This reaction may be illustrated by the preparation of *benzalazine* from benzaldehyde:

$$2C_6H_5CHO + N_2H_4,H_2SO_4 \xrightarrow[NH_3]{Aq.} C_6H_5CH{=}N{-}N{=}CHC_6H_5 + H_2SO_4 + 2H_2O$$

Stir a mixture of 2·4 g. of powdered hydrazine sulphate, 18 ml. of water and 2·4 ml. of concentrated aqueous ammonia (sp. gr. 0·88), and add 4·6 g. (4·4 ml.) of benzaldehyde (free from benzoic acid) dropwise, with stirring, over a period of 30–60 minutes. Stir the mixture for a further hour, collect the solid by suction filtration and wash it with water. Recrystallise from 8 ml. of rectified spirit. The yield of benzalazine (yellow needles), m.p. 92–93°, is 3·6 g.

The melting points of the various derivatives of a number of typical aromatic aldehydes are collected in Table **IV,135.**

TABLE IV,135. AROMATIC ALDEHYDES

Aldehyde	B.P.	M.P.	Dimedone	"Anhydride" of Dimedone	2:4-Dinitrophenylhydrazone	Semicarbazone	Oxime	Phenylhydrazone	*p*-Nitrophenylhydrazone
Benzaldehyde	179°	—	195°	200°	237°	224°	35°d	158°	192°
o-Chlorobenzaldehyde	213	11°	205	225	209	229 (146)	76d	86	249
m-Chlorobenzaldehyde	214	18	—	—	248	229	71d	134	216
p-Chlorobenzaldehyde	214	47	—	—	265	232	107 (140)	127	220
o-Bromobenzaldehyde	230	22	—	—	—	214	102	—	240
m-Bromobenzaldehyde	234	—	—	—	—	205	72d	141	220
p-Bromobenzaldehyde	—	67	—	—	—	228	111	113	208
o-Iodobenzaldehyde	—	37	—	—	—	206	108	79	—
m-Iodobenzaldehyde	—	57	—	—	—	226	62	155	212
p-Iodobenzaldehyde	—	78	—	—	—	224	—	121	201
Salicylaldehyde (1)	197	—	—	208	252	231	63	143	228
m-Hydroxybenzaldehyde	240	108	—	—	259	198	90	130	222
p-Hydroxybenzaldehyde	—	116	189	246	280	224	72	178	266
o-Methoxybenzaldehyde	236	38	—	—	253	215	92	—	205
m-Methoxybenzaldehyde	230	—	—	—	—	—	40	—	171
Anisaldehyde (2)	248	2	145	243	254	209	132 (165)	121	161
o-Nitrobenzaldehyde	—	44	—	—	265	256	103	156	263
m-Nitrobenzaldehyde	—	58	—	—	292	246	122	121	247
p-Nitrobenzaldehyde	—	106	—	—	320	221	133	159	249
o-Aminobenzaldehyde	—	40	—	—	—	247	135	221	220
m-Aminobenzaldehyde	—	Amorphous	—	—	—	280d	195	162	226
p-Aminobenzaldehyde	—	72	—	—	—	173	124	156	—
o-Tolualdehyde	200	—	167	215	194	212	49	106	222
m-Tolualdehyde	199	—	172	206	194	223	60	91	157
p-Tolualdehyde	204	—	—	—	233	234	80	112	201
Protocatechuicaldehyde (3)	—	153	—	145	275	230	157	176	—
Resorcylaldehyde (4)	—	136	—	—	286	260	192	158	—
2 : 3-Dimethoxybenzaldehyde	—	54	—	—	—	231	99	138	—

TABLE IV,135. AROMATIC ALDEHYDES (*continued*)

Aldehyde	B.P.	M.P.	Dimedone	"Anhydride" of Dimedone	2:4-Dinitrophenylhydrazone	Semicarbazone	Oxime	Phenylhydrazone	*p*-Nitrophenylhydrazone
2 : 4-Dimethoxybenzaldehyde	—	69°	—	—	—	—	106°	—	—
Veratraldehyde (5) . .	285°	58	—	—	264°	177°	95	121°	—
p-Dimethylaminobenzaldehyde	—	74	—	—	325	222	185	148	182°
Phenylacetaldehyde .	194	34	165°	126°	121	156	99	63	151
Cinnamaldehyde . .	252	—	213	175	225d	215	139	168	195
Hydrocinnamaldehyde .	224	—	—	—	149	127	94	—	123
Cuminaldehyde (6) . .	235	—	171	173	241	211	52	129	190
Piperonal (7) . . .	263	37	178	220	265	234	110	106	200
Vanillin (8) . . .	—	81	197	228	269	239	117	105	228
Hexahydrobenzaldehyde .	162	—	—	—	—	173	91	—	—
α-Naphthaldehyde . .	292	34	—	—	—	221	98	80	234
β-Naphthaldehyde . .	—	61	—	—	270	245	156	206	230
2 : 4-Dichlorobenzaldehyde	—	72	—	—	—	—	—	—	—
2 : 6-Dichlorobenzaldehyde	—	71	—	—	—	—	150	—	—
3 : 4-Dichlorobenzaldehyde	248	44	—	—	—	—	119	—	277

(1) *o*-Hydroxybenzaldehyde.
(2) *p*-Methoxybenzaldehyde.
(3) 3 : 4-Dihydroxybenzaldehyde.
(4) 2 : 4-Dihydroxybenzaldehyde.
(5) 3 : 4-Dimethoxybenzaldehyde.
(6) *p-iso*Propylbenzaldehyde.
(7) 3 : 4-Methylenedioxybenzaldehyde.
(8) 4-Hydroxy-3-methoxybenzaldehyde.

AROMATIC KETONES

Aromatic ketones may be prepared :—

1. By the **Friedel and Crafts reaction.** The condensation of an acid chloride or an acid anhydride with an aromatic hydrocarbon in the presence of anhydrous aluminium chloride generally gives a good yield of the aromatic ketone :

$$RCOCl + HAr \xrightarrow{AlCl_3} RCOAr + HCl$$

$$Ar'COCl + HAr \xrightarrow{AlCl_3} Ar'COAr + HCl$$

$$(RCO)_2O + HAr \xrightarrow{AlCl_3} RCOAr + RCOOH$$

It should be noted that the Friedel-Crafts acylation differs from the Friedel-Crafts alkylation (compare Sections **IV,3-4** and discussion preceding Section **IV,1**) in one important respect. The alkylation requires catalytic quantities of aluminium chloride, but for acylation a molecular equivalent of aluminium chloride is necessary for each carbonyl group present in the acylating agent. This is because aluminium chloride is capable of forming rather stable complexes with the carbonyl group ; these complexes probably possess an oxonium structure $\rangle C{=}O^+,AlCl_3^-$. Complex formation thus requires an equivalent quantity of metal halide and a slight excess over the molecular amount is employed in order to ensure that the free reagent may be present to act as a catalyst : thus 1·1 and 2·2 molecular equivalents of aluminium chloride are generally employed for acid chlorides and acid anhydrides respectively. Excess of benzene or of toluene may be used as a solvent (when either of these substances constitutes one of the reactants), otherwise carbon disulphide or nitrobenzene is usually used. Friedel-Crafts acylation is free of two features which complicate the alkylation reaction, namely, (i) polysubstitution and (ii) rearrangement of groups. There is usually no difficulty in arresting the acylation with the introduction of a single acyl group into the aromatic nucleus. Preliminary mixing of the acyl and aluminium halides often gives good results ; this procedure reduces any tendency of the benzene homologue to isomerise or disproportionate (where this is possible).

The use of aliphatic acid anhydrides in place of acid chlorides offers many advantages ; these include :

(*a*) The greater ease of obtaining the anhydrides in a state of purity and their availability as commercial products (acetic, propionic, *n*-butyric and succinic anhydrides).

(*b*) The handling of disagreeable acid chlorides is avoided.

(*c*) The absence of any appreciable quantities of by-products and of resinous substances.

(*d*) The resulting ketones are almost pure after one distillation. The reaction is smooth and the yield is generally good.

The examples of the Friedel and Crafts reaction described include the following :—

$$C_6H_6 + CH_3COCl \xrightarrow{AlCl_3} \underset{\text{Acetophenone}}{C_6H_5COCH_3} + HCl$$

$$C_6H_6 + (CH_3CO)_2O \xrightarrow{AlCl_3} C_6H_5COCH_3 + CH_3COOH$$

$$\underset{\text{Toluene}}{CH_3C_6H_5} + (CH_3CO)_2O \xrightarrow{AlCl_3} \underset{p\text{-Methylacetophenone}}{p\text{-}CH_3C_6H_4COCH_3} + CH_3COOH$$

$$\underset{\text{Naphthalene}}{C_{10}H_8} + CH_3COCl \xrightarrow[C_6H_5NO_2]{AlCl_3} \underset{\text{Methyl β-naphthyl ketone (main product)}}{C_{10}H_7COCH_3} + HCl$$

$$C_6H_6 + \underset{n\text{-Butyryl chloride}}{CH_3CH_2CH_2COCl} \xrightarrow{AlCl_3} \underset{\text{Butyrophenone}}{C_6H_5COCH_2CH_2CH_3} + HCl$$

$$C_6H_5Br + (CH_3CO)_2O \xrightarrow{AlCl_3} \underset{p\text{-Bromoacetophenone}}{p\text{-}BrC_6H_4COCH_3} + CH_3COOH$$

$$C_6H_6 + \underset{\text{Benzoyl chloride}}{C_6H_5COCl} \xrightarrow{AlCl_3} \underset{\text{Benzophenone}}{C_6H_5COC_6H_5} + HCl$$

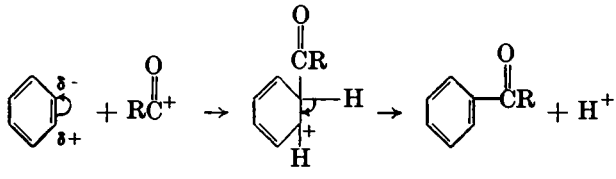
A further example is given below illustrating the use of a dibasic anhydride (succinic anhydride) : the succinoylation reaction is a valuable one since it leads to aroyl carboxylic acids and ultimately to polynuclear hydrocarbons. This general scheme of synthesis of substituted hydrocarbons through the use of succinic anhydride is sometimes called the **Haworth reaction.** Thus α-tetralone (see below) may be reduced by the Clemmensen method to tetralin (tetrahydronaphthalene) and the latter converted into naphthalene either catalytically or by means of sulphur or selenium (compare Section, VI,33).

The *mechanism* of acylation with acyl halides is usually regarded as involving the acyl cation (acyl carbonium or acylium ion) :

$$RCOCl + AlCl_3 \longrightarrow RCCl{=}O^+,AlCl_3^- \text{ (oxonium complex)}$$

$$RCCl{=}O^+,AlCl_3^- \rightleftharpoons [RCO]^+[AlCl_4]^-$$

$$RCOCl + AlCl_3 \longrightarrow [RCO]^+[AlCl_4]^- \rightleftharpoons [RCO]^+ + [AlCl_4]^-$$



$$H^+ + [AlCl_4]^- \longrightarrow HCl + AlCl_3$$

It is probable that, in general, acylation also occurs by the oxonium complex:

$$RCCl{=}O^+,AlCl_3^- + ArH \longrightarrow RCAr{=}O,AlCl_3 + HCl$$

With acid anhydrides, an acyl chloride is probably formed first :

$$(RCO)_2O + 2AlCl_3 \longrightarrow RCOCl,AlCl_3 + RCO.O.AlCl_2$$

Benzophenone is more conveniently prepared from benzene and excess of carbon tetrachloride :

$$2C_6H_6 + CCl_4 \xrightarrow{AlCl_3} \underset{\text{Benzophenone dichloride}}{C_6H_5CCl_2C_6H_5} \xrightarrow{H_2O} \underset{\text{Benzophenone}}{C_6H_5COC_6H_5} + 2HCl$$

2. By catalytic reduction of αβ-unsaturated ketones, prepared from aldehydes by the Claisen - Schmidt reaction (see under *Aromatic Aldehydes*), for example :

$$\underset{\text{Benzalacetophenone}}{C_6H_5CH{=}CHCOC_6H_5} + H_2 \xrightarrow{Pt} \underset{\text{Benzylacetophenone}}{C_6H_5CH_2CH_2COC_6H_5}$$

3. By dropping an aromatic acid either alone or mixed with an aliphatic acid into a tube containing a thoria catalyst deposited on pumice and heated to 400–450°. This method is generally employed for the preparation of mixed aromatic - aliphatic ketones. Excess of the aliphatic acid is usually present since this leads to by-products which are easily separated and also tends to increase the yield of the desired ketone at the expense of the symmetrical ketone of the aromatic acid. Thus :—

$$\underset{\text{Phenylacetic acid}}{C_6H_5CH_2COOH} + \underset{\text{Aliphatic acid}}{RCOOH} \xrightarrow{ThO_2} \underset{\text{Benzyl alkyl ketone}}{C_6H_5CH_2COR}$$

The by-products are formed in accordance with the following schemes :—

$$2RCOOH \xrightarrow{ThO_2} R_2CO \text{ (dialkyl ketone)} + CO_2 + H_2O$$

$$2C_6H_5CH_2COOH \xrightarrow{ThO_2} (C_6H_5CH_2)_2CO \text{ (dibenzyl ketone)} + CO_2 + H_2O$$

The dibenzyl ketone has a very high b.p. (*ca.* 200°/21 mm.) and this remains in the flask when the unsymmetrical ketone has been removed by distillation. The dialkyl ketone has a comparatively low b.p. and is therefore easily removed by fractionation under normal pressure ; acetone is most simply separated by washing with water. In this way **methyl benzyl ketone** ($R = CH_3$), **ethyl benzyl ketone** ($R = CH_3CH_2$) and ***n*-propyl benzyl ketone** ($R = CH_3CH_2CH_2$) are prepared. By using hydrocinnamic acid in place of phenylacetic acid :

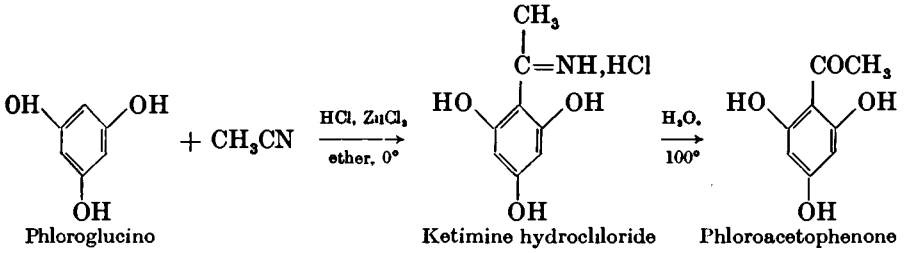
$$\underset{\text{Hydrocinnamic acid}}{C_6H_5CH_2CH_2COOH} + \underset{\text{Aliphatic acid}}{RCOOH} \xrightarrow{ThO_2} \underset{\beta\text{-Phenylethyl alkyl ketone}}{C_6H_5CH_2CH_2COR}$$

methyl β-phenyl ethyl ketone ($R = CH_3$), **ethyl β-phenylethyl ketone** ($R = CH_3CH_2$) and ***n*-propyl β-phenylethyl ketone** ($R = CH_3CH_2CH_2$) are obtained.

4. By the condensation of a nitrile with a phenol or phenol ether in the presence of zinc chloride and hydrogen chloride : a hydroxyaryl- or alkoxyaryl-ketone is produced. The procedure is termed the **Hoesch reaction** and is clearly an extension of the Gattermann aldehyde reaction (Section **IV,121**). The reaction gives the best results with polyhydric phenols and their ethers : with simple monohydric phenols the imino ester hydrochloride is frequently the sole product for example :

$$C_6H_5OH + CH_3CN \xrightarrow[ZnCl_2]{HCl} C_6H_5O{-}C(CH_3){=}NH,HCl$$

The reaction is illustrated by the following example :



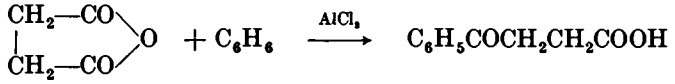
Phloroglucino — Ketimine hydrochloride — Phloroacetophenone

5. By the **Fries reaction.** This is a variant of the Friedel-Craft reaction ; it consists in the conversion of an ester of a phenol to the corresponding *o*- and *p*-hydroxyketone, or a mixture of both, by treatment with anhydrous aluminium chloride :

$$2C_6H_5OCOR \xrightarrow{AlCl_3} o\text{-}HO{-}C_6H_4{-}COR + p\text{-}HO{-}C_6H_4{-}COR$$

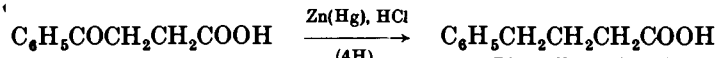
For further details, see Section **IV,107** and discussion preceding Section **IV,101**.

The preparation of the cyclic ketone **α-tetralone** possesses a number of interesting features. Succinic anhydride is condensed with pure benzene in the presence of anhydrous aluminium chloride (slightly over two equivalents; see 1 above) to yield **β-benzoylpropionic acid**:



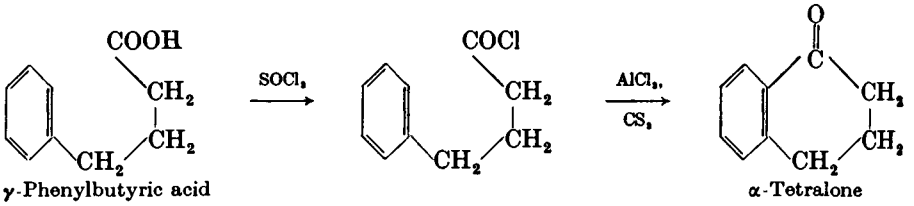
Succinic anhydride — β-Benzoylpropionic acid

The latter is reduced by *Clemmensen's method* in the presence of a solvent immiscible with the hydrochloric acid (toluene);



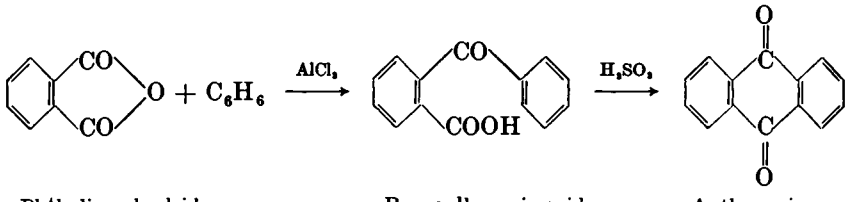
γ-Phenylbutyric acid

The **γ-phenylbutyric acid** is cyclised to α-tetralone by converting it into the acid chloride with thionyl chloride or phosphorus pentachloride and then an intramolecular Friedel and Crafts reaction is carried out:



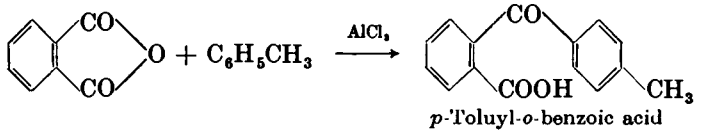
γ-Phenylbutyric acid — α-Tetralone

The **synthesis of anthraquinone** is instructive. Phthalic anhydride condenses with benzene in the presence of aluminium chloride (slightly more than two equivalents, see 1 above) to yield ***o*-benzoylbenzoic acid**, and the latter is heated with concentrated sulphuric acid:

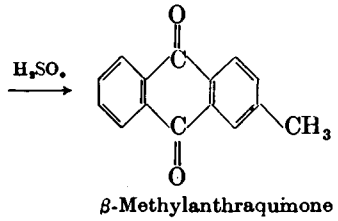


Phthalic anhydride — *o*-Benzoylbenzoic acid — Anthraquinone

Toluene similarly yields **β-methylanthraquinone**:

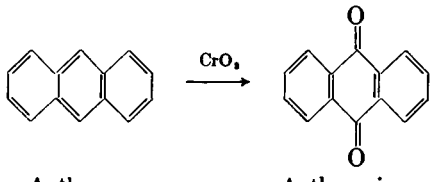


p-Toluyl-*o*-benzoic acid



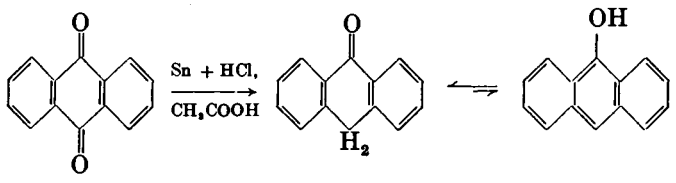
β-Methylanthraquinone

Anthraquinone may also be prepared by the oxidation of pure anthracene with a solution of chromium trioxide in glacial acetic acid :



Anthracene Anthraquinone

Reduction of anthraquinone with tin and concentrated hydrochloric acid in the presence of boiling glacial acetic acid gives **anthrone** ; this substance (keto form) under certain conditions passes into the enol form, **anthranol** :

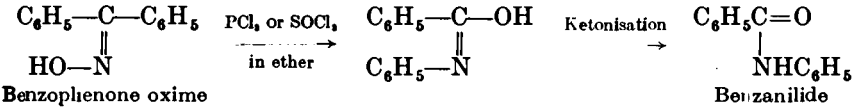


Anthraquinone Anthrone Anthranol

Benzophenone condenses with hydroxylamine hydrochloride in the presence of excess of sodium hydroxide solution to yield **benzophenone oxime**, m.p. 142° :

$$(C_6H_5)_2CO + H_2NOH,HCl + NaOH \longrightarrow (C_6H_5)_2C{=}NOH + NaCl + 2H_2O$$

By treatment of this oxime with phosphorus pentachloride or thionyl chloride in ether solution, smooth conversion into benzanilide, m.p. 163°, results. The change of any oxime into a substituted amide under the conditions mentioned is usually termed the **Beckmann rearrangement.** The above example may be represented :



Benzophenone oxime Benzanilide

IV,136. ACETOPHENONE

Method 1 (with acetyl chloride). Equip a dry 500 ml. round-bottomed or bolt-head flask with a reflux condenser, and fit the top of the condenser with a two-hole cork, one opening for a separatory funnel and the other for a delivery tube connected to an inverted funnel which dips *just* below the surface of about 200 ml. of water in a beaker (compare Fig. *II*, *13*, 8). Place 40 g. of anhydrous, finely-powdered aluminium chloride (see Section **IV,2**) and 88 g. (100 ml.) of dry A.R. benzene in the flask and cool the latter in a bath of *cold* water (*not* ice water since benzene may crystallise). Through the separatory funnel at the top of the condenser add 29 g. (27 ml.) of redistilled acetyl chloride slowly during half an hour and shake the flask frequently to ensure thorough mixing of the

contents. When all the acetyl chloride has been introduced, heat the flask on a water bath at 50° for 1 hour in order to complete the reaction: much hydrogen chloride is evolved, which is absorbed by the water. Cool and pour the reaction mixture into about 250 ml. of water and a little crushed ice contained in a 750 ml. flask; decomposition occurs with the evolution of heat and a dark oil (largely a solution of acetophenone in benzene) separates on the surface. Cork the flask and shake to complete the decomposition; if any solid remains undissolved, add a little concentrated hydrochloric acid to dissolve it. Pour the mixture into a separatory funnel, run off and discard the lower layer, wash the benzene layer with dilute sodium hydroxide solution (to remove the hydrogen chloride), then with water, and dry over anhydrous magnesium sulphate or calcium chloride. Recover the solvent by distillation from a boiling water bath; use the apparatus shown in Fig. *II*, *13*, 4 (100 ml. distilling flask). When most of the benzene has been removed, replace the dropping funnel by a 360° thermometer and the water condenser by short air condenser (Fig. *II*, *13*, 2). Continue the distillation by careful heating over a gauze or, better, in an air bath (Fig. *II*, *5*, 3)—*CAUTION*: there may be some benzene in the residual oil—and collect the acetophenone at 195–202° (pure acetophenone boils at 201°); the colourless oil crystallises on cooling in ice and has m.p. 20°. The yield is 27 g.

Method 2 (**with acetic anhydride**). Proceed exactly as in *Method 1*, but use 80 g. of powdered, anhydrous aluminium chloride, 108 g. (123 ml.) of dry A.R. benzene, and 26 g. (24 ml.) of redistilled acetic anhydride (1). Add the acetic anhydride during half an hour whilst the contents of the flask are thoroughly shaken; much heat is evolved in the reaction. Heat on a boiling water bath for 30 minutes (or until the evolution of hydrogen chloride almost ceases) to complete the reaction, cool, and pour the contents of the flask into a mixture of 150 g. of crushed ice and 150 ml. of concentrated hydrochloric acid contained in a beaker or flask. Stir or shake until all the aluminium salts are dissolved. Transfer the mixture to a separatory funnel, add 25–30 ml. of ether, shake and separate the upper (largely benzene) layer. Extract the aqueous layer with 25 ml. of ether and add this to the benzene solution. Wash the combined benzene and ether extracts with 50 ml. of 10 per cent. sodium hydroxide solution (or until the washings remain alkaline), then with water, separate the organic layer and dry it with anhydrous magnesium sulphate or calcium chloride. Remove the ether and benzene and isolate the acetophenone, b.p. 199–202° (2), as in *Method 1*. The yield is 25 g.

Notes.

(1) An alternative apparatus for conducting the preparation by both methods utilises a two-way adapter as in Fig. *II*, *13*, 9. The preparation may be carried out more conveniently in a three-necked flask provided with a mechanical stirrer; full details are given below under *p*-methylacetophenone.

(2) The b.p. under reduced pressure is 88–89°/16 mm. It solidifies on cooling: m.p. 20°.

Cognate Preparations

***p*-Methylacetophenone.** In a 1 litre three-necked flask, equipped with a separatory funnel carrying a calcium chloride (or cotton wool)

guard tube, a mercury-sealed mechanical stirrer, and a double surface reflux condenser attached to a gas absorption device (Fig. *II*, *8*, 1, *c*), place 150 g. of finely-powdered, anhydrous aluminium chloride and 253 ml. of sodium-dried toluene (free from sulphur compounds; see Section **II**,47,*16*). Set the stirrer in motion and add 51 g. (47·5 ml.) of redistilled acetic anhydride slowly through the separatory funnel; the addition requires 15 minutes, during which time the temperature rises to about 90° and much hydrogen chloride is evolved. Heat the mixture on a water bath, with stirring, for 30 minutes or until there is practically no evolution of gas. Cool the reaction mixture to room temperature and pour it into a mixture of 300 g. of crushed ice and 300 ml. of concentrated hydrochloric acid: stir until the aluminium salts dissolve completely. Separate the toluene layer, wash it with water, then with 10 per cent. sodium hydroxide solution until the washings remain alkaline, and finally with water: dry over a little anhydrous magnesium sulphate. Distil the residue from a Claisen flask with fractionating side arm (Figs. *II*, *24*, 2-5) at atmospheric pressure until the temperature rises to about 125°, then allow to cool and distil under reduced pressure. Collect the *p*-methylacetophenone at 93-94°/7 mm. (the b.p. under atmospheric pressure is 225°); the yield is 58 g.

Methyl β-naphthyl ketone (β-Acetonaphthalene). * Equip a 1 litre three-necked flask with a mercury-sealed mechanical stirrer and a dropping funnel. Place 64 g. of resublimed naphthalene and 350 g. (291 ml.) of pure nitrobenzene in the flask and stir until dissolved. To the homogeneous solution add 43·5 g. (38·5 ml.) of redistilled acetyl chloride. Cool to − 5° in a freezing mixture of ice and salt and introduce, whilst stirring vigorously, 73·5 g. of finely-powdered, anhydrous aluminium chloride in small portions during 90 minutes; do not allow the temperature to rise above 0°. The aluminium chloride dissolves and a deep green solution results. Remove the stirrer from the central aperture and replace it by a solid rubber stopper: into the side necks of the flask fit respectively a drawn-out capillary tube and a tube leading through a filter flask trap and a manometer to a water filter pump. Reduce the pressure to 15–20 mm. (take adequate precautions against collapse of the flask); hydrogen chloride is copiously evolved and a vigorous ebullition occurs in the mixture. When no more gas is evolved, add an excess of crushed ice and separate the nitrobenzene layer. Wash the latter successively with two 100 ml. portions of dilute hydrochloric acid and 100 ml. of 5 per cent. sodium carbonate solution. Use either of the following methods for isolating the pure β-acetonaphthalene from the accompanying α-isomer (about 10 per cent.)

1. Steam distil from a 1·5 litre three-necked flask until the odour of nitrobenzene is no longer perceptible in the distillate (6–12 hours). Extract the cold residue with three 100 ml. portions of ether, dry the combined extracts with anhydrous magnesium sulphate, and distil off the ether. The residue solidifies and consists of almost pure methyl β-naphthyl ketone, m.p. 52°; the yield is 30 g. Upon recrystallisation from glacial acetic acid, the m.p. is raised to 54°.

* For a more detailed discussion of this reaction, see Section IV,164, *Note 1.*

2. Distil the dry (anhydrous magnesium sulphate) nitrobenzene solution under reduced pressure. Nitrobenzene passes over at 95–100°/16 mm. and the temperature then rises rapidly to 170°/15 mm.; collect the fraction of b.p. 170–180°/15 mm. Transfer whilst still liquid to a porcelain basin; it solidifies on cooling. Spread it on a porous tile to absorb the small proportion of liquid α-ketone which is present: the resulting yield of crude methyl β-naphthyl ketone, m.p. 40–42°, is 50 g. Two recrystallisations from glacial acetic acid (or from glacial acetic acid - water) give the almost pure β-ketone, m.p. 53°.

IV,137. BUTYROPHENONE

Equip a 1500 ml. three-necked flask with an efficient mercury-sealed stirrer, a separatory funnel protected by a calcium chloride (or cotton wool) tube, and a double surface reflux condenser attached to a gas absorption device (Fig. *II*, *8*, 1, *c*). Weigh out 140 g. of finely-powdered, anhydrous aluminium chloride under sodium-dried A.R. benzene, and transfer the solid to the flask already containing 231 g. (263 ml.) of anhydrous A.R. benzene. Place 105 g. (102 ml.) of *n*-butyryl chloride, b.p. 100–102° (Section **III,87**) in the separatory funnel, run in 3–4 ml. into the flask and stir vigorously. Warm the flask gently to start the reaction (*i.e.*, until hydrogen chloride is evolved), remove the source of heat, and continue the addition during 2 hours. The reaction mixture darkens considerably. Reflux for 30 minutes to complete the reaction and allow to cool. Transfer the reaction mixture to a large separatory funnel and allow it to " drip " into about 2 litres of cold water in a 4-litre beaker, cooled externally in an ice bath, and vigorously agitated with an efficient mechanical stirrer. Separate the upper oily layer, wash it with 10 per cent. sodium hydroxide solution, then with water, and dry over anhydrous magnesium sulphate. Remove the benzene (Fig. *II*, *13*, 4, but use a 150 ml. Claisen flask), and distil the residue through an air condenser from an air bath. Collect the butyrophenone (a colourless liquid) at 227–230°. The yield is 75 g.

Cognate Preparation

Propiophenone $C_6H_5COCH_2CH_3$. Use 231 g. (263 ml.) of sodium-dried A. R. benzene, 140 g. of anhydrous aluminium chloride and 90 g. (84·5 ml.) of propionyl chloride (prepared from propionic acid; compare Section **III,87**). The yield of propiophenone, b.p. 214–217°, is 78 g.

An improved yield is obtained by the following process. Add a mixture of 75 g. (70·5 ml.) of propionyl chloride and 90 g. (103 ml.) of sodium-dried A.R. benzene to a vigorously stirred suspension of 75 g. of finely-powdered anhydrous aluminium chloride in 100 ml. of dry carbon disulphide. Then introduce more of the aluminium chloride (about 15 g.) until no further evolution of hydrogen chloride occurs. The yield of propiophenone, b.p. 123°/25 mm., is about 90 g.

IV,138. *p*-BROMOACETOPHENONE

In a 1-litre three-necked flask, equipped as in Section **IV,137**, place 78·5 g. (52·5 ml.) of dry bromobenzene (Section **IV,18**), 200 ml. of dry

carbon disulphide (*CAUTION :* see Section **II,14**) and 150 g. of finely-powdered, anhydrous aluminium chloride. Stir the mixture and heat on a water bath until gentle refluxing commences ; add 51 g. (47·5 ml.) of redistilled acetic anhydride slowly through the dropping funnel (30–60 minutes). Maintain gentle refluxing during the addition of the acetic anhydride and for 1 hour afterwards. Distil off most of the carbon disulphide on a water bath (Fig. *II*, *41*, 1 but with stirrer in position in the central aperture), allow the reaction mixture to cool somewhat and *while still warm* pour it slowly with stirring into a mixture of 500 g. of crushed ice and 300 ml. of concentrated hydrochloric acid. Decompose any residue in the flask and add it to the main product. Extract with 150 ml. and 100 ml. portions of benzene or ether, wash the combined extracts twice with water, once with 10 per cent. sodium hydroxide solution and twice with water. Dry the extract with anhydrous magnesium sulphate or calcium chloride, remove the solvent (Fig. *II*, *13*, 4 but replace the distilling flask by a Claisen flask with fractionating side arm, Figs. *II*, *24*, 2–5), and distil the residue under reduced pressure. The *p*-bromoacetophenone boils at 130°/15 mm. or at 117°/7 mm. and a 3° fraction should be collected ; it crystallises to a white solid, m.p. 50°. The yield is 75 g.

The b.p. under atmospheric pressure has been given as 255·5°/736 mm.

COGNATE PREPARATIONS

These are all prepared in the same manner, viz., 0·5 mol of the derivative of the aromatic hydrocarbon, 150 g. of finely-powdered anhydrous aluminium chloride and 0·5 mol of the acid anhydride. Thus :—

***p*-Chloroacetophenone.** From 56 g. (51 ml.) of chlorobenzene (Section **IV,17**). The yield of product, b.p. 124–126°/24 mm., m.p. 20–21°, is 60 g. The b.p. under atmospheric pressure is 237°.

***p*-Methoxyacetophenone.** From 54 g. (54·5 ml.) of anisole (Section **IV,104**). The yield of *p*-methoxyacetophenone, b.p. 139°/15 mm., is 70 g. The b.p. under atmospheric pressure is 265°.

IV,139. BENZOPHENONE

Method 1. Into the three necks of a 1 litre three-necked flask fit respectively a double surface reflux condenser, an efficient mechanical stirrer, and through a two-hole cork, a separatory funnel and a thermometer. Attach a trap (Fig. *II*, *8*, 1, *c*) to the top of the condenser for absorbing the hydrogen chloride evolved. Place 91 g. of powdered anhydrous aluminium chloride and 200 ml. of dry carbon tetrachloride (1) in the flask, surround the latter with an ice bath, and, when the temperature has fallen to 10–15°, introduce 10 ml. of sodium-dried A.R. benzene. The reaction commences immediately (hydrogen chloride is evolved and the temperature rises) ; add salt to the ice bath in order to get more efficient cooling. When the temperature commences to fall after the reaction has once started, add a mixture of 110 ml. of dry A.R. benzene and 110 ml. of dry carbon tetrachloride at such a rate that the temperature is maintained between 5° and 10° (2). The addition usually requires 1-2 hours ; continue the stirring for a further 3 hours while maintaining the temperature at 10°, and then allow to stand overnight.

Immerse the flask in ice, start the stirrer, and add about 500 ml. of water through the separatory funnel; the excess of carbon tetrachloride usually refluxes during the addition. Distil off as much as possible of the carbon tetrachloride on a water bath, and then distil the mixture with steam (Fig. *II*, *41*, 1) during 30 minutes to remove the residual carbon tetrachloride (3) and to hydrolyse the benzophenone dichloride to benzophenone. Separate the upper benzophenone layer and extract the aqueous layer with 40 ml. of benzene. Dry the combined benzene extract and benzophenone with anhydrous magnesium sulphate. Remove the benzene with the aid of an air bath (Fig. *II*, *13*, 4 but replace the distilling flask by a 200 ml. Claisen flask with fractionating side arm, Figs. *II*, *24*, 2–5) until the temperature rises to about 90°, allow to cool somewhat, and distil under diminished pressure. Collect the benzophenone at 187–190°/15 mm.; it solidifies to a white solid, m.p. 47–48°, on cooling. The yield is 105 g.

Notes.

(1) The carbon tetrachloride may be dried by distilling the commercial product and rejecting the first 10 per cent. of the distillate.

(2) Below 5°, the reaction is too slow; above 10°, appreciable amounts of tarry matter are formed.

(3) About 220 ml. of carbon tetrachloride are recovered; this contains a little benzene, but may be used, after drying and distilling, in another run.

Method 2. Into a 500 ml. round-bottomed flask place 120 ml. of dry A.R. benzene, and 35 g. (29 ml.) of redistilled benzoyl chloride. Weigh out 30 g. of finely-powdered, anhydrous aluminium chloride into a dry corked test-tube, and add the solid, with frequent shaking, during 10 minutes to the contents of the flask. Fit a reflux condenser to the flask, and heat on a water bath for 3 hours or until hydrogen chloride is no longer evolved. Pour the contents of the flask while still warm into a mixture of 200 g. of crushed ice and 100 ml. of concentrated hydrochloric acid. Separate the upper benzene layer (filter first, if necessary), wash it with 50 ml. of 5 per cent. sodium hydroxide solution, then with water, and dry with anhydrous magnesium sulphate. Isolate the benzophenone as in *Method 1*. The yield is 30 g.

IV,140. BENZYLACETOPHENONE

Place a solution of 10·4 g. of benzalacetophenone, m.p. 57° (Section **IV,130**) in 75 ml. of pure ethyl acetate (Section **II,47**,*19*) in the reaction bottle of the catalytic hydrogenation apparatus and add 0·2 g. of Adams' platinum oxide catalyst (for full experimental details, see Section **III,150**). Displace the air with hydrogen, and shake the mixture with hydrogen until 0·05 mol is absorbed (10–25 minutes). Filter off the platinum, and remove the ethyl acetate by distillation. Recrystallise the residual benzylacetophenone from about 12 ml. of alcohol. The yield of pure product, m.p. 73°, is 9 g.

IV,141. METHYL BENZYL KETONE

Use the apparatus described in Section **III,72** and adjust the furnace for a working temperature of 400–450°. Although a manganous oxide catalyst gives satisfactory results, thoria is more convenient in practice.

Preparation of thoria catalyst. Dissolve 276 g. of commercially pure thorium nitrate in the minimum volume of water (*ca.* 450 ml.) in a large beaker, and add slowly a solution of 106 g. of A.R. anhydrous sodium carbonate in 400 ml. of water with mechanical stirring. Allow the thorium carbonate to settle, decant as much as possible of the mother liquor, and wash it once by decantation with 500 ml. of water. Make the resulting moist precipitate into a thick paste with distilled water and stir in pumice (4–8 mesh) until most of the suspension appears to be absorbed. Dry the impregnated pumice in quantities of approximately 200 g. Heat in a large evaporating dish upon an electric hot plate and stir constantly with a thick glass rod ; stop the heating when the fragments of pumice no longer stick one to another. Sieve the resulting pumice ; 250 g. of a white powder (largely thorium carbonate but containing some oxide) are recovered, and can be used for impregnating more pumice. The total weight of pumice catalyst thus prepared is about 1400 g. ; the exact weight will, of course, depend upon the grade of the pumice.

Preparation of the ketone. Fill the tube with thoria catalyst, but insert small loose plugs of glass wool after each approximately 15 cm. column of catalyst ; the latter device will reduce the danger of carbonisation blocking the tube. Set up the apparatus as in Fig. *III*, *72*, 1 and heat the tube to 400–450° in a slow stream of nitrogen when carbon dioxide (and generally oxides of nitrogen) are evolved ; 6–12 hours are usually required for the complete decomposition of the thorium salt deposited upon the pumice. Place a solution of 170 g. of pure phenylacetic acid (m.p. 77°) in 225 g. of glacial acetic acid in the funnel, and adjust its rate of flow into the catalyst tube to 1 drop every 2 or 3 seconds. Also pass a slow stream of carbon dioxide or nitrogen (1 bubble per second) through the side tap in order to keep the gases in motion ; the rate of flow is estimated by passing the inert gas through a concentrated sulphuric acid wash bottle or " bubbler " before it enters the furnace. When all the acid mixture has passed through the catalyst tube, separate the lower aqueous layer of the product and treat the organic layer with 10–20 per cent. sodium hydroxide solution until the washings are alkaline to litmus and then twice with water. Extract the aqueous layer twice with 50 ml. portions of benzene, wash the extracts successively with sodium hydroxide solution (until alkaline) and water, and add the resulting benzene solution to the main product. Dry with anhydrous magnesium sulphate, remove the benzene under atmospheric pressure, and distil the residue under reduced pressure preferably from a Claisen flask with fractionating side arm (Figs. *II*, *24*, 2–5). Collect the methyl benzyl ketone at 102–102·5°/20 mm. ; the yield is 85 g. The residue in the flask is **dibenzyl ketone** ; it may be purified by transferring to a smaller flask and redistilling (b.p. 200°/21 mm. ; m.p. 34–35°).

Cognate Preparations

Ethyl benzyl ketone. Use 204 g. of phenylacetic acid (m.p. 77°) and 333 g. (335·5 ml.) of propionic acid (b.p. 139–141°), but omit the extraction with benzene when working up the distillate. Distil the dried

product from a 500 ml. round-bottomed flask through an efficient fractionating column {*e.g.*, a Widmer column (Fig. *II*, *17*, 1) or a well-lagged Hempel column filled with $\frac{3}{16}''$ or $\frac{1}{4}''$ glass rings (Fig. *II*, *15*, 3) or a modified Hempel column (Fig. *II*, *15*, 5)}. Collect the diethyl ketone at 99·5–102·5° (160 g.), and when the temperature rises to 130° (b.p. 103-130° : 7 g.) transfer the residue to a 250 ml. Claisen flask and distil under reduced pressure. The ethyl benzyl ketone passes over mainly at 118–123°/22 mm. (105 g.); the residue of high boiling point (34 g.) consists largely of dibenzyl ketone. Pure ethyl benzyl ketone may be obtained by redistilling the fraction b.p. 118–123°/22 mm. and collecting the fraction of b.p. 113-115°/17 mm.

***n*-Propyl benzyl ketone.** Use 204 g. of pure phenylacetic acid and 396 g. (414 ml.) of *n*-butyric acid (b.p. 161–164°). Upon working up as for ethyl benzyl ketone 180 g. of di-*n*-propyl ketone, b.p. 140–145° (mainly 143–145°), 108 g. of crude *n*-propyl benzyl ketone, b.p. 240-260°, and 49 g. of crude dibenzyl ketone (residue in flask) are obtained. Redistil the fraction of b.p. 240–260° and collect the *n*-propyl benzyl ketone at 243-247° (the pure ketone boils at 244°).

Methyl β-phenylethyl ketone. Use 100 g. of hydrocinnamic acid (m.p. 49–50°) (Section **IV,163**) and 160 g. of glacial acetic acid. The yield of methyl β-phenylethyl ketone, b.p. 230–235°, is 70 g. (the pure ketone boils at 234°.

Ethyl β-phenylethyl ketone. Use 100 g. of pure hydrocinnamic acid and 200 g. (201·5 ml.) of pure propionic acid. Fractionation of the distillate yields 70 g. of diethyl ketone (b.p. 100-102°), 72 g. of ethyl β-phenylethyl ketone (b.p. 245–249°; the pure ketone boils at 248°), and 18 g. of crude di-β-phenylethyl ketone (high b.p. residue).

***n*-Propyl β-phenylethyl ketone.** Use 100 g. of pure hydrocinnamic acid and 235 g. (245·5 ml.) of pure *n*-butyric acid. Upon working up as for ethyl benzyl ketone the following yields are obtained: 98 g. of di-*n*-propyl ketone, b.p. 140–144°; 65 g. of *n*-propyl β-phenylethyl ketone, b.p. 139–143°/17 mm.; and 22 g. of crude di-β-phenylethyl ketone (high b.p. residue). The required ketone, upon redistillation, boils almost completely at 138–139°/16 mm.

IV,142. PHLOROACETOPHENONE

Place 25·2 g. of dry phloroglucinol (1), 16·4 g. (20·9 ml.) of anhydrous acetonitrile (Section **III,111**) (2), 100 ml. of sodium-dried ether and 5 g. of finely-powdered, fused zinc chloride in a 300 ml. bolt-head flask carrying a two-hole rubber stopper into which are fitted a wide gas delivery tube (an inverted thistle funnel is satisfactory) and a calcium chloride (or cotton wool) guard tube. Cool the flask in an ice-salt mixture and pass a rapid stream of dry hydrogen chloride (Section **II,48,*1***) through the solution for 2 hours with occasional shaking. Allow the flask to stand in an ice chest for 24 hours, and again pass dry hydrogen chloride into the pale orange mixture for a further 2 hours. Stopper the flask and leave it in an ice chest (or refrigerator) for 3 days. A bulky orange-yellow precipitate of the ketimine hydrochloride is formed. Decant the ether

and wash the solid with two 25 ml. portions of anhydrous ether. Transfer the solid with the aid of about 1 litre of hot water to a 2 litre round-bottomed flask provided with a reflux condenser. Boil the yellow solution vigorously over a wire gauze for 2 hours, allow to cool somewhat, add 4–5 g. of decolourising carbon, boil the solution for 5 minutes longer, and filter the hot solution with suction through a preheated Buchner funnel. Extract the decolourising carbon with two 100 ml. portions of boiling water and add the filtrate to the main product. Allow to stand overnight, and filter the pale yellow or colourless needles of phloroacetophenone at the pump, dry at 120° to remove the molecule of water of crystallisation, and preserve in a tightly-stoppered bottle. The yield is 29 g., m.p. 217–219°. This product is pure enough for many purposes, but may be obtained absolutely pure by recrystallisation from hot water (35 ml. per gram); m.p. 218–219°.

Notes.

(1) Phloroglucinol contains two molecules of water of crystallisation; these are removed by heating for 12 hours at 120°.

(2) The acetonitrile may be dried over anhydrous calcium sulphate or by distilling from phosphoric oxide.

IV,143. α-TETRALONE

β-Benzoylpropionic acid. Equip a 1 litre three-necked flask with a mechanical stirrer and two efficient reflux condensers, and place in it 175 g. of sodium-dried A.R. benzene and 34 g. of succinic anhydride (Section **III,92**). Stir the mixture and add 100 g. of powdered, anhydrous aluminium chloride all at once. The reaction usually starts immediately —hydrogen chloride is evolved and the mixture becomes hot; if there is no apparent reaction, warm gently. Heat in an oil bath to gentle refluxing, with continued stirring, for half an hour. Allow to cool, immerse the flask in a bath of cold water, and slowly add 150 ml. of water from a separatory funnel inserted into the top of one of the condensers. Introduce 50 ml. of concentrated hydrochloric acid and separate the benzene by steam distillation (Fig. *II*, *41*, 1). Transfer the hot mixture to a 600 ml. beaker; the β-benzoylpropionic acid separates as a colourless oil, which soon solidifies. Cool in ice, filter off the acid at the pump, and wash with 100 ml. of cold dilute hydrochloric acid (1 : 3 by volume) and then with 100 ml. of cold water. Dissolve the crude acid in a solution of 40 g. of anhydrous sodium carbonate in 250 ml. of water by boiling for 10–15 minutes; filter the solution with suction to remove the small amount of aluminium hydroxide and wash with two 25 ml. portions of hot water. Treat the *hot* filtrate with 2 g. of decolourising carbon, stir for 5 minutes and filter at the pump through a preheated Buchner funnel. Transfer the hot filtrate to a 1 litre beaker, cool to about 50°, and cautiously acidify with 65–70 ml. of concentrated hydrochloric acid. Cool to 0° in a freezing mixture of ice and salt, filter, wash thoroughly with cold water, dry for 12 hours upon filter papers, and then to constant weight at 45–50°. The yield of practically pure β-benzoylpropionic acid, m.p. 115°, is 57 g.

γ-Phenylbutyric acid. Prepare amalgamated zinc from 120 g. of zinc wool contained in a 1-litre round-bottomed flask (Section **III,50,** *13*), decant the liquid as completely as possible, and add in the following order 75 ml. of water, 180 ml. of concentrated hydrochloric acid, 100 ml. of pure toluene (1) and 50 g. of β-benzoylpropionic acid. Fit the flask with a reflux condenser connected to a gas absorption device (Fig. *II*, *8*, 1, *c*), and boil the reaction mixture vigorously for 30 hours; add three or four 50 ml. portions of concentrated hydrochloric acid at approximately six hour intervals during the refluxing period in order to maintain the concentration of the acid. Allow to cool to room temperature and separate the two layers. Dilute the aqueous portion with about 200 ml. of water and extract with three 75 ml. portions of ether. Combine the toluene layer with the ether extracts, wash with water, and dry over anhydrous magnesium or calcium sulphate. Remove the solvents by distillation under diminished pressure on a water bath (compare Fig. *II*, *37*, 1), transfer the residue to a Claisen flask, and distil under reduced pressure (Fig. *II*, *19*, 1). Collect the γ-phenylbutyric acid at 178–181°/19 mm.; this solidifies on cooling to a colourless solid (40 g.) and melts at 47-48°.

Note.

(1) The procedure for the Clemmensen reduction is somewhat different from that previously described (Sections III,9, and IV,6); the chief modification of moment is the use of toluene. The concentration of organic material in the aqueous layer is considerably reduced; this results in less high b.p. products being formed, thus leading to a better yield of a purer product.

α-Tetralone. Place 32 g. of γ-phenylbutyric acid and 32 g. (20 ml.) of pure thionyl chloride (Section **II,49,***6*) in a 500 ml. round-bottomed flask, fitted with a reflux condenser connected at its upper end by a tube leading to a gas absorption trap (Fig. *II*, *8*, 1, *c*). Heat the mixture cautiously on a water bath until the acid melts, remove from the water bath, and allow the reaction to proceed. After about 30 minutes hydrogen chloride is no longer evolved: complete the reaction by warming on a water bath for 10 minutes. Connect the flask to a water pump (through an intermediate empty wash bottle to act as a trap), and remove the excess of thionyl chloride *completely* by first heating on a water bath for 10 minutes and then for 2–3 minutes over a small flame. The resulting γ-phenylbutyryl chloride (a nearly colourless liquid) requires no further purification.

To the cold acid chloride add 175 ml. of pure carbon disulphide, cool in ice, add 30 g. of powdered anhydrous aluminium chloride in one lot, and immediately attach a reflux condenser. When the evolution of hydrogen chloride ceases (about 5 minutes), slowly warm the mixture to the boiling point on a water bath. Reflux for 10 minutes with frequent shaking; the reaction is then complete. Cool the reaction mixture to 0°, and decompose the aluminium complex by the cautious addition, with shaking, of 100 g. of crushed ice. Then add 25 ml. of concentrated hydrochloric acid, transfer to a 2-litre round-bottomed flask and steam distil, preferably in the apparatus, depicted in Fig. *II*, *41*, 3 since the α-tetralone is only moderately volatile in steam. The carbon disulphide passes over first, then there is a definite break in the distillation, after which the α-tetralone distils completely in about 2 litres of distillate.

Separate the oil, and extract the aqueous layer with three 100 ml. portions of benzene. Combine the oil and benzene extracts, dry with anhydrous magnesium sulphate, remove the solvent, and distil the residue under diminished pressure. Collect the α-tetralone at 105–107°/2 mm. (or at 135–137°/15 mm.). The yield is 23 g.

IV,144. o-BENZOYLBENZOIC ACID

Equip a 750 ml. three-necked flask with a mercury-sealed mechanical stirrer and a reflux condenser connected with a gas absorption trap (Fig. *II*, *8*, 1, *c*); insert a rubber stopper in the third neck. Place 25 g. of pure phthalic anhydride (see Section **III,170**, *Note 1*) and 100 ml. of sodium-dried A.R. (or thiophene-free) benzene in the flask; start the stirrer and add 50 g. of powdered anhydrous aluminium chloride from a stoppered test-tube in four portions or, alternatively, use the device shown in Fig. *II*, *7*, 12, *c* or *d*. If the reaction does not commence after the addition of the first 12 g. of aluminium chloride, warm for a few seconds on a water bath. Have an ice bath or wet towel in readiness should the reaction become too vigorous. When all the aluminium chloride has been added and the evolution of hydrogen chloride slackens, warm very cautiously on a water bath and ultimately reflux the mixture until the evolution of gas practically ceases. Cool the flask, add crushed ice slowly until the dark mass is completely decomposed, and then run in concentrated hydrochloric acid (35–40 ml.) until the solution clears. Steam distil (Fig. *II*, *41*, 1) to remove the excess of benzene; the residue in the flask, when cooled in ice, largely solidifies and consists of crude *o*-benzoylbenzoic acid. Decant the aqueous solution through a Buchner funnel, wash the residue by decantation with a little cold water, and return the solid, collected on the filter, to the flask. Add a warm solution of 13·0 g. of anhydrous sodium carbonate in 200 ml. of water, and pass steam into the mixture until all the solid material, except particles of aluminium hydroxide and a little tarry material, dissolves; allow to cool slightly and add a few grams of decolourising carbon. Warm and filter the hot solution with suction. Place the filtrate in a 1 litre beaker, cool in ice, and cautiously acidify with concentrated hydrochloric acid while stirring well (16-17 ml. are required). The acid separates as an oil but it soon crystallises on stirring and cooling. Filter when ice cold, and wash with a little water. Dry in the air upon filter paper; the product, which is somewhat efflorescent, consists largely of the monohydrate, m.p. 94°.

To prepare pure anhydrous *o*-benzoylbenzoic acid, dissolve the air-dried (or the moist) product in about 175 ml. of benzene contained in a 500 ml. round-bottomed flask fitted with a reflux condenser and heat on a water bath. Transfer the benzene solution to a separatory funnel, run off any water present, and dry with anhydrous magnesium sulphate. Concentrate the benzene solution to about 75 ml. and add light petroleum. (b.p. 60–80°) to the hot solution until a slight turbidity is produced. Allow to cool spontaneously to room temperature, then cool in ice to about 5°, collect the crystals and dry. The yield of pure, anhydrous *o*-benzoylbenzoic acid, m.p. 128°, is 32 g.

COGNATE PREPARATION

p-Toluyl-o-benzoic acid. Use 25 g. of pure phthalic anhydride, 100 g. (115·5 ml.) of thiophene-free toluene and 50 g. of anhydrous aluminium chloride. The air-dried product consists largely of the monohydrate; this becomes anhydrous upon drying at 100° and melts at 138–139°. The yield of anhydrous *p*-toluyl-*o*-benzoic acid is 39 g. It may be recrystallised from toluene.

IV,145. ANTHRAQUINONE

Method 1. Mix 10 g. of *o*-benzoylbenzoic acid (preceding Section) with 90 g. (46 ml.) of fuming sulphuric acid (20 per cent. SO_3) in a 250 ml. round-bottomed flask protected by a calcium chloride (or cotton wool) guard tube. Heat upon a water bath with occasional shaking for 2 hours. Cool, and pour the reaction mixture into crushed ice contained in a 600 ml. beaker; heat the mixture to the boiling point for a few minutes in order to obtain a more granular product. Filter off the crude anthraquinone at the pump, wash it with hot water, then with a little dilute ammonia solution to remove any unchanged acid, and drain well. Recrystallise the product from boiling glacial acetic acid; filter off the purified crystals, wash with a little alcohol and dry at 100–120°. The yield of pure anthraquinone, m.p. 286°, is 7 g.

COGNATE PREPARATION

β-Methylanthraquinone. Use 10·5 g. of *p*-toluyl-*o*-benzoic acid (preceding Section) and 90 g. (46 ml.) of fuming sulphuric acid (20 per cent. SO_3). Recrystallise the product from alcohol in the presence of a little decolourising carbon. The yield of pure β-methylanthraquinone, m.p. 176°, is 7·5 g.

Method 2. Dissolve 10 g. of finely-powdered, pure anthracene in 110–120 ml. of boiling glacial acetic acid contained in a 500 ml. round-bottomed flask provided with a reflux condenser. Prepare a solution of 20 g. of chromium trioxide in 15 ml. of water and then add 50–75 ml. of glacial acetic acid. Add the chromium trioxide solution slowly (during 1 hour) to the boiling anthracene solution by means of a separatory funnel fitted into the top of the condenser with a grooved cork; boil for a further 15 minutes. Allow the deep green solution to cool and pour it into 500 ml. of cold water. Filter the crude anthraquinone by *gentle* suction, wash with a little hot water, then with a hot *dilute* solution of sodium hydroxide and finally with cold water until the washings are colourless, and drain well. Recrystallise from glacial acetic acid as in *Method 1.* The yield is 11 g., m.p. 286°. Alternatively, dry the crude product in the steam oven, and sublime it from a small evaporating dish (compare Fig. *II*, *45*, 1): beautiful yellow needles are obtained.

IV,146. ANTHRONE

Place 52 g. of anthraquinone, 50 g. of granulated tin and 375 ml. of glacial acetic acid in a 1 litre round-bottomed flask fitted with a reflux condenser. Heat the contents of the flask to boiling and add 125 ml. of

concentrated hydrochloric acid in 10 ml. portions during 2 hours. By this time all the anthraquinone should have passed into solution ; if not, add more tin and hydrochloric acid. Filter the liquid with suction through a sintered glass funnel, and add 50 ml. of water. Cool the solution to about 10° when the anthrone will crystallise out. Filter the crystals at the pump on a Buchner funnel and wash with water. Dry upon filter paper or upon a porous tile : the yield of crude anthrone, m.p. about 153°, is 40 g. Recrystallise from a 3 : 1 mixture of benzene and light petroleum, b.p. 60–80° (10-12 ml. per gram) ; this gives 30 g. of pure anthrone, m.p. 155°.

IV,147. BENZOPHENONE OXIME AND BECKMANN REARRANGEMENT

Place a mixture of 25 g. of benzophenone (Section **IV,139**), 15 g. of hydroxylamine hydrochloride, 50 ml. of rectified spirit and 10 ml. of water in a 500 ml. round-bottomed flask. Add 28 g. of sodium hydroxide (pellet form) in portions with shaking ; if the reaction becomes too vigorous, cool the flask with running tap water. When all the sodium hydroxide has been added, attach a reflux condenser to the flask, heat to boiling and reflux for 5 minutes. Cool, and pour the contents of the flask into a solution of 75 ml. of concentrated hydrochloric acid in 500 ml. of water contained in a 1 litre beaker. Filter the precipitate at the pump, wash thoroughly with cold water, and dry in an electric oven at 40° or in a vacuum desiccator. The yield of benzophenone oxime, m.p. 142°, is 26·5 g. It may be recrystallised from methyl alcohol (4 ml. per gram) but the m.p. is unaffected. The oxime is gradually decomposed by oxygen and traces of moisture into benzophenone and nitric acid ; it should be preserved in a vacuum desiccator filled with pure dry carbon dioxide.

Beckmann rearrangement of benzophenone oxime to benzanilide. Dissolve 2 g. of benzophenone oxime in 20 ml. of anhydrous ether in a small conical flask and add 3 g. of powdered phosphorus pentachloride (or 3 ml. of pure thionyl chloride). Distil off the solvent and other volatile products on a water bath (*CAUTION :* ether), add 25 ml. of water, boil for several minutes and break up any lumps which may be formed. Decant the supernatant liquid, and recrystallise, in the same vessel, from boiling alcohol. The product is benzanilide, m.p. 163° ; confirm this by a mixed m.p. determination with an authentic specimen.

IV,148. REACTIONS AND CHARACTERISATION OF AROMATIC KETONES

Aromatic ketones usually have relatively high boiling points, but distil with little or no decomposition. Many are solids. The vapours generally burn with a smoky flame. They react with the 2 : 4-dinitrophenyll hydrazine reagent (Section **III,74,*l***) or with the phenylhydrazine reagent

(Section **IV,135,5**), but are unaffected by the dimedone reagent (Section **III,70,** *2*). The general reactions are similar to those already given under *Aliphatic Ketones* (Section **III,74**). Owing to their higher molecular weight, such derivatives as oximes and phenylhydrazones are frequently quite satisfactory.

The preparation of crystalline derivatives, including 2 : 4-dinitrophenyl hydrazones, semicarbazones, oximes, phenylhydrazones and *p*-nitrophenylhydrazones can be carried out as described under *Aromatic Aldehydes*, Section **IV,135.**

The melting points of various derivatives of a number of typical aromatic ketones are collected in Table **IV,148.**

TABLE IV,148. **AROMATIC KETONES**

Ketone	B.P.	M.P.	2 : 4-Dinitrophenylhydrazone	Semicarbazone	Oxime	Phenylhydrazone	*p*-Nitrophenylhydrazone	Other Derivatives
Acetophenone	202°	20°	250°(237)	199°	59°	105°	185°	Benzal, 58°
o-Chloroacetophenone	229	—	206	160 (179)	113	—	215	—
m-Chloroacetophenone	228	—	—	232	88	—	176	—
p-Chloroacetophenone	236	20	231	201	95	114	239	—
o-Bromoacetophenone	112°/10	—	—	177	—	—	—	—
m-Bromoacetophenone	131°/16	8	—	238	—	—	—	—
p-Bromoacetophenone	256	51	230	208	129	126	—	—
p-Iodoacetophenone	—	85	—	—	—	—	—	—
o-Methylacetophenone (1)	216	—	159	203	61	—	—	—
m-Methylacetopheneone	220	—	207	198	55	—	—	—
p-Methylacetophenone	224	28	258	205	88	96	198	—
o-Hydroxyacetophenone	215	—	—	210	117	110	—	—
m-Hydroxyacetophenone	—	96	—	195	—	—	—	—
p-Hydroxyacetophenone	—	109	261	199	145	151	—	—
o-Methoxyacetophenone	245	—	—	183	83	114	—	—
m-Methoxyacetophenone	240	—	—	196	—	—	—	—
p-Methoxyacetophenone	258	39	220	198	87	142	—	—
o-Nitroacetophenone	159°/16	—	—	—	—	—	—	—
m-Nitroacetophenone	—	81	228	257	132	135	—	—
p-Nitroacetophenone	—	81	—	—	—	132	—	—
o-Aminoacetophenone	251	20	—	290	109	108	—	—
m-Aminoacetophenone	—	99	—	196	148	—	—	—
p-Aminoacetophenone	294	106	—	250	—	—	—	—
Resacetophenone (2)	—	147	—	218	199	159	—	Dibenzoyl, 81 ; diacetyl, 38
Phloroacetophenone (3)	—	219	—	—	—	—	—	Tribenzoyl, 118 ; triacetyl, 103
Propiophenone (4)	218	19	191	174	53	147	—	—
n-Butyrophenone (5)	230	12	190	188	50	—	—	—
iso-Butyrophenone (6)	222	—	163	181	94	73	—	—
n-Valerophenone (7)	242	—	166	166	52	162	—	—
Benzyl methyl ketone	216	27	156	198	69	87	145	—
Benzyl ethyl ketone	226	—	—	136	—	—	—	—

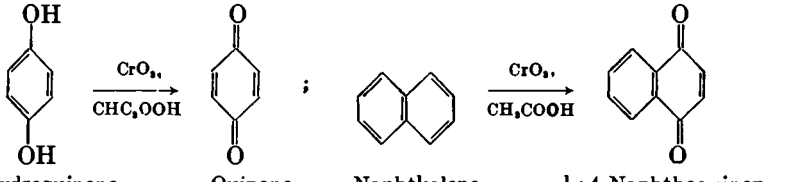
TABLE IV,148. **AROMATIC KETONES (*continued*)**

Ketone	B.P.	M.P.	2 : 4-Dinitrophenylhydrazone	Semicarbazone	Oxime	Phenylhydrazone	*p*-Nitrophenylhydrazone	Other Derivatives
Benzophenone	306°	49°	238°	165°	144°	137°	155°	—
p-Chlorobenzophenone	323	78	185	—	156 (95)	106	—	—
p-Bromobenzophenone	350	82	230	—	169	126	—	—
Desoxybenzoin (8)	320	60	204	148	98	116	163	Benzal, 102°
Dibenzyl ketone	331	35	100	146	125	129	—	Benzal, 162
Phenyl *p*-tolyl ketone	326	60	200	122	154	109	—	—
Di-*p*-tolyl ketone	335	95	229	—	163	100	—	—
Methyl α-naphthyl ketone	302	34	—	229	139	146	—	Picrate, 116 ; benzal, 126
Methyl β-naphthyl ketone	301	54	262	236	145	177	—	Picrate, 85
Benzoin	344	137	245	206	151 (99)	159	—	Benzoyl, 125 ; acetyl, 83
Benzil	347d	95	189	244Di	237	235Di	290	Quinoxaline, 126
Benzalacetone	262	42	227	186	116	157	166	Benzal, 112
Dibenzalacetone (9)	—	112	180	189	143	153	173	Picrate, 114
Benzalacetophenone (10)	347	58	245	168	115	119	—	Picrate, 97
Phenacyl alcohol (11)	—	86	—	146	70	112	—	Benzoyl, 118 ; acetyl, 49
Phenacyl bromide (12)	—	51	—	146	89	—	—	—
p-Bromophenacyl bromide	—	109	—	—	115	—	—	—
α-Hydrindone	242	42	258	233	146	128	235	Benzal, 113
α-Tetralone	129°/12	—	257	217	89 (103)	84	231	Benzal, 105
Fluorenone (13)	341	83	284	—	195	152	269	—
Acenaphthenone	—	121	—	—	175	90	—	Picrate, 113
p-Benzoquinone	—	116	186	243Di	140	—	—	Picrate, 79
1 : 2-Naphthaquinone	—	146	—	184	162	138	235	—
1 : 4-Naphthaquinone	—	125	—	247	198	—	278	—
Anthraquinone	—	285	—	—	224	183	—	—
9 : 10-Phenanthraquinone	—	207	313	—	158	165	245	—

(1) Methyl *o*-tolyl ketone.
(2) 2 : 4-Dihydroxyacetophenone.
(3) 2 : 4 : 6-Trihydroxyacetophenone.
(4) Ethyl phenyl ketone.
(5) *n*-Propyl phenyl ketone.
(6) *iso*-Propyl phenyl ketone.
(7) *n*-Butyl phenyl ketone.
(8) Phenyl benzyl ketone.
(9) Distyryl ketone.
(10) Chalkone.
(11) ω-Hydroxyacetophenone.
(12) ω-Bromoacetophenone.
(13) Diphenylene ketone.

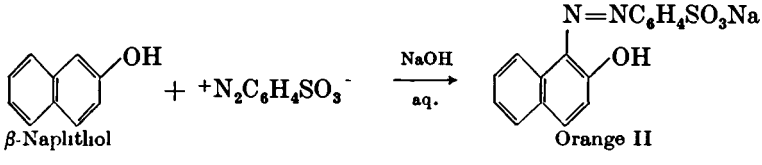
QUINONES

***p*-Benzoquinone** ("*quinone*") is obtained as the end product of the oxidation of aniline by acid dichromate solution. Industrially, the crude product is reduced with sulphur dioxide to hydroquinone, and the latter is oxidised either with dichromate mixture or in very dilute sulphuric acid solution with sodium chlorate in the presence of a little vanadium pentoxide as catalyst. For the preparation in the laboratory, it is best to oxidise the inexpensive hydroquinone with chromic acid or with sodium chlorate in the presence of vanadium pentoxide. Naphthalene may be converted into 1 : 4-naphthoquinone by oxidation with chromic acid.

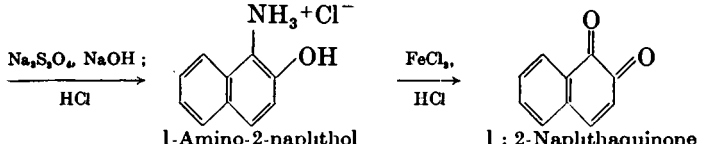


Hydroquinone Quinone Naphthalene 1 : 4-Naphthoquinone

A fairly general procedure consists in coupling a phenol or naphthol with a diazotised amine, reducing the product to an aminophenol or aminonaphthol, and oxidising the hydroxy compound with acid ferric chloride solution. This method is illustrated by the preparation of **β (or 1 : 2)-naphthoquinone** :



β-Naphthol Orange II



1-Amino-2-naphthol hydrochloride 1 : 2-Naphthaquinone

When a solution of, say, 1 g. of hydroquinone in 4 ml. of rectified spirit is poured into a solution of 1 g. of quinone in 30 ml. of water, **quinhydrone** $C_6H_4O_2{,}C_6H_4(OH)_2$, a complex of equimolecular amounts of the two components, is formed as dark green crystals having a glistening metallic lustre, m.p. 172°. In solution, it is largely dissociated into quinone and hydroquinone. Quinhydrone is more conveniently prepared by the partial oxidation of hydroquinone with a solution of iron alum.

The preparation of anthraquinone and of β-methylanthraquinone is described in Section **IV,145**.

IV,149. *p*-BENZOQUINONE ("QUINONE")

Method 1. Cool a solution of 33 g. of hydroquinone in 150 ml. of 60 per cent. acetic acid contained in a 600 ml. beaker to below 5° in an ice bath. Dissolve 42 g. of chromic anhydride in 70 ml. of water, and add 30 ml. of glacial acetic acid. By means of a separatory funnel with bent stem and supported over the beaker, add the chromic anhydride solution

to the mechanically-stirred hydroquinone solution at such a rate that the temperature does not rise above 10° ; the addition takes about 2 hours. Filter the mixture at once and wash the quinone several times with 10 ml. portions of ice cold water. Spread the material upon filter paper until dry, but no longer or the quinone will be lost through sublimation. The yield of quinone (a bright yellow crystalline solid), m.p. 115°, is 21 g. ; it darkens when exposed to light.

Impure quinone may be purified by placing it in a distilling flask attached to a condenser and passing a rapid current of steam into the flask : the quinone sublimes and collects in the receiver. It is separated from the water by filtration and dried ; the m.p. is 116°. The vapour has a penetrating odour and attacks the eyes.

Method 2. In a 1 litre round-bottomed flask, provided with a mechanical stirrer, place 0·5 g. of vanadium pentoxide (catalyst), 500 ml. of 2 per cent. sulphuric acid, 55 g. of hydroquinone and 30 g. of sodium chlorate. Stir the mixture vigorously for about 4 hours. Greenish-black quinhydrone is first formed and this is converted into yellow quinone ; the temperature of the mixture rises to about 40° (do not allow it to exceed this temperature). Cool the flask in running water, filter the mixture at the pump, and wash it with 50 ml. of cold water. Dry the quinone upon filter paper in the air (see *Method 1*) or in a desiccator over anhydrous calcium chloride. The yield is 45 g., m.p. 111-112°. The crude quinone may be purified by steam distillation as in *Method 1*, or by recrystallisation from boiling light petroleum, b.p. 100–120° (12 ml. per gram) : the resulting pure, bright yellow quinone has m.p. 115° and the recovery is about 95 per cent.

COGNATE PREPARATION

1 : 4-Naphthoquinone. Place a solution of 120 g. of pure chromium trioxide in 150 ml. of 80 per cent. aqueous acetic acid in a 2-litre three-necked flask, fitted with a thermometer, mechanical stirrer and 1-litre dropping funnel. Surround the flask by a mixture of ice and salt and, when the temperature has fallen to 0°, add a solution of 64 g. of pure naphthalene in 600 ml. of glacial acetic acid, with constant stirring, over a a period of 2–3 hours whilst maintaining the internal temperature at 10–15°. Continue the stirring overnight, during which time the reaction mixture and bath attain room temperature. Allow the dark green solution to stand for 3 days and stir occasionally. Pour the reaction mixture into 5–6 litres of water, collect the crude naphthoquinone by suction filtration, wash with 200 ml. of water and dry in a desiccator. Recrystallise from 500 ml. of petroleum ether (b.p. 80–100°). The yield of pure 1 : 4-naphthoquinone, m.p. 124–125°, is 17 g.

IV,150. 1 : 2-NAPHTHOQUINONE

Place 20 g. of Orange II (Section **IV,79**) in a 600 ml. beaker and dissolve it in 250 ml. of water at 40–50°. Add, with stirring, 24–25 g. of sodium hyposulphite ($Na_2S_2O_4$) ; this discharges the colour and yields a pink or cream-coloured, finely-divided precipitate of α-amino-β-naphthol (compare Section **IV,76**). Heat the mixture nearly to boiling until it commences to froth considerably, then cool to 25° in ice, filter on a

Buchner funnel and wash with a little cold water. Transfer the precipitate to a beaker containing a solution of 0·25 g. of stannous chloride in 5 ml. of concentrated hydrochloric acid diluted with 100 ml. of water; upon stirring the aminonaphthol dissolves and a small amount of insoluble matter remains. The function of the stannous chloride is as an antioxidant, preventing the readily oxidisable aminonaphthol hydrochloride from undergoing appreciable change. Stir the solution for 5 minutes with 2 g. of decolourising carbon, and filter at the pump. If crystalline material should separate at any stage, dissolve it by warming and by the addition of a little water if necessary. Transfer the clear solution to a beaker, add 25 ml. of concentrated hydrochloric acid and warm until the solid dissolves. Cool to 0°, filter the almost colourless crystals of the aminonaphthol hydrochloride with suction, and wash with 25 ml. of dilute hydrochloric acid (1 : 4 by volume). *From this point all operations must be carried out rapidly.* In the meantime, prepare the oxidising solution by dissolving 30 g. of crystallised ferric chloride in a mixture of 10 ml. of concentrated hydrochloric acid and 25 ml. of water by heating, cool to room temperature by adding *ca.* 30 g. of crushed ice, and filter the solution at the pump. Wash the crystalline 1 : 2-aminonaphthol hydrochloride into a 600 ml. beaker with water, add 150 ml. of water and a few drops of concentrated hydrochloric acid, and dissolve the precipitated solid by stirring and warming to about 35°. If necessary, filter rapidly by suction from a trace of residue, transfer to a 500 ml. round-bottomed flask, add the ferric chloride solution all at once whilst shaking the flask vigorously. The quinone separates rapidly as a voluminous micro-crystalline yellow precipitate. Filter on a Buchner funnel and wash it thoroughly with water at 30° to remove all traces of acid. Dry the product upon filter paper in an atmosphere free from acid fumes. The yield of β-naphthoquinone, which melts with decomposition at 145–147°, is 7 g. It should not be powdered, for it becomes highly electrified.

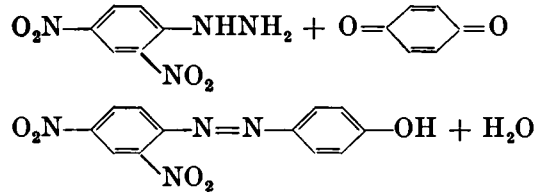
IV,151. QUINHYDRONE

Dissolve 100 g. of iron alum (ferric ammonium sulphate) in 300 ml. of water at 65°. Pour the solution, with stirring, into a solution of 25 g. of hydroquinone in 100 ml. of water contained in a 600 ml. beaker. The quinhydrone is precipitated in fine needles. Cool the mixture in ice, filter with suction, and wash three or four times with cold water. Dry in the air between filter paper. The yield of quinhydrone, m.p. 172°, is 15 g. It contains a trace of iron, but this has no influence upon the e.m.f. of the quinhydrone electrode provided that the washing of the crude material has been thorough. The quinhydrone should be stored in a tightly-stoppered bottle.

IV,152. REACTIONS AND CHARACTERISATION OF QUINONES

The number of quinones normally encountered in routine qualitative organic analysis is very limited; the following notes will be found useful for their detection and characterisation.

(i) **General properties.** All quinones are coloured (generally yellow) crystalline solids. They are usually insoluble in water, soluble in ether, and sublime on heating. Frequently the vapour has a penetrating odour and attacks the eyes. The carbonyl groups of quinones often do not react in a normal manner with carbonyl group reagents, because of their oxidising properties: thus quinones are reduced by sodium bisulphite. Crystalline products are usually formed with one molecule of phenylhydrazine and of 2 : 4-dinitrophenylhydrazine, but these are not always of normal structure. Thus *p*-benzoquinone reacts with 2 : 4-dinitrophenylhydrazine hydrochloride in hot alcoholic solution to give 2′ : 4′-dinitrobenzene-azophenol-4, m.p. 185-186° :



(ii) **Sodium hydroxide solution.** Dark solutions are formed on warming owing to decomposition. Upon acidification, an amorphous solid may be precipitated.

(iii) **Hydriodic acid.** Compounds of the *p*-benzoquinone type liberate iodine from hydriodic acid.

Dissolve 0·1 g. of the quinone in a little rectified spirit. Add 10 ml. of 10 per cent. aqueous potassium iodide solution to a mixture of 5 ml. of alcohol and 5 ml. of concentrated hydrochloric acid, and then introduce the quinone solution. Iodine is liberated immediately. This test is also given by other oxidising agents.

(iv) **Reduction with zinc powder and acid.** Simple *p*-quinones are reduced to hydroquinones in the following manner. Dissolve or suspend 0·5 g. of the quinone in dilute hydrochloric acid (1 : 5) and add a little zinc powder. When the solution is colourless, filter, neutralise with sodium bicarbonate, extract the dihydric phenol with ether, remove the solvent, and identify (Section **IV,114**).

Sulphurous acid produces a similar result, but some hydroquinone sulphonic acid is simultaneously produced.

(v) **Reduction with zinc powder and caustic alkali.** Compounds of the anthraquinone type are reduced to oxanthrols (compare Section **IV,146**).

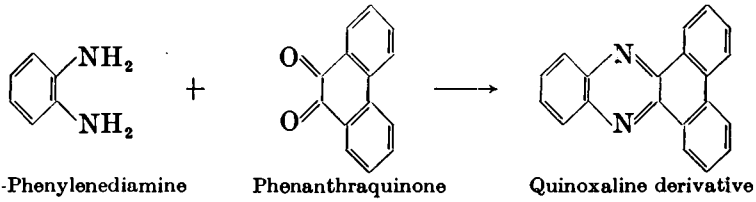
Treat 0·1 g. of the quinone with dilute sodium hydroxide and zinc powder. Upon boiling the mixture a red colour is produced : this disappears when the solution is shaken owing to aerial oxidation to the original quinone.

(vi) **Distillation with zinc powder.** Quinones derived from polycyclic hydrocarbons may be reduced to the parent hydrocarbon as follows. Grind 0·5 of the compound with 3–4 g. of zinc powder, pour the mixture into a Pyrex test-tube and cover it with an equal volume of zinc powder. Clamp the tube horizontally at the open end. Heat the zinc powder first, then the mixture of zinc powder and the compound to a dull red heat : the hydrocarbon sublimes into the cooler part of the tube. Remove the sublimate ; determine the m.p. and identify it by the preparation of the picrate (Section **IV,9**).

(vii) **Reaction with semicarbazide hydrochloride.** Many simple quinones yield crystalline mono-semicarbazones by the following procedure. Dissolve 0·2 g. of semicarbazide hydrochloride in a little water, add 0·2 g. of the quinone and warm. The mono-semicarbazone is immediately formed as a yellow precipitate. Filter and recrystallise from hot water ; any di- (or *bis*-) semicarbazone will remain undissolved.

Ortho quinones (and also aromatic α-diketones, *e.g.*, benzil) react with *o*-phenylenediamine to yield **quinoxalines** as follows. Dissolve the substance

in alcohol or in glacial acetic acid, add an equivalent amount of *o*-phenylenediamine in alcoholic solution and warm for 15 minutes on a water bath. Cool, dilute with water, filter and recrystallise from dilute alcohol. The quinoxaline from phenanthraquinone has m.p. 217°; from benzil, 124°.



o-Phenylenediamine Phenanthraquinone Quinoxaline derivative

Characterisation

1. **Reduction to hydroquinone.** Dissolve, or suspend, 0·5 g. of the quinone in 5 ml. of ether or benzene and shake vigorously with a solution of 1·0 g. of sodium hydrosulphite ($Na_2S_2O_4$) in 10 ml. of *N* sodium hydroxide until the colour of the quinone has disappeared. Separate the alkaline solution of the hydroquinone, cool it in ice, and acidify with concentrated hydrochloric acid. Collect the product (extract with ether, if necessary) and recrystallise it from alcohol or water.

2. **Reductive acetylation.** Suspend 0·5 g. of the quinone in 2·5 ml. of pure acetic anhydride, and add 0·5 g. of zinc powder and 0·1 g. of powdered, anhydrous sodium acetate. Warm the mixture gently until the colour of the quinone has largely disappeared and then boil for 1 minute. Add 2 ml. of glacial acetic acid and boil again to dissolve the product and part of the precipitated zinc acetate. Decant the hot solution from the zinc acetate and zinc, and wash the residue with 3–4 ml. of hot glacial acetic acid. Combine the solutions, heat to boiling, carefully add sufficient water to hydrolyse the acetic anhydride and to produce a turbidity. Cool the mixture in ice, filter off the diacetate of the hydroquinone, and recrystallise it from dilute alcohol or from light petroleum.

3. **Thiele acetylation.** Quinones, when treated with acetic anhydride in the presence of perchloric acid or of concentrated sulphuric acid, undergo simultaneous reductive acetylation and substitution to yield triacetoxy derivatives, *e.g.*, benzoquinone gives 1 : 2 : 4-triacetoxybenzene.

Add 0·1 ml. of concentrated sulphuric acid or of 72 per cent. perchloric acid cautiously to a cold solution of 0·01 mol (or 1·0 g.) of the quinone in 3–5 ml. of acetic anhydride. Do not permit the temperature to rise above 50°. Allow to stand for 15–30 minutes and pour into 15 ml. of water. Collect the precipitated solid and recrystallise it from alcohol.

The properties of a number of quinones are summarised in Table **IV,152.**

TABLE IV,152. **QUINONES**

Quinone	M.P.	Semi-carbazone	Oxime	Hydro-quinone	Diacetate of hydro-quinone	Thiele acetylation product	Other Derivatives
Thymoquinone	45°	204°	162°	143°	74°	—	—
p-Toluquinone	69	179	135	124	52	114°	—
2-Methylnaphthoquinone (1 : 4)	106	247	167	—	—	113	—
Duroquinone	112	—	—	239	207	—	—
p-Benzoquinone	116	243d	240d	171	123	97	Picrate, 179°
α-Naphthoquinone (1 : 4)	125	247	198	176	128	135	—
β-Naphthoquinone (1 : 2)	146d	184	162	103	105	135	—
β-Methylanthraquinone	177	—	—	—	217	—	—
o-Toluquinone	195	—	140	—	—	—	—
Camphorquinone	199	236	170	—	—	—	Quinoxaline, 78
Quinizarin	201	—	—	—	—	207	—
9 : 10-Phenanthraquinone	206	220d	158	148	202	—	Quinoxaline, 220
Acenaphthenequinone	261	192	222 Di	—	—	—	Quinoxaline, 241
Anthraquinone	286	—	224	180	260	—	—
Chloranil (1)	290*	—	—	232	251	—	—
Alizarin	290	—	—	—	182	—	—

(1) Tetrachloro-*p*-benzoquinone.

* Sealed tube.

AROMATIC CARBOXYLIC ACIDS

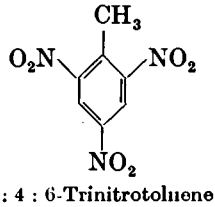
Aromatic carboxylic acids may be prepared :—

1. By the oxidation of a side chain, provided the molecule contains no other groups (*e.g.*, amino NH_2 and hydroxyl OH) which are affected by oxidising agents, for example :

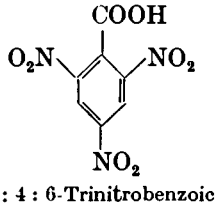
$$\underset{\text{Benzyl chloride}}{C_6H_5CH_2Cl} \xrightarrow[KMnO_4]{\text{Alkaline}} \underset{\text{Benzoic acid}}{C_6H_5COOH}$$

$$\underset{p\text{-Nitrotoluene}}{p\text{-}NO_2C_6H_4CH_3} \xrightarrow[H_2SO_4]{Na_2Cr_2O_7} \underset{p\text{-Nitrobenzoic acid}}{p\text{-}NO_2C_6H_4COOH}$$

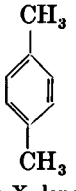
$$\underset{o\text{- or }p\text{-Chlorotoluene}}{ClC_6H_4CH_3} \xrightarrow{KMnO_4} \underset{o\text{- or }p\text{-Chlorobenzoic acid}}{ClC_6H_4COOH}$$



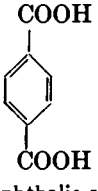
$\xrightarrow[H_2SO_4]{Na_2Cr_2O_7}$



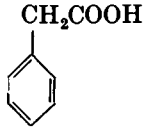
2 : 4 : 6-Trinitrotoluene — 2 : 4 : 6-Trinitrobenzoic acid



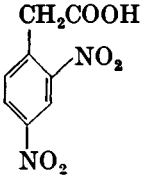
$\xrightarrow[H_2SO_4]{Na_2Cr_2O_7}$



p-Xylene — Terephthalic acid



$\xrightarrow[HNO_3]{\text{Fuming}}$



Phenylacetic acid — 2 : 4-Dinitrophenylacetic acid

The last example illustrates nitration by means of fuming nitric acid with retention of the side chain.

2. By the hydrolysis of nitriles. The nitriles may be easily prepared either from amines by the Sandmeyer reaction (Section **IV,66**) or by the action of cuprous cyanide upon aryl halides (compare Section **IV,163**). Benzyl cyanide

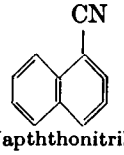
is conveniently obtained by the action of aqueous-alcoholic sodium cyanide upon benzyl chloride. The following examples are given :—

C_6H_5CN (Benzonitrile) $\xrightarrow[\text{aq.}]{\text{NaOH}}$ C_6H_5COOH (see Section IV,66) (Benzoic acid)

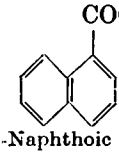
o- or *p*-$CH_3C_6H_4CN$ (*o*- or *p*-Tolunitrile) $\xrightarrow[\text{or 75\% } H_2SO_4]{\text{NaOH aq.}}$ *o*- or *p*-$CH_3C_6H_4COOH$ (*o*- or *p*-Toluic acid)

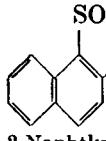
$C_6H_5CH_2CN$ (Benzyl cyanide) $\xrightarrow[CH_3COOH]{50\% H_2SO_4}$ $C_6H_5CH_2COOH$ (Phenylacetic acid)

p-$NO_2C_6H_4CH_2CN$ (*p*-Nitrobenzyl cyanide) $\xrightarrow[H_2SO_4]{\text{Dilute}}$ *p*-$NO_2C_6H_4CH_2COOH$ (*p*-Nitrophenylacetic acid)

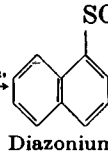

α-Napththonitrile

$\xrightarrow[CH_3COOH]{\text{Dilute } H_2SO_4}$

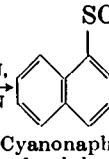

α-Naphthoic acid


2-Naphthylamine-1-sulphonic acid

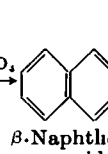
$\xrightarrow[HCl]{NaNO_2}$

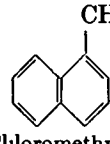

Diazonium compound

$\xrightarrow[KCN]{CuCN,}$

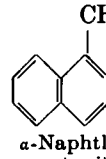

K 2-Cyanonaphthalene-1-sulphonate

$\xrightarrow{H_2SO_4}$

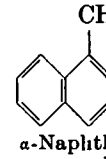

β-Naphthoic acid


α-Chloromethylnaphthalene

$\xrightarrow{KCN}$


α-Naphthylacetonitrile

$\xrightarrow[H_2SO_4]{\text{Dil.}}$


α-Naphthylacetic acid

α-Naphthylacetic acid is an important growth promoting plant hormone.

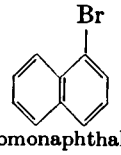
The hydrolysis of arylacetonitriles may be arrested at the arylacetamide stage by treatment with concentrated hydrochloric acid at about 40° ; thus benzyl cyanide yields **phenylacetamide** :

$$C_6H_5CH_2CN \xrightarrow[40°]{H_2O,\ HCl,} C_6H_5CH_2CONH_2$$

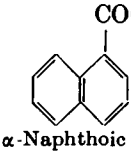
3. By carbonation of Grignard reagents, for example :

$$\underset{\text{Bromobenzene}}{C_6H_5Br} + Mg \longrightarrow C_6H_5MgBr \xrightarrow{CO_2} C_6H_5COOMgBr \xrightarrow{H_2O} \underset{\text{Benzoic acid}}{C_6H_5COOH} + Mg(OH)Br$$

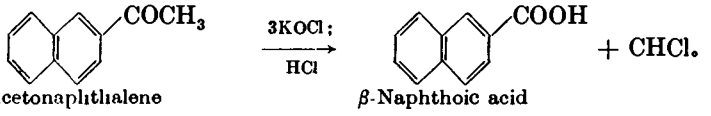
Similarly $\underset{\text{Benzyl chloride}}{C_6H_5CH_2Cl} \xrightarrow[H_2O]{Mg\ ;\ CO_2;} \underset{\text{Phenylacetic acid}}{C_6H_5CH_2COOH}$


α-Bromonaphthalene

$\xrightarrow[H_2O]{Mg;\ CO_2;}$


α-Naphthoic acid

4. By the hypohalite oxidation of aceto compounds, for example :



β-Acetonaphthalene β-Naphthoic acid

5. By the malonic ester synthesis (compare Section **III,165**), for example :

$$CH_2(COOC_2H_5)_2 \xrightarrow{NaOC_2H_5} Na[CH(COOC_2H_5)_2] \xrightarrow{C_6H_5CH_2Cl}$$

$$(C_6H_5CH_2)CH(COOC_2H_5)_2 \xrightarrow[\text{and heat}]{\text{Hydrolyse}} \underset{\text{Hydrocinnamic acid}}{C_6H_5CH_2CH_2COOH}$$

Hydrocinnamic acid may also be prepared by the reduction of cinnamic acid with sodium and alcohol or with sodium amalgam or with hydrogen in the presence of Adams' platinum oxide catalyst (Section **III,150**) :

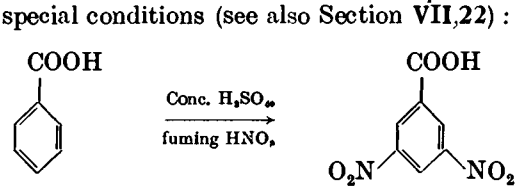
$$C_6H_5CH{=}CHCOOH \xrightarrow[Na—Hg \text{ or } PtO_2 + H_2]{Na + C_2H_5OH \text{ or}} C_6H_5CH_2CH_2COOH$$

The preparation of a number of miscellaneous acids is described.

***m*-Nitrobenzoic acid.** Although *m*-nitrobenzoic acid is the main product of the direct nitration of benzoic acid with potassium nitrate and concentrated sulphuric acid, the complete separation of the small quantity of the attendant *para* isomer is a laborious process. It is preferable to nitrate methyl benzoate and hydrolyse the resulting methyl *m*-nitrobenzoate, which is easily obtained in a pure condition :

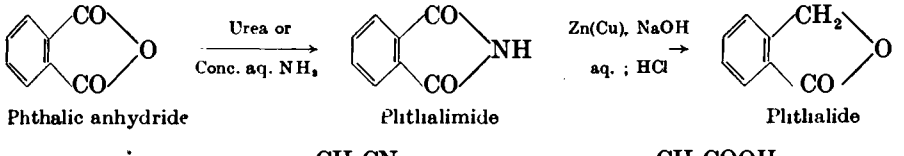
$$\underset{\text{Methyl benzoate}}{C_6H_5COOCH_3} \xrightarrow{HNO_3} \underset{\text{Methyl } m\text{-nitrobenzoate}}{m\text{-}NO_2C_6H_4COOCH_3} \xrightarrow{\text{Hydrolysis}} \underset{m\text{-Nitrobenzoic acid}}{m\text{-}NO_2C_6H_4COOH}$$

3 : 5-Dinitrobenzoic acid. This acid may be prepared by the nitration of benzoic acid with a mixture of concentrated sulphuric acid and fuming nitric acid under special conditions (see also Section **VII,22**) :

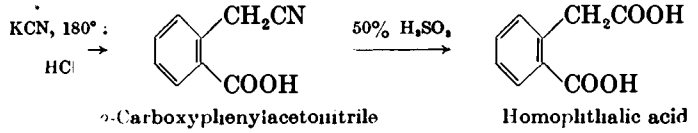


Benzoic acid 3 : 5-Dinitrobenzoic acid

Homophthalic acid. This is a four-stage preparation with phthalic anhydride as the starting material :

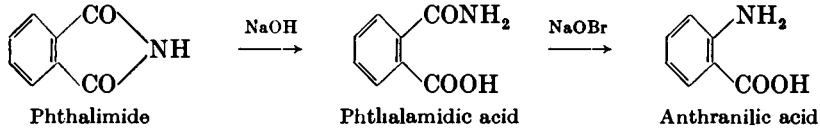


Phthalic anhydride Phthalimide Phthalide



2-Carboxyphenylacetonitrile Homophthalic acid

Anthranilic acid. This substance, the *ortho* amino derivative of benzoic acid, may be conveniently prepared by the action of sodium hypobromite (or sodium hypochlorite) solution upon phthalimide in alkaline solution at 80°. The ring in phthalimide is opened by hydrolysis to phthalamidic acid and the latter undergoes the Hofmann reaction (compare Section **III,116**) :



Phthalimide — Phthalamidic acid — Anthranilic acid

Diphenylacetic acid. The reduction of benzilic acid with red phosphorus and a little iodine in 98 per cent. acetic acid solution yields diphenylacetic acid :

$$(C_6H_5)_2C(OH)COOH \xrightarrow{2H} (C_6H_5)_2CHCOOH$$

Benzilic acid — Diphenylacetic acid

It is believed that the red phosphorus is the true reducing agent and the iodine (or iodide) functions as a hydrogen carrier. This procedure replaces the obsolete method of heating with red phosphorus and concentrated hydriodic acid in a sealed tube.

Mandelic acid. This preparation is an example of the synthesis of an α-hydroxy acid by the cyanohydrin method. To avoid the use of the very volatile and extremely poisonous liquid hydrogen cyanide, the cyanohydrin (mandelonitrile) is prepared by treatment of the sodium bisulphite addition compound of benzaldehyde (not isolated) with sodium cyanide :

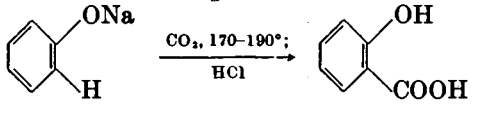
$$C_6H_5CHO \xrightarrow{NaHSO_3} C_6H_5CH(OH)SO_3Na \xrightarrow{NaCN} C_6H_5CH(OH)CN$$

Benzaldehyde — Bisulphite Compound — Mandelonitrile

$$\xrightarrow{HCl} C_6H_5CH(OH)COOH + NH_4Cl$$

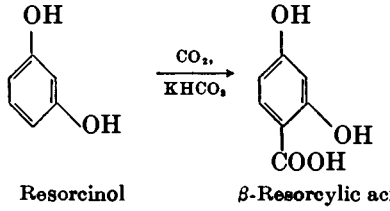
Mandelic Acid

Salicylic acid. The preparation of salicylic acid by passing carbon dioxide into dry sodium phenoxide at 170-190° is the classical example of the **Kolbe-Schmitt reaction.** The latter is a method for introducing a carboxyl group directly into a phenol nucleus.



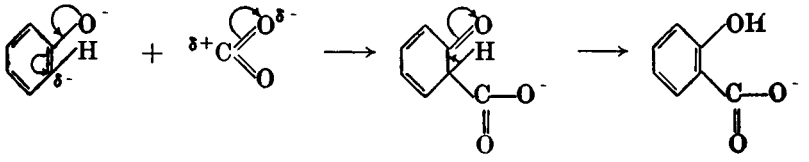
Sodium phenoxide — Salicylic acid

The reaction is particularly facile with di- and tri-hydric phenols. Thus **β-resorcylic acid** is readily obtained by passing carbon dioxide through a boiling aqueous solution of the potassium or sodium salt of resorcinol :

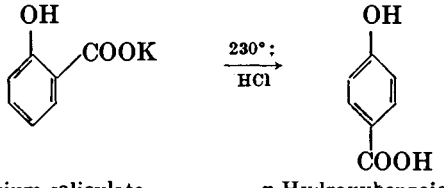


Resorcinol — β-Resorcylic acid

The *mechanism* of the reaction appears to involve the attack by an activated carbon dioxide molecule at the activated *ortho* position in the phenoxide ion :



It is of interest to record that ***p*-hydroxybenzoic acid** may be prepared by the thermal rearrangement of potassium salicylate at 230° ;



Potassium salicylate — *p*-Hydroxybenzoic acid

Phenylpropiolic acid. This is an example of an aromatic acetylenic acid, and is made by adding bromine to the ethylenic linkage in ethyl cinnamate, and treating the resulting dibromide with alcoholic potassium hydroxide which eliminates two molecules of hydrogen bromide :

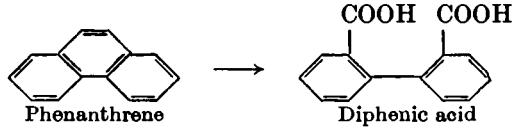
$$C_6H_5CH{=}CHCOOC_2H_5 \xrightarrow[CCl_4]{Br_2\ in} C_6H_5CHBrCHBrCOOC_2H_5$$

Ethyl cinnamate — Ethyl $\alpha\beta$-dibromo-β-phenylpropionate

$$\xrightarrow[H_2SO_4]{Alc.\ KOH;} C_6H_5C{\equiv}CCOOH$$

Phenylpropiolic acid

Diphenic acid. Phenanthrene upon oxidation in acetic acid solution at 85° with 30 per cent. hydrogen peroxide gives diphenic acid (diphenyl-2 : 2′-dicarboxylic acid) : no phenanthraquinone is formed under these experimental conditions. The reaction is essentially an oxidation of phenanthrene with *peracetic acid.* (For another method of preparation, see Section **IV,74.**)



Phenanthrene — Diphenic acid

IV,153. BENZOIC ACID

From Benzyl Chloride

Method 1. Into a 500 ml. bolt-head flask equipped with a reflux condenser, place 4 g. of anhydrous sodium carbonate, 200 ml. of water, 9 g. of potassium permanganate, 5 g. (4·5 ml.) of benzyl chloride (Section **IV, 22**) and a few chips of porous porcelain. Boil the mixture gently until the reaction is complete (60–90 minutes), *i.e.*, until the liquid running down from the condenser contains no oily drops of unchanged benzyl chloride. Manganese dioxide is precipitated. Allow to cool, acidify with contrated hydrochloric acid (about 40 ml.), and add a 20 per cent. aqueous solution of crystallised sodium sulphite ($Na_2SO_3,7H_2O$) with shaking until the manganese dioxide is completely dissolved and only the white

precipitate of benzoic acid remains. When the mixture is cold, filter off the benzoic acid at the pump and wash it with cold water. Recrystallise from boiling water. The benzoic acid is obtained as colourless needles, m.p. 121·5°. The yield is 4 g.

Method 2. Into a 250 ml. bolt-head flask provided with a reflux condenser, place 10 g. (9 ml.) of benzyl chloride, 50 ml. of water, 20 ml. of concentrated nitric acid and a few fragments of porous porcelain. Boil vigorously for 5–6 hours, by the end of which time oxidation should be complete. Cool the flask under the tap, shaking vigorously to prevent the formation of lumps. Filter the solid at the pump on a Buchner funnel and wash with cold water. Transfer the solid to a beaker containing 1–2 g. of decolourising carbon and about 400 ml. of water; heat to boiling until the acid dissolves. Filter through a hot water funnel or through a preheated Buchner funnel and filter flask, and allow the filtrate to cool. When cold, filter the benzoic acid with suction on a clean Buchner funnel, press well with a large glass stopper, wash with small quantities of cold water, and drain as dry as possible. Dry upon filter paper in the air. The yield is 8 g., m.p. 121·5°.

By Carbonation of the Grignard Reagent

Equip a 500 ml. round-bottomed flask with a reflux condenser (preferably of the double surface type) and a calcium chloride (or cotton wool) guard tube; it is important that the apparatus be thoroughly dry. Place 8·0 g. of dry magnesium turnings, a small crystal of iodine, 15 g. (10 ml.) of dry bromobenzene (Section **IV,18**) and 20 ml. of sodium-dried ether in the flask. If the magnesium does not react within a few minutes, warm the flask on a water bath so that the ether refluxes gently and then remove the bath. This will generally start the reaction. The formation of the Grignard reagent will be indicated by the disappearance of the iodine colour, the production of a cloudiness, and the gentle boiling of the ether. Replace the guard tube by a separatory funnel containing a solution of 38 g. (25·5 ml.) of dry bromobenzene in 140 ml. of anhydrous ether and carrying a calcium chloride (or cotton wool) guard tube in its mouth; fit the separatory funnel into the top of the condenser by a grooved cork. Run this solution slowly into the flask at such a rate that the ether boils gently from the heat of reaction alone without the application of external heating. This operation occupies about 30 minutes. Replace the separatory funnel by the guard tube and reflux the mixture gently on a water bath (*CAUTION*: ether) for 30 minutes in order to complete the reaction. The solution will now be either cloudy or slightly dark in colour; the magnesium will have disintegrated and only a little will remain unattacked.

Place 80 g. (roughly weighed) of Dry Ice in the form of small lumps in a dry 1 or 1·5 litre beaker (for method of handling, see Section **III,84**). Pour the solution of the Grignard reagent slowly and steadily on to the solid carbon dioxide with stirring, taking care to retain any unreacted magnesium in the flask. There is a vigorous reaction and the Grignard reagent addition compound sets to a stiff mass. Continue the stirring until all the Dry Ice has evaporated. Add 200 g. of crushed ice and then 60 ml. of dilute hydrochloric acid (1 : 1 by volume); stir until most

of the solid has decomposed. Transfer the mixture to a separatory funnel, wash the beaker with 50 ml. of technical ether, and add the extract to the mixture in the separatory funnel. Withdraw the aqueous layer. Wash the ether layer twice with 30 ml. portions of water. Extract the ether solution with two 100 ml. portions of 5 per cent. sodium hydroxide solution, and run the aqueous layer into a clean beaker. [Place the ether in the *ETHER RESIDUES* bottle.] Treat the combined aqueous layers with 1–2 g. decolourising carbon and a Whatman ashless tablet, and filter by suction. Acidify the filtrate with dilute hydrochloric acid, cool and collect the precipitate of benzoic acid on a Buchner funnel. Recrystallise from hot water and dry upon filter paper in the air (see Section IV,153). The yield of pure benzoic acid, m.p. 121°, is 20 g.

COGNATE PREPARATION

Phenylacetic acid. Use 5·0 g. of magnesium, 25 g. (23 ml.) of redistilled benzyl chloride (Section IV,22) and 75 ml. of sodium-dried ether. Allow the reaction mixture to warm to 15° and then decompose it with dilute hydrochloric or sulphuric acid. Filter off the crude acid and recrystallize it from water. The yield of pure phenylacetic acid, m.p. 76–77°, is 11 g.

Note.

Phenylacetic acid is appreciably soluble in water, so that the yield is poor; it may be improved by evaporating the filtrates to a small volume and extracting with ether.

IV,154. *p*-NITROBENZOIC ACID

Place 46 g. of *p*-nitrotoluene, 136 g. of crystallised sodium dichromate ($Na_2Cr_2O_7,2H_2O$) and 300 ml. of water in a 1-litre round-bottomed flask fitted with a mechanical stirrer. By means of a dropping funnel supported above the flask, add 340 g. (185 ml.) of concentrated sulphuric acid during about 30 minutes to the well-stirred mixture. The heat of dilution of the acid causes the *p*-nitrotoluene to melt and oxidation takes place; if the reaction shows signs of becoming vigorous, the rate of addition must be reduced. When all the sulphuric acid has been introduced and the temperature of the mixture commences to fall, attach a reflux condenser to the flask, and heat to gentle boiling for half an hour. Cool and pour the reaction mixture into 400–500 ml. of water. Filter the crude *p*-nitrobenzoic acid at the pump and wash it with about 200 ml. of water. Transfer the solid to a 1-litre beaker, add about 200 ml. of 5 per cent. sulphuric acid (11 g. or 6 ml. of concentrated sulphuric acid added to 200 ml. of water) and digest on a water bath, with agitation, in order to remove the chromium salts as completely as possible; allow to cool and filter again. Transfer the acid to a beaker, break up any lumps of material, and treat it with 5 per cent. sodium hydroxide solution until the liquid remains alkaline (360–400 ml.). The *p*-nitrobenzoic acid passes into solution, any unchanged *p*-nitrotoluene remains undissolved and chromium salts are converted into chromic hydroxide and/or sodium chromite. Add about 5 g. of decolourising carbon, warm to about 50° with stirring for 5 minutes, and filter with suction. Run the alkaline solution of sodium *p*-nitrobenzoate into about 450 ml. of well-stirred

15 per cent. sulphuric acid (74 g. or 40 ml. of concentrated sulphuric acid in 400 ml. of water). Do not add the acid to the alkaline solution, for in this way the acid is liable to be contaminated by the sodium salt. Filter the purified acid at the pump, wash it thoroughly with cold water, and dry it in the steam oven. The yield of *p*-nitrobenzoic acid, m.p. 237°, is 48 g.: this is sufficiently pure for most purposes. Upon recrystallisation from benzene or from glacial acetic acid, the m.p. is raised to 239°.

IV,155. 2 : 4 : 6-TRINITROBENZOIC ACID

In a 1 litre bolt-head flask, mounted in an empty water bath, place 720 g. (392 ml.) of concentrated sulphuric acid and add 72 g. of commercial trinitrotoluene. Stir the mixture mechanically with a powerful stirrer and introduce powdered crystallised sodium dichromate ($Na_2Cr_2O_7,2H_2O$) in small quantities until the temperature of the mixture reaches 40°: now fill the empty water bath with cold water and add the sodium dichromate at such a rate that the temperature is maintained at 45–55°. The total weight of sodium dichromate required is 110 g. Stir the mixture for a further 2 hours at 45–55°, and pour into a beaker containing 800 g. of crushed ice. Filter off the trinitrobenzoic acid and wash it carefully with cold water until free from chromium salts (the acid is appreciably soluble in water). Transfer the solid to a 1-litre bolt-head flask, provided with a stirrer and containing 400 ml. of water. Add 15 per cent. sodium hydroxide solution from a separatory funnel, with vigorous stirring, until a *faint* red colour persists for 5 minutes; discharge the colour with a few drops of acetic acid. Filter off the unattacked trinitrotoluene and wash it with a little water. Precipitate the trinitrobenzoic acid from the filtrate by the addition of a slight excess of 50 per cent. sulphuric acid. Cool in ice, filter the acid at the pump and wash it free from salts with ice-cold water. Dry the 2 : 4 : 6-trinitrobenzoic acid in the air: it melts at 228° (decomp.) and the yield is 55 g.

IV,156. 2 : 4-DINITROPHENYLACETIC ACID

Place 25 g. of phenylacetic acid (Section **IV,160**) in a 500 ml. round-bottomed flask, cool the latter in running water and add 250 ml. of fuming nitric acid, rather slowly at first and then more rapidly. The addition occupies about 15 minutes. Attach a condenser to the flask, reflux the solution for 1 hour, and pour into about 500 ml. of cold water. When cold, filter the crude 2 : 4-dinitrophenylacetic acid at the pump and wash it with cold water: the resulting acid, after drying at 100°, is almost pure (m.p. 181°) and weighs 31 g. Recrystallise it from 300 ml. of 20 per cent. alcohol. Collect the first main crop (25 g.), and allow the mother liquor to stand overnight when a further 2 g. of pure acid is obtained; dry at 100°. The yield of pure 2 : 4-dinitrophenylacetic acid, m.p. 183°, is 27 g.

IV,157. *o*-CHLOROBENZOIC ACID

Method 1. Place 1250 ml. of water, 75 g. of pure potassium permanganate and 50 g. of *o*-chlorotoluene (Section **IV,61**) in a 2·5-litre three-necked flask equipped with a mechanical stirrer and reflux condenser.

Stir the mixture and reflux gently until practically all the permanganate colour has disappeared (about 2 hours). At this point add 37·5 g. more of potassium permanganate and reflux the mixture again until the permanganate colour disappears (about 2 hours); the colour of the solution can easily be seen by removing the flame and stopping the refluxing. Finally, add a second 37·5 g. of potassium permanganate and continue refluxing until the permanganate colour has disappeared (about 2–4 hours) (1). Steam distil the mixture (Fig. *II*, *41*, 1) to remove unreacted *o*-chlorotoluene (about 12 g.). Filter the hot contents of the flask from the manganese dioxide with suction (2) and wash with two 125 ml. portions of hot water. Concentrate the filtrate to about 800 ml. (Fig. *II*, *37*, 1) (3), and precipitate the *o*-chlorobenzoic acid by cautiously adding 75 ml. of concentrated hydrochloric acid with continual stirring. When cold, filter with suction, wash the acid with cold water, and dry at 100°. The yield of *o*-chlorobenzoic acid, m.p. 138–139°, is 42 g. Upon recrystallisation from hot water or from toluene (*ca.* 4 ml. per gram), the m.p. is raised to 139–140°.

$$o\text{-}ClC_6H_4CH_3 + 2KMnO_4 \longrightarrow o\text{-}ClC_6H_4COOK + 2MnO_2 + KOH + H_2O$$

Notes.

(1) A somewhat lower yield is obtained if all the potassium permanganate (150 g.) is added all at once and, furthermore, the reaction may become violent. Addition in three portions results in a more controllable reaction.

(2) The addition of a Whatman filter tablet or of a little diatomaceous earth (Super Cel, etc.) assists in the filtration of the finely divided manganese dioxide.

(3) If the acid is precipitated before the solution is concentrated, the yield is considerably reduced (*ca.* 25 g.). If the concentrated solution is not clear, it may be clarified by the addition of 1 g. of decolourising carbon.

Method 2. Dissolve 14 g. of anthranilic acid (Section **IV,170**) in a solution of 20 ml. of concentrated hydrochloric acid and 100 ml. of water. Cool to about 5°, and diazotise by the gradual addition of a cold solution of 7 g. of sodium nitrite in 25 ml. of water to an end point with starch-potassium iodide paper (compare Section **IV,60**). In the meantime prepare a solution of cuprous chloride as follows. Dissolve 26 g. of crystallised copper sulphate and 12 g. of sodium chloride in 50 ml. of water in a 750 ml. round-bottomed flask. Heat the solution to boiling, then add 80 ml. of concentrated hydrochloric acid and 14 g. of copper turnings, and continue the heating under reflux until the solution is practically colourless. (Alternatively, prepare the cuprous chloride by the method given in Section **II,50,1**.) Cool in ice, and then add the cold diazonium solution slowly and with shaking. The reaction proceeds rapidly and with frothing: allow the mixture to stand for 2–3 hours with frequent shaking. Filter the precipitated *o*-chlorobenzoic acid and wash it with a little cold water. Recrystallise the crude acid from hot water containing a little alcohol to which a little decolourising carbon has been added. The yield of pure *o*-chlorobenzoic acid, m.p. 138–139°, is 14 g.

$$o\text{-}HOOCC_6H_4NH_2 \xrightarrow[HCl]{NaNO_2} o\text{-}HOOCC_6H_4N_2^+Cl^- \xrightarrow{CuCl} o\text{-}HOOCC_6H_4Cl$$

COGNATE PREPARATIONS

p-Chlorobenzoic acid. Proceed exactly as for *o*-chlorobenzoic acid. Use 1250 ml. of water, 50 g. of *p*-chlorotoluene (Section **IV,61**), and 75 g., 37·5 g. and 37·5 g. of potassium permanganate. When the oxidation is complete, steam distil the mixture to recover any unreacted *p*-chlorotoluene (3·4 g.). Filter the reaction mixture from hydrated manganese dioxide and wash the precipitate with two 100 ml. portions of water. Precipitate the *p*-chlorobenzoic acid in the filtrate (1) by the addition of 75 ml. of concentrated hydrochloric acid. Filter the cold solution with suction, wash with cold water, and dry in an oven at 100°. The yield of *p*-chlorobenzoic acid, m.p. 234–235°, is 55 g. Recrystallisation from hot water raises the m.p. to 238–239°.

Note.

(1) If the filtrate has a faint permanganate colour, add a few drops of sodium bisulphite solution until the solution is colourless. In this case (compare *o*-chlorobenzoic acid) concentration of the solution before precipitation only increases the yield by about 1 g. and may cause occlusion of inorganic salts.

o-Iodobenzoic acid. Dissolve 14 g. of anthranilic acid in dilute sulphuric acid and diazotise it as described in *Method 2*. Introduce into the resulting clear solution, with stirring, a solution of 26 g. of potassium iodide in dilute sulphuric acid, heat the mixture to boiling for 10 minutes and then cool. Collect the *o*-iodobenzoic acid by suction filtration, and recrystallise from hot water. The yield is almost quantitative; m.p. 162°.

IV,158. TEREPHTHALIC ACID

Place 25 g. (29 ml.) of pure *p*-xylene, 140 g. of crystallised sodium dichromate ($Na_2Cr_2O_7,2H_2O$) and 300 ml. of water in a 1 litre three-necked flask equipped with a reflux condenser, a mercury-sealed mechanical stirrer and a separatory funnel. Add through the separatory funnel 340 g. (185 ml.) of concentrated sulphuric acid to the well-stirred mixture at such a rate that the reaction is under control; this usually occupies 60–90 minutes. When all the acid has been introduced and the temperature begins to fall, reflux the mixture gently for half an hour. Cool and pour the reaction mixture (which contains some solid matter) into about 500 ml. of ice water and allow to stand for 1 hour. Filter the crude terephthalic acid with suction, and wash it with 50 ml. of cold water followed by 25 ml. of ether. Purify the acid by dissolving it in 5 per cent. sodium hydroxide solution (about 120 ml. are required), filter from any chromic hydroxide, and run the alkaline solution into about 450 ml. of well-stirred 15 per cent. sulphuric acid (74 g. or 40 ml. of concentrated sulphuric acid in 400 ml. of water). Filter the purified acid at the pump, wash it thoroughly with cold water, and dry at 100°. The yield of colourless terephthalic acid is 17 g.; it sublimes without melting at 300° and is almost insoluble in water and alcohol.

IV,159. o-TOLUIC ACID

Prepare *o*-tolunitrile, b.p. 94–96°/20 mm., from *o*-toluidine following the method given in Section **IV,66** under p-*Toluidine*. Also prepare 600 g. of 75 per cent. sulphuric acid by adding 450 g. (245 ml.) of con-

centrated sulphuric acid cautiously, with stirring and cooling, to 150 ml. of water. Place the latter in a 1 litre three-necked flask, equipped with a separatory funnel, a mechanical stirrer and reflux condenser. Heat the solution in an oil bath to about 150°, stir, and add 220 g. of *o*-tolunitrile during 2 hours. Continue the stirring for a further 2 hours while the temperature is maintained at 150–160°; finally raise the temperature to 190° and stir for another hour. Some crystalline solid will appear in the condenser at this stage. Allow the reaction mixture to cool, pour into ice water, and filter off the precipitated acid. Dissolve the crude acid in an excess of 10 per cent. sodium hydroxide solution, filter off any insoluble material (probably *o*-toluamide, m.p. 141°) through a sintered glass funnel while still hot, and acidify the filtrate with dilute sulphuric acid. Collect the *o*-toluic acid on a Buchner funnel, dry in the air and recrystallise from benzene (about 500 ml.). The yield of pure *o*-toluic acid, m.p. 102–103°, is 200 g.

***p*-Toluic acid** may be similarly prepared, if required in quantity, from *p*-tolunitrile (Section **IV,66**).

IV,160. PHENYLACETIC ACID (*from Benzyl Cyanide*)

Preparation of benzyl cyanide. Place 100 g. of powdered, technical sodium cyanide (97–98 per cent. NaCN) (*CAUTION*) and 90 ml. of water in a 1 litre round-bottomed flask provided with a reflux condenser. Warm on a water bath until the sodium cyanide dissolves. Add, by means of a separatory funnel fitted into the top of the condenser with a grooved cork, a solution of 200 g. (181·5 ml.) of benzyl chloride (Section **IV,22**) in 200 g. of rectified spirit during 30–45 minutes. Heat the mixture in a water bath for 4 hours, cool, and filter off the precipitated sodium chloride with suction; wash with a little alcohol. Distil off as much as possible of the alcohol on a water bath (wrap the flask in a cloth) (Fig. *II*, *13*, 3). Cool the residual liquid, filter if necessary, and separate the layer of crude benzyl cyanide. (Sometimes it is advantageous to extract the nitrile with ether or benzene.) Dry over a little anhydrous magnesium sulphate, and distil under diminished pressure from a Claisen flask, preferably with a fractionating side arm (Figs. *II*, *24*, 2–5). Collect the benzyl cyanide at 102–103°/10 mm. The yield is 160 g.

This product is sufficiently pure for the preparation of phenylacetic acid and its ethyl ester, but it contains some benzyl *iso*-cyanide and usually develops an appreciable colour on standing. The following procedure removes the *iso*-cyanide and gives a stable water-white compound. Shake the once-distilled benzyl cyanide vigorously for 5 minutes with an equal volume of warm (60°) 50 per cent. sulphuric acid (prepared by adding 55 ml. of concentrated sulphuric acid to 100 ml. of water). Separate the benzyl cyanide, wash it with an equal volume of saturated sodium bicarbonate solution and then with an equal volume of half-saturated sodium chloride solution. Dry with anhydrous magnesium sulphate and distil under reduced pressure. The loss in washing is very small (compare n-*Butyl Cyanide*, Section **III,113**, in which concentrated hydrochloric acid is employed).

Hydrolysis of benzyl cyanide to phenylacetic acid. Into a 500 ml. round-bottomed flask, provided with a reflux condenser, place 100 ml.

of water, 100 ml. of concentrated sulphuric acid and 100 ml. of glacial acetic acid : add 100 g. (98 ml.) of benzyl cyanide. Heat under reflux for 45–60 minutes ; hydrolysis is then complete. Pour the mixture into 2–3 volumes of water with stirring. Filter the crude acid at the pump. Melt the crude material under water, and wash it two or three times with small volumes of hot water ; the acid solidifies on cooling (1). Test a small portion for the presence of phenylacetamide (m.p. 155°) by dissolving in sodium carbonate solution. If a clear solution results, phenylacetamide is absent : if the solution is not clear, shake the whole of the crude product with excess of sodium carbonate solution, filter, and precipitate the phenylacetic acid from the clear filtrate by the addition of dilute sulphuric acid. Filter off the phenylacetic acid and recrystallise it from hot water or, better, light petroleum (b.p. 40–60°). The yield of pure acid, m.p. 77°, is 50 g. Small quantities of acid may be recovered from the mother liquors by extraction with ether, but this is rarely worth while.

$$C_6H_5CH_2CN + H_2SO_4 + 2H_2O \longrightarrow C_6H_5CH_2COOH + NH_4HSO_4$$

Note.

(1) Another method of purification consists in distillation under reduced pressure. The fraction of b.p. 140–150°/20 mm. is collected separately ; it solidifies on standing, melts at 76–76·5°, and is practically pure.

Hydrolysis of benzyl cyanide to phenylacetamide. In a 1500 ml. three-necked flask, provided with a thermometer, reflux condenser and *efficient* mechanical stirrer, place 100 g. (98 ml.) of benzyl cyanide and 400 ml. of concentrated hydrochloric acid. Immerse the flask in a water bath at 40°. and stir the mixture vigorously : the benzyl cyanide passes into solution within 20–40 minutes and the temperature of the reaction mixture rises to about 50°. Continue the stirring for an additional 20–30 minutes after the mixture is homogeneous. Replace the warm water in the bath by tap water at 15°, replace the thermometer by a dropping funnel charged with 400 ml. of cold distilled water, and add the latter with stirring : crystals commence to separate after about 50–75 ml. have been introduced. When all the water has been run in, cool the mixture externally with ice water for 30 minutes (1), and collect the crude phenylacetamide by filtration at the pump. Remove traces of phenylacetic acid by stirring the wet solid for about 30 minutes with two 50 ml. portions of cold water ; dry the crystals at 50–80°. The yield of phenylacetamide, m.p. 154–155°, is 95 g. Recrystallisation from benzene or rectified spirit raises the m.p. to 156°.

Note.

(1) The suspension of phenylacetamide may be further hydrolysed to phenylacetic acid by refluxing with stirring until the solid dissolves. The mixture becomes turbid after 30 minutes and the product begins to separate as an oil : refluxing is continued for 6 hours, the mixture is cooled first with tap water and then by an ice-water bath for about 4 hours. The crude phenylacetic acid is filtered at the pump, washed with two 50 ml. portions of cold water, and dried in a desiccator. The resulting crude acid melts at 69-70° ; it may be purified by recrystallisation from light petroleum (b.p. 40–60°) or, better, by vacuum distillation.

COGNATE PREPARATIONS

α-Naphthylacetonitrile. Place a mixture of 56 g. of α-chloromethylnaphthalene (Section **IV,23**), 29 g. of potassium cyanide, 125 ml. of ethanol and 50 ml. of water in a 500 ml. round-bottomed flask fitted with a double-surface reflux condenser, and reflux for 1 hour. Distil off the alcohol, transfer the residue to a separatory funnel, wash it with water, filter from a small amount of solid, transfer to a dish and dry under reduced pressure (vacuum desiccator charged with anhydrous calcium chloride). Distil under diminished pressure and collect the α-naphthylacetonitrile at 155–160°/9 mm. (1) : the yield is 38 g.

Note.

(1) A little naphthalene may pass over first owing to impurities in the original α-chloromethylnaphthalene.

α-Naphthylacetic acid. Heat a mixture of 36 g. of the acetonitrile, 45 ml. of concentrated sulphuric acid, 45 ml. of glacial acetic acid and 45 ml. of water under reflux for 45 minutes. Pour the hot reaction mixture slowly and with good stirring into about 800 ml. of ice-cold water. Collect the precipitated solid by suction filtration and dry it at 100°; the yield of crude acid, m.p. 116–118°, is 42 g. Purify the acid by dissolving it in about 180 ml. of 50 per cent. ethanol, treating the boiling solution with a little decolourising carbon, filtering, and precipitating the acid by dilution with cold water. (Occasionally, a little oily matter, soluble in alcohol, is present ; this is readily removed by placing the filtered solution in a separatory funnel and adding a little water ; the oil separates first and is run off from the bottom of the funnel.) The recovery of pure acid, m.p. 130°, is about 75 per cent.

IV,161. *p*-NITROPHENYLACETIC ACID

***p*-Nitrobenzyl cyanide.** Place a mixture of 275 ml. of concentrated nitric acid with an equal volume of concentrated sulphuric acid in a 2-litre three-necked flask, fitted with a thermometer, a mechanical stirrer and a dropping funnel. Cool the mixture to 10° in an ice bath, and run in 100 g. (98 ml.) of benzyl cyanide (Section **IV,160**) at such a rate (about 1 hour) that the temperature remains at about 10° and does not rise above 20°. Remove the ice bath, stir the mixture for 1 hour and pour it on to 1200 g. of crushed ice. A pasty mass slowly separates ; more than half of this is *p*-nitrobenzyl cyanide, the other components being the *ortho* isomeride and a variable amount of an oil. Filter the mass on a sintered glass funnel, press well to remove as much oil as possible, and then dissolve in 500 ml. of boiling rectified spirit. The *p*-nitrobenzyl cyanide crystallises on cooling. Filter this off at the pump and recrystallise from 80 per cent. alcohol. The yield of *p*-nitrobenzyl cyanide, m.p. 115-116°, is 75 g. Another recrystallisation raises the m.p. to 116-117°.

$$C_6H_5CH_2CN + HNO_3 \longrightarrow p\text{-}NO_2C_6H_4CH_2CN \text{ (main product)} + H_2O$$

***p*-Nitrophenylacetic acid.** Prepare a diluted sulphuric acid by adding 150 ml. of concentrated sulphuric acid cautiously to 140 ml. of water. Place 50 g. of *p*-nitrobenzyl cyanide in a 500 ml. round-bottomed

flask, pour in about two-thirds of the sulphuric acid and shake well until all the solid is moistened with the acid. Wash down any nitrile adhering to the walls of the flask into the liquid with the remainder of the acid. Attach a reflux condenser to the flask and support it in a 10 cm. hole in a large sheet of asbestos board resting on a tripod. Heat to the boiling point and boil for 15 minutes. Dilute the rather dark reaction mixture with an equal volume of cold water and cool to 0°. Filter with suction, and wash several times with ice water. Dissolve the solid in 800 ml. of boiling water (add decolourising carbon, if necessary) and filter rapidly through a hot water funnel supporting a fluted filter paper. If any solid remains on the filter, dissolve it in the minimum volume of boiling water and filter into the main filtrate. Collect the pale yellow needles of *p*-nitrophenylacetic acid which separates on cooling, and dry at 100°. The yield of acid, m.p. 151–152°, is 53 g.

IV,162. *p*-AMINOPHENYLACETIC ACID

The acid is conveniently prepared by the reduction of *p*-nitrophenylacetic acid with ammonium sulphide (hydrogen sulphide in ammoniacal solution).

$$p\text{-}NO_2C_6H_4CH_2COOH + 3NH_4HS \longrightarrow p\text{-}NH_2C_6H_4CH_2COONH_4 + 2NH_3 + 2H_2O + 3S$$

$$p\text{-}NH_2C_6H_4CH_2COONH_4 + CH_3COOH \longrightarrow p\text{-}NH_2C_6H_4CH_2COOH + CH_3COONH_4$$

Fit a 750 ml. flask with a two-holed rubber stopper carrying a wide delivery tube (which ends well below the middle of the flask) and a glass stopcock. Place 250 ml. of approximately 6*N* ammonia solution (sp. gr. *ca.* 0·95) in the flask and add, slowly and with shaking, 50 g. of *p*-nitrophenylacetic acid (Section **IV,161**). Immerse the flask in an ice bath and saturate the mixture with hydrogen sulphide : keep the temperature below 50° and open the stopcock from time to time in order to expel the hydrogen which has accumulated, due to free iron in commercial ferrous sulphide. Remove the stopper from the flask and gently boil the solution of ammonium *p*-aminophenylacetate in the fume cupboard until nearly all of the excess of hydrogen sulphide and of ammonia have been expelled : the colour of the solution changes from a dark orange-red to a pale yellow. Filter off the sulphur at the pump, and add 20 ml. of glacial acetic acid with stirring to the hot filtrate. Filter off the *p*-aminophenylacetic acid when cold. It is contaminated with a little sulphur, which can be removed by recrystallisation from 2 litres of hot water. The yield of pure acid, m.p. 199-200°, is 32 g.

IV,163. α-NAPHTHOIC ACID

Method 1. **α-Naphthonitrile.** Place 80 g. (54 ml.) of redistilled α-bromonaphthalene (Section **IV,20**), 43 g. of dry powdered cuprous cyanide (Section **II,50,3**) and 36 g. (37 ml.) of dry pure pyridine (1) (Section **II,47,22**) in a 250 ml. round-bottomed flask fitted with a ground-in reflux condenser carrying a calcium chloride (or cotton wool) guard tube, and heat the mixture in a metal bath at 215–225° for

15 hours (2). Pour the resulting dark brown solution while still hot (*ca.* 100°) into a litre flask containing 180 ml. of concentrated ammonia solution, sp. gr. 0·88, and 180 ml. of water. Add 170 ml. of benzene, stopper the flask and shake until all the lumps have disintegrated. When cold, add 100 ml. of ether and filter through a sintered glass funnel (3). Add a further 50 ml. of ether, transfer to a separatory funnel, separate the ether-benzene layer and wash it successively with (i) four 125 ml. portions of dilute ammonia solution (or until the organic layer is colourless), (ii) two 125 ml. portions of dilute hydrochloric acid (1 : 1) (any precipitate which separates should be filtered off), (iii) two 125 ml. portions of water, and (iv) two 125 ml. portions of saturated sodium chloride solution. Finally dry with anhydrous magnesium sulphate, remove the ether and benzene by distillation from a water bath (Fig. *II*, *13*, 4 but with a Claisen flask with fractionating side arm as in Figs. *II*, *24*, 2–5), and distil under reduced pressure. Collect the α-naphthonitrile at 166–169°/18 mm. as a colourless liquid. The yield is 50 g.

Notes.

(1) Much heat is liberated when pyridine is added to the mixture.

(2) The metal bath may be replaced by a bath of hydrogenated cotton seed oil or of Silicone oil.

(3) The cuprammonium solution attacks filter paper.

α-Naphthoic acid. In a 750 ml. or 1 litre flask equipped with a reflux condenser, place 50 g. of α-naphthonitrile, 100 ml. of glacial acetic acid, 100 ml. of water and 100 ml. of concentrated sulphuric acid. Heat in an oil bath at 115–120° for 1·5 hours : do not allow the temperature to rise above 120° as the α-naphthoic acid formed tends to lose carbon dioxide at higher temperatures and the yield will be reduced. Dilute the cold reaction mixture, which contains much crystalline solid, with an equal volume of water and filter at the pump ; if the product consists of large lumps, transfer it first to a glass mortar and thoroughly grind it to a fine paste. Wash with water until free from mineral acid. Dissolve the crude acid in dilute aqueous sodium carbonate solution, heat for a short time to separate the resinous impurities, and filter the hot solution. Acidify the clear filtrate with a slight excess of dilute sulphuric acid (compare order of addition under p-*Nitrobenzoic Acid*, Section **IV,154**), collect the voluminous precipitate of almost pure α-naphthoic acid, wash until free from inorganic salts, and dry at 100°. Recrystallise from toluene or from light petroleum (b.p. 80–100°). The yield of pure α-naphthoic acid, m.p. 160–161°, is 55 g.

Method 2. Equip a 1 litre three-necked flask with a double surface reflux condenser, a mechanical stirrer and a separatory funnel, and place 12·2 g. of dry magnesium turnings, a crystal of iodine, 50 ml. of sodium-dried ether and 7·5 g. (5 ml.) of α-bromonaphthalene (Section **IV,20**) in the flask. If the reaction does not start immediately, reflux gently on a water bath until it does ; remove the water bath. Stir the mixture, and add a solution of 96 g. (65 ml.) of α-bromonaphthalene in 250 ml. of anhydrous ether from the separatory funnel at such a rate that the reaction is under control (1·5–2 hours). Place a water bath under the flask and continue the stirring and refluxing for a further 30 minutes. The Grignard reagent collects as a heavy oil in the bottom of the flask :

add 270 ml. of anhydrous benzene to the warm liquid in order to dissolve it completely. Cool the flask in a freezing mixture of ice and salt. In the meantime, replace the reflux condenser by a wide lead-in tube, 10 mm. in diameter and adjusted so that the end is about 5 cm. above the reaction mixture; this is necessary in order to prevent clogging in the subsequent reaction. Also replace the separatory funnel by a two-holed rubber stopper supporting a thermometer (with the bulb immersed in the reaction mixture) and a glass tube drawn out to fine capillary: the latter will permit the carbon dioxide which does not react to escape slowly and thus prevent the pressure in the flask becoming too great. When the temperature has fallen to —7°, pass dry carbon dioxide into the well-stirred mixture through the wide gas-inlet tube (1). Adjust the rate of flow of the gas so that the temperature does not rise above — 2°. The reaction is complete (*ca.* 1·5 hours) when the temperature falls below — 7° and does not rise on increasing the current of gas. Cool the flask in ice and add 25 per cent. sulphuric acid, with stirring, until no further reaction takes place and all the magnesium has disappeared. Separate the upper layer, and extract the aqueous layer with two 50 ml. portions of ether. Extract the clear ether-benzene extracts with three 50 ml. portions of 25 per cent. sodium hydroxide solution. Acidify the alkaline extracts with 50 per cent. sulphuric acid, filter off the crude α-naphthoic acid at the pump, wash with cold water until free from sulphate and dry at 100°. Dissolve the crude acid (67 g.) in 200 ml. of hot toluene, add a small amount of Filter-Cel (a diatomaceous earth), and filter the solution through a preheated Buchner funnel. Cool the filtrate in ice, filter and wash with cold toluene until the filtrate is nearly colourless. The yield of slightly coloured α-naphthoic acid, m.p. 160–161°, is 60 g.

Note.

(1) Alternatively, the solution of the Grignard reagent may be poured on to solid carbon dioxide (Dry Ice)—for experimental details, see under n-*Valeric Acid*, Section III,84.

IV,164. β-NAPHTHOIC ACID

Method 1

Prepare a solution containing about 100 g. of potassium hypochlorite from commercial calcium hypochlorite ("H.T.H.") as detailed under ββ-*Dimethylacrylic Acid*, Section **III,142**, *Note 1*, and place it in a 1500 ml. three-necked flask provided with a thermometer, a mechanical stirrer and a reflux condenser. Warm the solution to 55° and add through the condenser 85 g. of β-acetonaphthalene (methyl β-naphthyl ketone) (1). Stir the mixture vigorously and, after the exothermic reaction commences, maintain the temperature at 60–70° by frequent cooling in an ice bath until the temperature no longer tends to rise (*ca.* 30 minutes). Stir the mixture for a further 30 minutes, and destroy the excess of hypochlorite *completely* by adding a solution of 25 g. of sodium bisulphite in 100 ml. of water: make sure that no hypochlorite remains by testing the solution with acidified potassium iodide solution. Cool the solution, transfer the reaction mixture to a 2-litre beaker and cautiously acidify with 100 ml. of concentrated hydrochloric acid. Filter the crude acid at the pump,

wash with water, and drain as completely as possible. Dry at 100° and recrystallise the dry acid (85 g.; m.p. 181–183°) from rectified spirit (about 300 ml.). The yield of pure, colourless β-naphthoic acid, m.p. 184–185°, is 75 g.

Note.

(1) The commercial product, m.p. 53–55°, may be used. Alternatively the methyl β-naphthyl ketone may be prepared from naphthalene as described in Section IV,136. The Friedel-Crafts reaction in nitrobenzene solution yields about 90 per cent. of the β-ketone and 10 per cent. of the α-ketone; in carbon disulphide solution at — 15°, the proportions are 65 per cent. of the α- and 35 per cent. of the β-isomer. With chlorobenzene as the reaction medium, a high proportion of the α-ketone is also formed. Separation of the liquid α-isomer from the solid β-isomer in such mixtures (which remain liquid at the ordinary temperature) is readily effected through the picrates; the picrate of the liquid α-aceto compound is less soluble and the higher melting.

The reaction in chlorobenzene solution may be carried out as follows. Dissolve 1500 g. of pure naphthalene in 1500 g. (1355 ml.) of chlorobenzene, add 120 g. of finely-powdered, anhydrous aluminium chloride and 100 g. (90·5 ml.) of pure acetyl chloride, following the method given under p-*Bromoacetophenone* (Section IV,138), during 1 hour. Allow the reaction mixture to stand overnight, pour it upon crushed ice, separate the organic layer, wash it well with water, and dry with anhydrous magnesium sulphate. Distil off the chlorobenzene at normal pressure (*i.e.*, until the temperature rises to 140°) and then distil the residue under reduced pressure. A low b.p. fraction containing about 30 g. of naphthalene passes over first, followed by the mixed methyl naphthyl ketones at 138-145°/3 mm. (71 g.). Dissolve the ketone fraction in 100 ml. of rectified spirit and add a warm solution of 95 g. of picric acid in 900 ml. of rectified spirit. Cool, separate the almost pure picrate of methyl α-naphthyl ketone, m.p. 115–116° (71 g.); upon recrystallisation the m.p. rises to 119°. Concentrate the mother liquor successively to 500 ml. and 250 ml., and collect the crystals which separate after each concentration and cooling; 80 g. of the picrate of methyl β-naphthyl ketone, m.p. 82°, are obtained. Decompose the β-picrate, m.p. 82°, with sodium carbonate or dilute ammonia solution, separate the ketone, dry and distil under reduced pressure: pure methyl β-naphthyl ketone, b.p. 170–171°/11 mm., m.p. 55°, is thus isolated. Decomposition of the α-picrate, m.p. 119°, similarly yields pure methyl α-naphthyl ketone, b.p. 166–167°/12 mm.

Method 2

Diazotise 223 g. of 2-naphthylamine-1-sulphonic acid as detailed under *β-Bromonaphthalene* in Section IV,62. Prepare cuprous cyanide from 125 g. of cupric sulphate pentahydrate (Section IV,66) and dissolve it in a solution of 65 g. of potassium cyanide in 500 ml. of water contained in a 1-litre three-necked flask. Cool the potassium cuprocyanide solution in ice, stir mechanically, and add the damp cake of the diazonium compound in small portions whilst maintaining the temperature at 5–8°. Nitrogen is soon evolved and a red precipitate forms gradually. Continue the stirring for about 10 hours in the cold, heat slowly to the boiling point, add 250 g. of potassium chloride, stir, and allow to stand. Collect the orange crystals which separate by suction filtration; recrystallise first from water and then from alcohol; dry at 100°. The product is almost pure potassium 2-cyanonaphthalene-1-sulphonate. Transfer the product to a 2-litre round-bottomed flask, add a solution prepared from 400 ml. of concentrated sulphuric acid and 400 g. of crushed ice, and heat the mixture under reflux for 12 hours. Collect the β-naphthoic acid formed (some of which sublimes from the reaction mixture) by suction filtration

on a sintered glass funnel, wash well with water, and dry at 100°; recrystallise from rectified spirit. The yield of β-naphthoic acid, m.p. 184–185°, is 130 g.

IV,165 DIPHENIC ACID (*from Phenanthrene*)

Equip a 2·5 litre three-necked flask with a mechanical stirrer, a reflux condenser and a thermometer. Dissolve 89 g. (0·5 mol) of pure phenanthrene (1) in 1 litre of glacial acetic acid in the flask and warm to 85° on a water bath. Introduce 345 ml. of 30 per cent. hydrogen peroxide solution (2·75 mols) during 40 minutes; the temperature falls to about 80° and some phenanthrene may precipitate. After the addition is complete, heat the mixture with stirring on a water bath for a further 3–4 hours. Reduce the volume of the solution to about half by distillation under reduced pressure and allow to cool. Filter off the considerable amount of diphenic acid which crystallises out on cooling. Keep the filtrate and evaporate it almost to dryness under reduced pressure: extract the residue with 375 ml. of 10 per cent. sodium carbonate solution by warming on a water bath, boil the extract with a little decolourising carbon, filter and add dilute hydrochloric acid until the *p*H is 4·5 (use narrow-range indicator paper). Stir the solution with a further small amount of active charcoal and filter off the tarry material; cool the clear solution to 0° and acidify with dilute hydrochloric acid. Collect the precipitate by suction filtration, wash with water and dry at 110°. The total yield of crude diphenic acid, m.p. 228°, is 83 g. Recrystallisation from glacial acetic acid raises the m.p. to 230°.

Note.

(1) **Technical phenanthrene may be purified as follows.** Dissolve 500 g. of technical 90 per cent. phenanthrene in 3 litres of ethanol in a 4-litre flask on a steam bath and decant the hot solution from any insoluble material: collect the solid which crystallises upon cooling the solution. Dissolve 250 g. of the crystallised product in 550 ml. of hot glacial acetic acid in a 1-litre three-necked flask provided with an efficient reflux condenser and a dropping funnel. To the boiling solution add gradually 18 ml. of an aqueous solution containing 15 g. of chromic anhydride; then add slowly 7·5 ml. of concentrated sulphuric acid from the dropping funnel. Reflux the solution for 15 minutes, and then pour it with vigorous stirring into 1125 ml. of water in a 3-litre round-bottomed flask. Filter when cold, wash with water, and dry in the air. Distil the product under reduced pressure (oil pump) and collect the phenanthrene at 148–149°/1 mm. Use a 500 ml. Claisen flask attached directly with a 10–14 mm. glass tube to a 500 ml. round-bottomed flask (compare Fig. *II, 19,* 3): an all-glass apparatus is necessary since the m.p. of the phenanthrene is relatively close to its boiling point under the pressure of the distillation. Recrystallise the distillate from ethanol: 200–225 g. of nearly white phenanthrene, m.p. 99°, are obtained.

IV,166. HYDROCINNAMIC ACID

Method 1. Place 11·5 g. of clean metallic sodium (compare Section **III,7,** *Note 1*), cut into small pieces, into a dry 1 litre round-bottomed flask fitted with a 25 cm. double surface reflux condenser. Introduce 250 ml. of absolute, but preferably "super-dry" (see Section **II,47,** *5*) ethyl alcohol all at once. A vigorous reaction ensues: if the condenser tends to become flooded with alcohol, cool the flask either by surrounding it with a wet towel or by directing the waste water from the condenser upon

it. When all the sodium has reacted, add with frequent shaking 80 g. (75 ml.) of diethyl malonate (Section **III,153**). Then add slowly, through a separatory funnel supported in the top of the condenser by means of a grooved cork, 64 g. (58 ml.) of freshly distilled benzyl chloride (Section **IV,22**). Remove the separatory funnel, introduce a calcium chloride (or cotton wool) guard tube into the top of the condenser and reflux the mixture, with occasional shaking, for 4 hours or until neutral to moist litmus. Rearrange the condenser for ordinary distillation (compare Fig. *II*, *13*, 3) and distil as much of the remaining ethyl alcohol as possible on a water bath : this process is assisted by wrapping the exposed part of the flask in a cloth. Add 250 ml. of water to the residue and separate the upper oily layer of crude ethyl benzylmalonate. Transfer the ester to a 500 ml. round-bottomed flask, provided with a reflux condenser, containing a solution of 75 g. of potassium hydroxide in 75 ml. of water. Reflux the mixture until hydrolysis is complete (no oily layer visible : about 2 hours) and remove the residual alcohol by distillation. Allow to cool and extract the resulting aqueous solution of potassium benzylmalonate with a little ether to remove any unhydrolysed oily matter ; if any solid salts separate, add just sufficient water to dissolve them. Heat the clear potassium benzylmalonate solution in a 750 ml. round-bottomed flask on a water bath to about 80° to remove the dissolved ether, fit a reflux condenser, and add 180 ml. of 10*N* sulphuric acid. When foaming has ceased, reflux the mixture for 3 hours. Cool, add water to dissolve any inorganic salt which has separated, and extract the oil with ether. Dry the ethereal solution over anhydrous magnesium sulphate, remove the ether (Fig. *II*, *13*, 4 but with a Claisen flask replacing the distilling flask) and distil the residue under diminished pressure. Collect the fraction, b.p. 164–172°/25 mm., separately ; this solidifies at room temperature. Recrystallise from hot water containing a little hydrochloric acid or, better, from light petroleum, b.p. 40–60°. The yield of hydrocinnamic acid, m.p. 47–48°, is 20 g.

Method 2. Dissolve 20 g. of cinnamic acid (Section **IV,124**) in 145 ml. of approximately *N* sodium hydroxide solution contained in a 500 ml. glass bottle, equipped with a mechanical stirrer. Add 350 g. of 2·5 per cent. sodium amalgam (Section **II,50,7**) gradually during 1 hour whilst the mixture is well-stirred. When hydrogen is no longer evolved, separate the mercury and wash it with water : add the washings to the solution and acidify the whole with dilute hydrochloric acid (1 : 1). Hydrocinnamic acid is precipitated, at first in the form of an oil, which solidifies on cooling and rubbing with a glass rod. Filter at the pump and recrystallise as in *Method 1*. The yield of hydrocinnamic acid, m.p. 47-48°, is 17 g.

IV,167. *m*-NITROBENZOIC ACID

Methyl *m*-nitrobenzoate. In a 1 litre round-bottomed or bolt-head flask, fitted with a mechanical stirrer, place 102 g. (94 ml.) of pure methyl benzoate (Section **IV,176**) : support a separatory funnel containing a mixture of 62·5 ml. of concentrated sulphuric acid and 62·5 ml. of concentrated nitric acid over the mouth of the flask. Cool the flask in an ice bath to 0-10°, and then run in the nitrating mixture, with stirring,

whilst maintaining the temperature of the reaction mixture between 5° and 15°; the addition requires about 1 hour. Continue the stirring for 15 minutes longer, and pour the mixture upon 700 g. of crushed ice. Filter off the crude methyl *m*-nitrobenzoate at the pump and wash it with cold water. Transfer the solid to a 500 ml. bolt-head flask and stir it with 100 ml. of ice-cold methyl alcohol in order to remove a small amount of the *ortho* isomeride and other impurities. Filter the cooled mixture with suction, wash it with 50 ml. of ice-cold methyl alcohol, and dry in the air. The practically colourless methyl *m*-nitrobenzoate weighs 115 g. and melts at 75–76°; it is sufficiently pure for conversion into *m*-nitrobenzoic acid. The pure ester, m.p. 78°, may be obtained by recrystallisation from an equal weight of methyl alcohol.

Hydrolysis of methyl *m*-nitrobenzoate to *m*-nitrobenzoic acid. Place 90·5 g. of methyl *m*-nitrobenzoate and a solution of 40 g. of sodium hydroxide in 160 ml. of water in a 1-litre round-bottomed flask equipped with a reflux condenser. Heat the mixture to boiling during 5–10 minutes or until the ester has disappeared. Dilute the reaction mixture with an equal volume of water. When cold pour the diluted reaction product, with vigorous stirring, into 125 ml. of concentrated hydrochloric acid. Allow to cool to room temperature, filter the crude acid at the pump and wash it with a little water. Upon drying at 100°, the crude *m*-nitrobenzoic acid, which has a pale brownish colour, weighs 80 g. and melts at 140°. Recrystallisation from 1 per cent. hydrochloric acid affords the pure acid, m.p. 141°, as a pale cream solid; the loss of material is about 5 per cent.

IV,168. 3:5-DINITROBENZOIC ACID

Method 1. Dissolve 50 g. of pure benzoic acid in 230 ml. of concentrated sulphuric acid in a litre flask equipped with a ground-in condenser. Add 73 ml. of fuming nitric acid (sp. gr. 1·5) a few ml. at a time. Shake the flask well and cool in ice water during the addition; much heat is evolved and a clear yellow solution results. Add a few fragments of porous porcelain and heat the mixture gradually on a water bath to 100° during 45 minutes. At 70–80° the reaction may (and usually does) become vigorous; moderate, when necessary, by cooling the flask in cold water. Maintain the mixture at 100° for 15 minutes with occasional shaking, and then transfer it to an oil bath at 100°; raise the temperature to 130° over 30 minutes and keep it at 130–140° for 1 hour. Allow the flask to cool: crystals commence to separate at about 90°. When cold, pour the reaction mixture into 3–4 litres of ice water, filter the separated crystals, wash with water, and dry. The yield of 3:5-dinitrobenzoic acid, m.p. 204°, is 50 g.: this acid is pure enough for most purposes. Upon recrystallisation from 50 per cent. alcohol (4·5 ml. per gram), the m.p. is raised to 207°.

Method 2. This preparation should be carried out in the fume cupboard since nitrous fumes are evolved. Place 62 g. of benzoic acid and 300 ml. of concentrated sulphuric acid in a 2-litre round-bottomed flask, warm on a water bath with shaking until the benzoic acid dissolves, and cool to 20°. Add 100 ml. of fuming nitric acid (sp. gr. 1·54) in portions

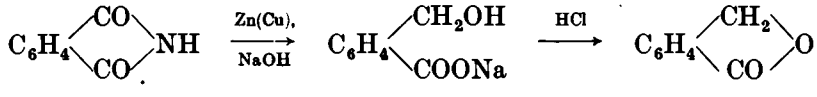
of 2-3 ml. Keep the temperature between 70° and 90° by means of external cooling with cold water ; avoid the evolution, in other than small quantities, of brown fumes. Cover the flask with a watch glass, and allow to stand for 1 hour or overnight. Heat the flask on a water bath for 4 hours ; considerable quantities of nitrous fumes are liberated. Allow to cool to room temperature, preferably with mechanical stirring, when yellow crystals will separate from the solution. Add a further 75 ml. of fuming nitric acid ; heat the mixture on a water bath for 3 hours, then in an oil bath at 135–145° for 3 hours. Allow the reaction mixture to cool and pour it into a mixture of 800 g. of finely-crushed ice and 800 ml. of water. Allow to stand for 30–60 minutes, filter off the crude 3 : 5-dinitrobenzoic acid at the pump, and wash it with water until free from sulphates. Recrystallise the crude acid (66 g. ; m.p. 201–202°) from 280 ml. of hot 50 per cent. alcohol. Collect the recrystallised material and dry in the steam oven. The yield of 3 : 5-dinitrobenzoic acid, m.p. 207°, is 62 g.

IV,169. HOMOPHTHALIC ACID

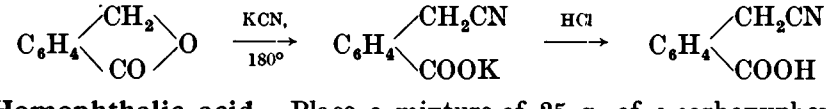
Phthalimide. *Method 1.* Place 100 g. of phthalic anhydride and 105 ml. of concentrated ammonia solution (sp. gr. 0·88) in a 1-litre round-bottomed flask fitted with a wide air condenser (⩽ 10 mm. in diameter). Heat first over a wire gauze and then over a free flame until the mixture is in a state of quiet fusion and forms a homogeneous melt (the temperature reaches 300° in about 1·5–2 hours ; all the water is evaporated during the first hour). Shake the flask occasionally during the heating and push down any material which sublimes into the condenser with a glass rod. Pour the contents of the flask whilst still hot into a porcelain basin or casserole, allow to cool, and grind to a fine powder in a mortar. The phthalimide (95 g.) is practically pure and melts at 233-234°. It may be recrystallised from alcohol, but the solubility is only slight (about 5 per cent.).

Method 2. Intimately mix 99 g. of pure phthalic anhydride and 20 g. of urea, and place the mixture in a 1 litre long-necked, round-bottomed flask. Heat the flask in an oil bath at 130–135°. When the contents have melted, effervescence commences and gradually increases in vigour : after 10–20 minutes, the mixture suddenly froths up to about three times the original volume (this is accompanied by a rise in temperature to 150–160°) and becomes almost solid. Remove the flame from beneath the bath and allow to cool. Add about 80 ml. of water to disintegrate the solid in the flask, filter at the pump, wash with a little water, and then dry at 100°. The yield of phthalimide, m.p. 233° (*i.e.*, it is practically pure) is 86 g. If desired, the phthalimide may be recrystallised from 1200 ml. of methylated spirit ; the first crop consists of 34 g. of m.p. 234°, but further quantities may be recovered from the mother liquor.

Phthalide. In a 1 litre bolt-head flask stir 90 g. of a high quality zinc powder to a thick paste with a solution of 0·5 g. of crystallised copper sulphate in 20 ml. of water (this serves to activate the zinc), and then add 165 ml. of 20 per cent. sodium hydroxide solution. Cool the flask in an ice bath to 5°, stir the contents mechanically, and add 73·5 g. of phthalimide in small portions at such a rate that the temperature does not rise above 8° (about 30 minutes are required for the addition). Continue the stirring for half an hour, dilute with 200 ml. of water, warm on a water bath until the evolution of ammonia ceases (about 3 hours), and concentrate to a volume of about 200 ml. by distillation under reduced pressure (Fig. *II*, *37*, 1). Filter, and render the filtrate acid to Congo red paper with concentrated hydrochloric acid (about 75 ml. are required). Much of the phthalide separates as an oil, but, in order to complete the lactonisation of the hydroxymethylbenzoic acid, boil for an hour : transfer while hot to a beaker. The oil solidifies on cooling to a hard red-brown cake. Leave overnight in an ice chest or refrigerator, and then filter at the pump. The crude phthalide contains much sodium chloride. Recrystallise it in 10 g. portions from 750 ml. of water : use the mother liquor from the first crop for the recrystallisation of the subsequent portion. Filter each portion while hot, cool in ice below 5°, filter and wash with small quantities of ice-cold water. Dry in the air upon filter paper. The yield of phthalide (transparent plates), m.p. 72–73°, is 47 g.



***o*-Carboxyphenylacetonitrile.** Into a 1 litre bolt-head flask, provided with a mechanical stirrer and a thermometer, place 40 g. of phthalide and 40 g. of powdered potassium cyanide. Heat the stirred mixture to 180–190° (internal temperature) in an oil bath for 4–5 hours. Allow to cool, add 400 ml. of distilled water and stir the mixture until all the solids are dissolved (about 1 hour). Filter off any unreacted phthalide. Add dilute hydrochloric acid (1 : 1) to the dark aqueous solution * until it becomes turbid (about 20 ml. are required), and continue the addition until the solution is slightly acid : filter off any dark impurities which may separate. Neutralise the solution carefully with sodium bicarbonate, add a few grams of decolourising carbon, stir the mixture for several minutes and filter. Acidify the nearly colourless filtrate with about 20 ml. of concentrated hydrochloric acid, cool in ice, and filter at the pump. The resulting *o*-carboxyphenylacetonitrile (40 g.) melts at 114–115° and is satisfactory for most purposes. It may be crystallised from benzene or glacial acetic acid, but with considerable loss.



Homophthalic acid. Place a mixture of 25 g. of *o*-carboxyphenylacetonitrile and 25 g. of 50 per cent. sulphuric acid in a 100 ml. flask, heat

* This operation should be conducted in a fume cupboard (hood) as hydrogen cyanide may be evolved.

the mixture on a water bath for 10–12 hours and then pour it into twice its volume of ice and water. Filter the precipitate at the pump and dry in the air. The yield of crude homophthalic acid is 21 g. Recrystallise by dissolving it in 500 ml. of boiling water, add decolourising carbon, filter the hot solution through a hot water funnel, and cool the filtrate in an ice bath : collect the acid and dry at 100°. The yield of practically colourless acid, m.p. 181°, is 17 g. The melting point depends upon the rate of heating ; immersion of the capillary in a bath at 170° gives a m.p. of 182–183°.

IV,170. ANTHRANILIC ACID

Prepare a solution of 30 g. of sodium hydroxide in 120 ml. of water in a 350 ml. conical flask and cool to 0° or below in a bath of ice and salt. Add 26·2 g. (8·4 ml.) of bromine in one portion and shake (or stir) until all the bromine has reacted. The temperature will rise somewhat ; cool again to 0° or below. Meanwhile, prepare a solution of 22 g. of sodium hydroxide in 80 ml. of water. Add 24 g. of finely-powdered phthalimide (Section **IV,169**) in one portion to the cold sodium hypobromite solution ; stir vigorously while swirling the contents of the flask and add the prepared sodium hydroxide solution rapidly. The solid will dissolve and the temperature will rise to about 70°. Warm the mixture to 80° for about 2 minutes. Filter, if necessary. Cool in ice and add concentrated hydrochloric acid slowly and with stirring until the solution is *just* neutral (about 60 ml. are required). [It is recommended that a little of the alkaline solution be set aside in case too much acid is added.] Precipitate the anthranilic acid completely by the gradual addition of glacial acetic acid (20–25 ml. are required) : it is advisable to transfer the mixture to a 1 litre beaker as some foaming occurs. Filter off the acid at the pump and wash with a little cold water. Recrystallise from hot water with the addition of a little decolourising carbon ; collect the acid on a Buchner funnel and dry at 100°. The yield of pure anthranilic acid, m.p. 145°, is 14 g.

IV,171. DIPHENYLACETIC ACID

Place 125 ml. of glacial acetic acid, 7·5 g. of purified red phosphorus (Section **II,50,5**) and 2·5 g. of iodine in a 500 ml. round-bottomed flask fitted with a reflux condenser. Allow the mixture to stand for 15–20 minutes with occasional shaking until all the iodine has reacted, then add 2·5 ml. of water and 50 g. of benzilic acid (Section **IV,127**). Boil the mixture under reflux for 3 hours, and filter the hot mixture at the pump through a sintered glass funnel to remove the excess of red phosphorus. Pour the hot filtrate into a cold, well-stirred solution of 12 g. of sodium bisulphite in 500 ml. of water ; the latter should be acid to litmus, produced, if necessary, by passing sulphur dioxide through the solution. This procedure removes the excess of iodine and precipitates the diphenylacetic acid as a fine white or pale yellow powder. Filter the solid with suction and dry in the air upon filter paper. The yield is 45 g., m.p.

142–144°. Upon recrystallisation from about 250 ml. of 50 per cent. alcohol, crystalline diphenylacetic acid, m.p. 144–145° (1), is obtained.

Note.

(1) Benzilic acid melts at 149–150°, *i.e.*, very close to that of diphenylacetic acid. The completeness of the reduction can easily be tested by treating a little of the product with concentrated sulphuric acid ; if even a trace of benzilic acid remains, the sulphuric acid will have a red colour.

IV,172. MANDELIC ACID

Into a 750 ml. wide-mouthed bottle, provided with a mechanical stirrer, place a solution of 25 g. of technical sodium cyanide (97–98 per cent. NaCN) in 100 ml. of water and 53 g. (51 ml.) of purified benzaldehyde (Section IV,115). Prepare a saturated solution of sodium bisulphite by stirring 250 g. of finely-powdered technical sodium bisulphite with 335 ml. of water and filtering to remove the excess of the salt. Stir the mixture in the bottle and add the sodium bisulphite solution slowly at first and then more rapidly (the addition occupies 10–15 minutes). During the addition of the first half of the solution, add 150 g. of crushed ice to the reaction mixture in several portions. Transfer the product to a separatory funnel and remove the layer of crude mandelonitrile (1). Place the latter at once (2) in a large evaporating dish, add 75 ml. of concentrated hydrochloric acid, cover with a clock glass, and allow the hydrolysis to proceed in the cold for 12 hours ; finally evaporate to dryness on a water bath. Grind the residue of slightly discoloured mandelic acid and inorganic salts to a fine powder in a mortar and wash it twice with 125 ml. portions of cold benzene : this process will remove most of the colouring matter and a negligible quantity of mandelic acid. To separate inorganic salts from the mandelic acid, extract the residue in a Soxhlet apparatus (Figs. *II,44*, 4–6) with about 200 ml. of benzene on a water bath. Allow the hot benzene extract to crystallise, collect the crystals on a Buchner funnel and dry in the air. The yield of pure *dl*-mandelic acid, m.p. 118°, is 35 g.

Notes.

(1) A small quantity of mandelonitrile may be obtained by extracting the aqueous layer with 25 ml. of benzene, evaporating the benzene, and adding the residue to the main portion. This extraction is hardly worth while except for large scale preparations.

(2) It is important to mix the mandelonitrile with hydrochloric acid immediately it has been separated from the water. Standing results in rapid conversion to the acetal of benzaldehyde and mandelonitrile $C_6H_5CH[OCH(CN)C_6H_5]_2$, and/or the *iso*-nitrile ; the yield of mandelic acid will, in consequence, be reduced.

IV,173. SALICYLIC ACID

Place 10 g. of clean sodium (cut into small pieces) in a 500 ml. round-bottomed flask fitted with a double surface reflux condenser. Introduce 100 g. (127 ml.) of absolute ethyl alcohol and allow the reaction to proceed as vigorously as possible ; if the alcohol tends to flood the condenser, cool the flask momentarily with a wet towel or by a stream of cold water. When all the sodium has reacted, add 40 g. of pure phenol. Distil off the

alcohol using a free flame : shake the flask frequently during the process until a powdery mass is produced. Transfer the solid rapidly to a dry mortar, powder rapidly, and transfer the powder to a 250 ml. distilling flask. Immerse the bulb of the flask in an oil bath, and insert a gas inlet tube in the mouth so that it terminates about 1 cm. above the sodium phenoxide. Heat the oil bath to 110° and pass dry carbon dioxide into the flask for 1 hour. Raise the temperature gradually during 4 hours to 190° (20° an hour) and finally maintain the temperature at 200° for 1·5 hours. Pass a fairly rapid stream of carbon dioxide into the flask during the whole of the heating period ; stir the contents of the flask frequently with a glass rod (this will necessitate removing the gas inlet tube momentarily) in order to expose a fresh portion of the solid to the action of the gas. Allow the reaction product to cool, transfer it to a large beaker and rinse the distilling flask several times with water. Precipitate the salicylic acid by the addition of excess of concentrated hydrochloric acid. Cool in ice, filter at the pump, and wash with a little cold water. Recrystallise the crude acid from hot water with the addition of a little decolourising carbon. The yield of air-dried salicylic acid, m.p. 159°, is 16 g.

Cognate Preparations

β-Resorcylic acid. Place a solution containing 40 g. of resorcinol, 200 g. of potassium bicarbonate and 400 ml. of water in a litre flask fitted with a reflux condenser and gas inlet tube. Heat gently on a steam bath for 4 hours ; then reflux vigorously over a flame for 30 minutes whilst passing a rapid stream of carbon dioxide through the solution. Acidify the solution whilst still hot by adding 180 ml. of concentrated hydrochloric acid from a separatory funnel with a long tube delivering acid to the bottom of the flask. Allow to cool to room temperature, chill in an ice bath, and collect the crude β-resorcylic acid by filtration with suction. Recrystallise by boiling the crude acid with 180–200 ml. of water in the presence of a little decolourising carbon, filter through a hot water funnel, and cool in an ice-salt mixture with stirring. Collect and dry the pure β-resorcylic acid ; the yield is 36 g., m.p. 216–217°.

p-Hydroxybenzoic acid. Place 100 g. of A.R. salicylic acid and 150 ml. of water in an 8″ porcelain dish and slowly stir in 60 g. of potassium carbonate. Evaporate the solution on a steam bath to a thick, pasty solid ; break this up into small pieces and dry at 105–110° for 2 hours. Finely grind the solid, dry for a further 2 hours at 105–110°, and grind again to a fine powder. Transfer the powder (a mixture of potassium salicylate and potassium carbonate) to a 500 ml. bolt-head flask immersed in an oil bath (*FUME CUPBOARD !*) so that only a small portion of the neck protrudes from the flask ; in this way, the phenol formed in the subsequent reaction distils out of the mixture. Heat the oil bath to 240° and maintain this temperature for 90 minutes ; stir the solid occasionally with a glass rod. When the reaction is complete (1), transfer the product while hot to a 2-litre flask containing 1 litre of hot water ; rinse the reaction flask with several portions of the hot solution. Acidify with concentrated hydrochloric acid (*ca.* 75 ml. are required), heat nearly to boiling, add 5 g. of decolourising carbon, filter, cool, and collect the brown

solid by suction filtration. Concentrate the filtrate to about 300 ml., cool and collect a second crop of the acid. Dissolve the crude acid in 300 ml. of hot water, boil for a few minutes with 5 g. of decolourising carbon, and filter. Cool the filtrate under the tap, filter the solid with suction, wash with 15 ml. of cold water and dry. The yield of *p*-hydroxybenzoic acid, m.p. 211–212°, is 40 g.

Note.

(1) This may be determined roughly by treating a small test portion with 3–4 ml. of hot water and acidifying with concentrated hydrochloric acid ; the absence of a precipitate in the warm solution indicates the essential completeness of the reaction. Salicylic acid is sparingly soluble and *p*-hydroxybenzoic acid is relatively soluble under these conditions.

IV,174. PHENYLPROPIOLIC ACID

Place a solution of 88 g. (84 ml.) of ethyl cinnamate (Section **IV,131**) in 50 ml. of carbon tetrachloride in a 500 ml. round-bottomed flask and fit it with a two-holed stopper. Immerse the flask in ice and insert a separatory funnel charged with 80 g. (25·5 ml.) of bromine in one hole of the stopper. Add the bromine slowly with frequent shaking. The halogen will disappear rapidly at first, but more slowly towards the end of the reaction ; no hydrogen bromide is evolved and the time of the addition is about 20–25 minutes. Allow the mixture to stand for 1 hour, pour the solution into a large evaporating dish and permit the excess of bromine and the carbon tetrachloride to evaporate spontaneously in the fume cupboard. The crude ethyl αβ-dibromo-β-phenylpropionate will remain as a solid cake ; this can be dried by pressing between large filter papers. The yield of crude ester, m.p. 66–71°, is 140 g. (1).

Dissolve 85 g. of potassium hydroxide in 400 ml. of rectified spirit by heating in a 1500 ml. round-bottomed flask, provided with a reflux condenser, on a water bath. Cool to 40–50°, and add 112 g. of the crude dibromo ester ; when the initial exothermic reaction has subsided, heat the mixture on a water bath for 5–6 hours. Pour the contents of the flask into a large beaker and, when cold, add concentrated hydrochloric acid with stirring until neutral to litmus. Cool, filter the precipitated solids at the pump, and wash with a little alcohol. Set the solids (*A*) aside. Transfer the filtrate to the original flask and distil the liquid (Fig. *II*, *13*, 3) from a wire gauze or from an air bath until the temperature of the vapour reaches 95°. Combine the residue in the flask with the precipitated solids (*A*), dissolve in 270 ml. of water, add about 300 g. of crushed ice, and cool the flask in an ice bath. Stir the mixture mechanically, and add 20 per cent. sulphuric acid slowly until the solution is strongly acid to Congo red. Allow to stand for 20 minutes, filter off the dark-coloured crude phenylpropiolic acid at the pump and wash it with three 15 ml. portions of 2 per cent. sulphuric acid. Dissolve the solid in about 300 ml. of 5 per cent. sodium carbonate solution, add 6 g. of decolourising carbon, and heat on a water bath for 30 minutes with occasional shaking. Filter through a fluted filter paper, cool the filtrate in ice, and then add 70 g. of crushed ice. Stir the solution mechanically and add 20 per cent. sulphuric acid slowly until acid to Congo red. After 20 minutes, filter

the precipitated acid by suction, wash with 15 ml. of 2 per cent. sulphuric acid, then with a little water, and dry in the air. The yield of pure phenylpropiolic acid, m.p. 134–135°, is 23 g.

Note.

(1) To obtain the pure dibromo ester, recrystallise from light petroleum, b.p. (60–80°); the recovery of the pure ester, m.p. 75°, is 85 per cent.

IV,175. REACTIONS AND CHARACTERISATION OF AROMATIC CARBOXYLIC ACIDS

Aromatic carboxylic acids are usually crystalline solids, burn with a smoky flame, and are generally sparingly soluble in water. They may be detected and characterised as already described under *Aliphatic Carboxylic Acids* (Section **III,85**).

An additional useful test is to **distil the acid or its sodium salt with soda lime.** Heat 0.5 g. of the acid or its sodium salt with 0·2 g. of soda lime in an ignition tube to make certain that there is no explosion. Then grind together 0·5 g. of the acid with 3 g. of soda lime, place the mixture in a Pyrex test-tube and cover it with an equal bulk of soda lime. Fit a wide delivery tube dipping into an empty test-tube. Clamp the tube near the mouth. Heat the soda lime first and then the mixture gradually to a dull-red heat. Examine the product: this may consist of aromatic hydrocarbons or derivatives, *e.g.*, phenol from salicylic acid, anisole from anisic acid, toluene from toluic acid, etc.

The melting points of the derivatives of a number of selected aromatic carboxylic acids are collected in Table **IV,175.**

TABLE IV,175. **AROMATIC CARBOXYLIC ACIDS**

Acid	B.P.	M.P	Anilide	*p*-Toluidide	Amide	*p*-Bromophenacyl Ester	*p*-Nitrobenzyl Ester	*p*-Phenylphenacyl Ester	S-Benzyl-*iso*-thiuronium Salt	Other Derivatives
Benzoic	249°	121°	162°	158°	129°	119°	89°	167°	167°	Hydrazide, 112°
o-Toluic	259	105	125	144	143	57	91	95	146	Hydrazide, 124
m-Toluic	263	111	126	118	95	108	87	136	140	Hydrazide, 97
p-Toluic	274	178	148	160	159	153	104	165	190	Hydrazide, 117
Phenylacetic	265	76	118	136	157	89	65	88	165	—
o-Chlorobenzoic	—	141	118	131	141	107	106	123	—	Hydrazide, 110
m-Chlorobenzoic	—	158	124	—	134	117	107	154	155	Hydrazide, 158
p-Chlorobenzoic	—	243	194	—	179	126	130	160	—	Hydrazide, 163
o-Bromobenzoic	—	150	141	—	155	102	110	98	171	—
m-Bromobenzoic	—	155	146	—	155	126	105	155	168	—
p-Bromobenzoic	—	252	197	—	189	134	141	160	—	Hydrazide, 164
o-Iodobenzoic	—	162	141	—	184	110	111	143	—	—
m-Iodobenzoic	—	187	—	—	186	128	121	—	—	—
p-Iodobenzoic	—	270	210	—	218	146	141	171	—	—
o-Nitrobenzoic	—	147	155	—	175	107	112	140	159	—
m-Nitrobenzoic	—	141	154	162	142	132	142	153	163	—
p-Nitrobenzoic	—	239	211	203	200	136	169	182	182	—
2 : 4-Dinitrobenzoic	—	183	—	—	204	158	142	—	—	—
3 : 5-Dinitrobenzoic	—	207	234	—	183	159	157	154	—	—
2 : 4 : 6-Trinitrobenzoic	—	228	—	—	264	—	—	—	—	—
Salicylic	—	158	135	156	139	140	98	148	148	Benzoyl, 132; *p*-nitrobenzoyl, 205
m-Hydroxybenzoic	—	201	157	163	167	176	108	—	—	Acetyl, 131
p-Hydroxybenzoic	—	213	197	204	162	191	192	240	145	Acetyl, 187
Resorcylic (1)	—	213	127	—	221	—	189	—	—	—
Protocatechuic (2)	—	199	167	—	212	—	188	—	—	—
Piperonylic (3)	—	229	—	—	169	—	—	—	—	—
o-Methoxybenzoic	—	101	131	—	129	—	113	131	—	—
m-Methoxybenzoic	—	110	—	—	—	—	—	—	—	—
Anisic (4)	—	184	171	186	163	152	132	160	185	—
Anthranilic	—	146	131	151	109	—	205	—	149	*N*-Benzoyl, 81; *N*-*p*-toluenesulphonyl, 217
m-Aminobenzoic	—	174	140	—	111	—	201	—	—	*N*-Acetyl, 248
p-Aminobenzoic	—	188	—	—	114	—	—	—	—	*N*-Acetyl, 250; *N*-benzoyl, 278
o-Ethoxybenzoic	—	25	—	—	132	—	—	—	—	—
m-Ethoxybenzoic	—	137	—	—	139	—	—	—	—	—
p-Ethoxybenzoic	—	198	170	—	202	—	110	—	—	—

Acid	B.P.	M.P.	Anilide	*p*-Toluidide	Amide	*p*-Bromophenacyl Ester	*p*-Nitrobenzyl Ester	*p*-Phenylphenacyl Ester	S-Benzyl-*iso*-thiuronium Salt	Other Derivatives
Phenoxyacetic	—	99°	101°	—	101°	148°	—	—	—	—
o-Chlorophenoxyacetic	—	146	121	—	150	—	—	—	—	—
m-Chlorophenoxyacetic	—	110	—	—	—	—	—	—	—	—
p-Chlorophenoxyacetic	—	157	125	—	133	136	—	—	—	—
α-Naphthoic	—	162	163	—	202	—	—	—	—	—
β-Naphthoic	—	185	170	191°	192	—	—	—	—	—
3-Hydroxy-2-naphthoic	—	223	244	222	218	—	—	—	—	—
Phthalic	—	*ca.*208d	251	—	220	153	155°	167°	158°	—
iso-Phthalic	—	347	—	—	280	179	203	280	216	Hydrazide, 220°
Terephthalic	—	subl. 300	337	—	—	225	264	—	204	—
3-Nitrophthalic	—	219	234	223	201	—	190	149	—	—
4-Nitrophthalic	—	165	—	—	200	—	—	120	—	—
Cinnamic	300°	133	153	168	147	146	117	182	183	—
o-Nitrocinnamic	—	240	—	—	185	142	132	146	—	—
m-Nitrocinnamic	—	205	—	—	196	178	174	—	—	—
p-Nitrocinnamic	—	287	—	—	217	191	187	192	—	—
Hydrocinnamic (5)	—	48	98	135	105	104	36	95	—	—
Benzylmalonic	—	120d	217	—	225	—	120	—	—	—
Phenylpropiolic	—	135	126	142	109	—	83	—	—	—
Hippuric	—	187	208	—	183	151	136	163	—	Hydrazide, 162
β-Phenylalanine (6)	—	273	—	—	140	—	222	—	—	*N*-Benzoyl, 188
dl-Mandelic	—	118	152	172	134	—	123	—	166	—
Benzilic	—	150	175	190	155	152	100	122	—	Acetyl, 98
Gallic	—	*ca.*240d	207	—	245	—	—	198d	—	Triacetyl, 172; tribenzoyl, 192
Vanillic (7)	—	210	—	—	—	—	141	—	—	Acetyl, 146; benzoyl, 178
o-Benzoylbenzoic	—	128	195	—	165	—	100	—	—	—
Acetylsalicylic	—	135	136	—	138	—	90	—	144	—
Hexahydrobenzoic (8)	233	31	144	—	186	—	—	—	—	—
Trimesic (9)	—	380	—	—	365	197	—	—	—	Tri-Me-ester, 144; tri-Et-ester, 135
Diphenic		229	230	—	212	—	186	—	—	—
Diphenylacetic	—	148	180	173	168	—	—	111	—	—

(1) 2 : 4-Dihydroxybenzoic acid.
(2) 3 : 4-Dihydroxybenzoic acid.
(3) 3 : 4-Methylenedioxybenzoic acid.
(4) *p*-Methoxybenzoic acid.
(5) β-Phenylpropionic acid.
(6) α-Amino-β-phenylpropionic acid.
(7) 4-Hydroxy-3-methoxybenzoic acid.
(8) *cyclo*Hexanecarboxylic acid.
(9) Benzene-1 : 3 : 5-tricarboxylic acid.

AROMATIC ESTERS

Aromatic esters may be prepared by methods similar to those already described for aliphatic esters (see discussion preceding Section III,95). These include :—

1. **From the acid.** By refluxing an aromatic acid (1 mol) with an excess (up to about 10 mols) of methyl or ethyl alcohol in the presence of a small proportion of concentrated sulphuric acid or hydrogen chloride (catalyst), the ester may be obtained in good yield. The excess of methyl or ethyl alcohol may be largely removed by distillation from a water bath or, less conveniently, by pouring into a large excess of water. For higher alcohols, *e.g.*, *n*-propyl or *n*-butyl alcohols, the proportion of alcohol may be considerably reduced (say, 1 mol of monobasic acid to 2 mols of alcohol) if a volume of pure dry benzene approximately equal to that of the alcohol is added. The following examples are given :

$$\underset{\text{Benzoic acid}}{C_6H_5COOH} + \underset{\text{Methyl alcohol}}{CH_3OH} \xrightarrow[\text{or HCl}]{H_2SO_4} \underset{\text{Methyl benzoate}}{C_6H_5COOCH_3} + H_2O$$

$$\underset{\text{Benzoic acid}}{C_6H_5COOH} + \underset{n\text{-Propyl alcohol}}{C_3H_7{}^{\alpha}OH} \xrightarrow[C_6H_6]{H_2SO_4} \underset{n\text{-Propyl benzoate}}{C_6H_5COOC_3H_7{}^{\alpha}} + H_2O$$

$$\underset{\text{Salicylic acid}}{o\text{-}HOC_6H_4COOH} + CH_3OH \xrightarrow{H_2SO_4} \underset{\text{Methyl salicylate}}{o\text{-}HOC_6H_4COOCH_3} + H_2O$$

Esterification with an aromatic alcohol may be readily achieved by using an excess of the acid. The latter is readily removed by washing with water and/or treatment with sodium bicarbonate solution, for example :

$$\underset{\text{Acetic acid}}{CH_3COOH} + \underset{\text{Benzyl alcohol}}{C_6H_5CH_2OH} \xrightarrow{H_2SO_4} \underset{\text{Benzyl acetate}}{CH_3COOCH_2C_6H_5} + H_2O$$

2. **From the nitrile.** By refluxing a mixture of the aromatic nitrile (with —CN group in side chain) with alcohol and concentrated sulphuric acid simultaneous hydrolysis and esterification occurs, for example :

$$\underset{\text{Benzyl cyanide}}{C_6H_5CH_2CN} + C_2H_5OH + H_2SO_4 + H_2O \longrightarrow \underset{\text{Ethyl phenylacetate}}{C_6H_5CH_2COOC_2H_5} + NH_4HSO$$

3. **From the acid chloride.** The interaction of the acid chloride of an aromatic acid with the calculated quantity of an alcohol or a phenol affords a good yield of the ester, for example :

$$\underset{\text{Cinnamic acid}}{C_6H_5CH{=}CHCOOH} + SOCl_2 \longrightarrow \underset{\text{Cinnamoyl chloride}}{C_6H_5CH{=}CHCOCl} + SO_2 + HCl$$

$$C_6H_5CH{=}CHCOCl + \underset{\text{Phenol}}{C_6H_5OH} \longrightarrow \underset{\text{Phenyl cinnamate}}{C_6H_5CH{=}CHCOOC_6H_5} + HCl$$

4. **By the Schotten-Baumann reaction.** Under the usual Schotten-Baumann conditions (compare discussion preceding Section IV,52, also Section IV,100, *2* and Section IV,114, *2*), esters are readily formed, for example :

$$\underset{\text{Benzoyl chloride}}{C_6H_5COCl} + \underset{\text{Phenol}}{C_6H_5OH} \xrightarrow[\text{aq.}]{NaOH} \underset{\text{Phenyl benzoate}}{C_6H_5COOC_6H_5} + HCl\ (\longrightarrow NaCl)$$

The esters formed with *p*-nitrobenzoyl chloride and 3 : 5-dinitrobenzoyl chloride (see Section **III,27,***1* and *2* and Section **IV,205**) must be included under this heading.

5. **From the mono-halogenated hydrocarbon.** The halogenated hydrocarbon is converted into the Grignard reagent and the latter allowed to react with diethyl carbonate, for example :

$$\underset{\alpha\text{-Bromonaphthalene}}{C_{10}H_7{}^{\alpha}Br} \xrightarrow{Mg} C_{10}H_7{}^{\alpha}MgBr \xrightarrow{(C_2H_5)_2CO_3} \underset{\text{Ethyl } \alpha\text{-naphthoate}}{C_{10}H_7{}^{\alpha}COOC_2H_5} + C_2H_5OMgBr$$

IV,176. METHYL BENZOATE

In a 500 ml. round-bottomed flask place a mixture of 30 g. of benzoic acid, 80 g. (101 ml.) of absolute methyl alcohol and 5 g. (2·7 ml.) of concentrated sulphuric acid. Add a few small chips of porous porcelain, attach a reflux condenser and boil the mixture gently for 4 hours (1). Distil off the excess of alcohol on a water bath (see Fig. *II*, *13*, 3) and allow to cool. Pour the residue into about 250 ml. of water contained in a separatory funnel and rinse the flask with a few ml. of water which are also poured into the separatory funnel. If, owing to the comparatively slight difference between the density of the ester and of water, difficulty is experienced in obtaining a sharp separation of the lower ester layer and water, add 10–15 ml. of carbon tetrachloride (2) and shake the mixture in the funnel vigorously ; upon standing, the heavy solution of methyl benzoate in the carbon tetrachloride separates sharply and rapidly at the bottom of the separatory funnel. Run off the lower layer carefully, reject the upper aqueous layer, return the methyl benzoate to the funnel and shake it with a strong solution of sodium bicarbonate until all free acid is removed and no further evolution of carbon dioxide occurs. Wash once with water, and dry by pouring into a small dry conical flask containing about 5 g. of anhydrous magnesium sulphate. Cork the flask, shake for about 5 minutes, and allow to stand for at least half an hour with occasional shaking. Filter the methyl benzoate solution through a small fluted filter paper directly into a small distilling flask containing a few chips of unglazed porcelain (" porous pot "). Fit the flask with a 360° thermometer and a condenser (a simple air condenser may be used, but a small Liebig's condenser with an empty water jacket is quite satisfactory). Distil from an air bath (Fig. *II*, *5*, 3) ; raise the temperature *slowly* at first (3) until all carbon tetrachloride has passed over and then heat more strongly. Collect the methyl benzoate (a colourless liquid) at 198–200°. The yield is 31 g.

Notes.

(1) Slightly improved results may be obtained by increasing the time of heating.

(2) Alternatively, the ester may be extracted with two 50 ml. portions of ether. The ethereal solution is washed with concentrated sodium bicarbonate solution (handle the separatory funnel cautiously as carbon dioxide is evolved) until effervescence ceases, then with water, and dried over anhydrous magnesium sulphate. The ether is removed with the aid of the apparatus depicted in Fig. *II*, *13*, 4, and the residual ester distilled.

(3) In view of the small quantity of carbon tetrachloride present, the use of a water condenser during the early stages of the distillation, although desirable for complete recovery of the solvent, is not essential.

COGNATE PREPARATIONS

Ethyl benzoate (*sulphuric acid as a catalyst*). Use 30 g. of benzoic acid, 115 g. (145 ml.) of absolute ethyl alcohol and 5 g. (2·7 ml.) of concentrated sulphuric acid. Reflux the mixture for 4 hours and work up as for *Methyl Benzoate*. The yield of ethyl benzoate, b.p. 212–214°, is 32 g.

Ethyl benzoate (*hydrogen chloride as a catalyst*). Pass dry hydrogen chloride (Section **II,48**, *1*) into a 500 ml. round-bottomed flask containing 115 g. (145 ml.) of absolute ethyl alcohol, cooled in an ice bath, until the increase in weight is 6 g. Add 30 g. of benzoic acid and reflux the mixture for 4 hours. Isolate the pure ester, b.p. 212–214°, as described for *Methyl Benzoate*. The yield is 32 g.

***n*-Propyl benzoate.** Into a 500 ml. round-bottomed flask place 30 g. of benzoic acid, 30 g. (37·5 ml.) of *n*-propyl alcohol, 50 ml. of sodium-dried A.R. benzene and 10 g. (5·4 ml.) of concentrated sulphuric acid. Reflux the mixture for 10 hours. Pour the reaction product into about 250 ml. of water, and extract with ether. Wash the ethereal extract with saturated sodium bicarbonate solution and then with water: dry over anhydrous magnesium sulphate. Distil off the ether and some of the benzene through a fractionating column, and distil the residue from a Claisen flask. Collect the *n*-propyl benzoate at 229–230°. The yield is 37 g.

***n*-Butyl benzoate.** Use 30 g. of benzoic acid, 37 g. (46 ml.) of *n*-butyl alcohol, 50 ml. of sodium-dried A.R. benzene and 10 g. (5·4 ml.) of concentrated sulphuric acid, and reflux the mixture for 12 hours. Work up the product as for *n-Propyl Benzoate*; after the ether and benzene have been removed under atmospheric pressure, distil the residue under reduced pressure. The yield of *n*-butyl benzoate, b.p. 119–120°/11 mm., is 35 g.

IV,177. METHYL SALICYLATE

In a 500 ml. round-bottomed flask place 28 g. of salicylic acid (Section **IV,173**) and 64 g. (81 ml.) of absolute methyl alcohol, and add cautiously, with shaking, 8 ml. of concentrated sulphuric acid, followed by a few fragments of porous porcelain. Fit the flask with a reflux condenser and reflux on a water bath for at least 5 hours. Distil off the excess of methyl alcohol on a water bath (see Fig. *II*, *13*, 3) and allow to cool. Pour the residue into about 250 ml. of water in a separatory funnel, shake the mixture and allow to stand. Run off the lower layer of ester (1) and discard the aqueous layer. Wash the ester successively with 25 ml. of water, concentrated sodium bicarbonate solution until all the free acid is removed, and water; dry over about 5 g. of anhydrous magnesium sulphate in a small conical flask for at least 30 minutes. Filter the ester through a fluted filter paper into a small distilling flask, and distil using an air condenser (compare Fig. *II*, *13*, 2) and an air bath (Fig. *II*, *5*, 3). Collect the pure methyl salicylate (a colourless oil of delightful fragrance, "oil of winter green") at 221–224°; the yield is 25 g. The ester may also be distilled under reduced pressure (see Fig. *II*, *20*, 1); the b.p. is 115°/20 mm. and a 2° fraction should be collected.

Note.

(1) If an emulsion should form during the washing process, add about 10 ml. of carbon tetrachloride (for details, see under *Methyl Benzoate*, Section IV,176).

COGNATE PREPARATION

Ethyl salicylate. Use 28 g. of salicylic acid, 84 g. (106 ml.) of absolute ethyl alcohol and 8 ml. of concentrated sulphuric acid. Reflux the mixture for at least 5 hours. The yield of ethyl salicylate (a colourless liquid), b.p. 231–234°, is 26 g. It is more convenient in practice to distil the liquid under reduced pressure: the boiling points under various pressures are given in Table II, 19.

IV,178. BENZYL ACETATE

Mix 31 g. (29·5 ml.) of benzyl alcohol (Section IV, 123 and Section IV,200) and 45 g. (43 ml.) of glacial acetic acid in a 500 ml. round-bottomed flask; introduce 1 ml. of concentrated sulphuric acid and a few fragments of "porous pot." Attach a reflux condenser to the flask and boil the mixture gently for 9 hours. Pour the reaction mixture into about 200 ml. of water contained in a separatory funnel, add 10 ml. of carbon tetrachloride (to eliminate emulsion formation owing to the slight difference in density of the ester and water, compare *Methyl Benzoate*, Section IV,176) and shake. Separate the lower layer (solution of benzyl acetate in carbon tetrachloride) and discard the upper aqueous layer. Return the lower layer to the funnel, and wash it successively with water, concentrated sodium bicarbonate solution (until effervescence ceases) and water. Dry over 5 g. of anhydrous magnesium sulphate, and distil under normal pressure (Fig. *II*, *13*, 2) with the aid of an air bath (Fig. *II*, *5*, 3). Collect the benzyl acetate a (colourless liquid) at 213–215°. The yield is 16 g.

IV,179. ETHYL PHENYLACETATE

Place 75 g. (74 ml.) of benzyl cyanide (Section IV,160), 125 g. (153 ml.) of rectified spirit and 150 g. (68 ml.) of concentrated sulphuric acid in a 750 ml. round-bottomed flask, fitted with an efficient reflux condenser. Reflux the mixture, which soon separates into two layers, gently for 8 hours, cool and pour into 350 ml. of water. Separate the upper layer. Dissolve it in about 75 ml. of ether (1) in order to facilitate the separation of the layers in the subsequent washing process. Wash the ethereal solution carefully with concentrated sodium bicarbonate solution until effervescence ceases and then with water. Dry over 10 g. of anhydrous magnesium sulphate for at least 30 minutes. Remove the solvent with the aid of the apparatus shown in Fig. *II*, *13*, 4 and distil from an air bath (Fig. *II*, *5*, 3). The ethyl phenylacetate passes over at 225–229° (mainly 228°) as a colourless liquid; the yield is 90 g. Alternatively, the residue after removal of the ether may be distilled in a Claisen flask under diminished pressure (Fig. *II*, *20*, 1); collect the ester at 116–118°/20 mm.

Note.

(1) The use of ether may be avoided by mixing the ester, after its isolation from the water layer, with about 20 ml. of carbon tetrachloride. The carbon tetrachloride solution then forms the lower layer in all washing operations (compare *Methyl Benzoate*, Section IV,176).

IV,180. PHENYL CINNAMATE

Into a 250 ml. Claisen flask place 72 g. of cinnamic acid (Section IV,124) and 60 g. (37 ml.) of redistilled thionyl chloride. Stopper the side arm, fit the flask with a reflux condenser the top of which is connected to a gas absorption device (Fig. *II,8*, 1, *c* or *d*), and mount the entire apparatus at an angle so that the condensate will not run into the side arm (compare Fig. *III, 31*, 1 or *III, 28*, 1). Heat the mixture on a water bath, cautiously at first, until hydrogen chloride ceases to be evolved (about 1 hour), allow to cool, and add 47 g. of pure (*e.g.*, A.R.) phenol. Heat the mixture on a water bath until no further evolution of hydrogen chloride is observed (about 1 hour). Then place the apparatus on an asbestos-centred wire gauze and heat the flask until the contents are brought just to the reflux temperature in order to complete the reaction : do not heat unduly long as prolonged heating leads to loss of product due to decomposition and polymerisation. Allow the reaction mixture to cool and distil under diminished pressure ; collect the fraction of b.p. 190–210°/15 mm. This solidifies to a pale yellow solid, m.p. 66–69°, weighing 98 g. Grind it to a powder in a glass mortar and wash the powder with 250 ml. of cold 2 per cent. sodium bicarbonate solution. Recrystallise from rectified spirit (150 ml.) : 81 g. of pure phenyl cinnamate (white crystals) of m.p. 75–76° are obtained.

IV,181. PHENYL BENZOATE

Dissolve 5 g. of phenol in 75 ml. of 10 per cent. sodium hydroxide solution contained in a wide-mouthed reagent bottle or conical flask of about 200 ml. capacity. Add 11 g. (9 ml.) of redistilled benzoyl chloride, cork the vessel securely, and shake the mixture vigorously for 15–20 minutes. At the end of this period the reaction is usually practically complete and a solid product is obtained. Filter off the solid ester with suction, break up any lumps on the filter, wash thoroughly with water and drain well. Recrystallise the crude ester from rectified (or methylated) spirit ; use a quantity of hot solvent approximately twice the minimum volume required for complete solution in order to ensure that the ester does not separate until the temperature of the solution has fallen below the melting point of phenyl benzoate. Filter the hot solution, if necessary, through a hot water funnel or through a Buchner funnel preheated by the filtration of some boiling solvent. Colourless crystals of phenyl benzoate, m.p. 69°, are thus obtained. The yield is 8 g.

Cognate Preparation

β-Naphthyl benzoate. Dissolve 7·2 g. of β-naphthol in 40 ml. of 5 per cent. sodium hydroxide solution in the cold ; add a little more water if necessary. If the solution is highly coloured, add 1·5 g. of decolourising

carbon and filter the cold solution through a hardened filter paper. Pour the solution into a 100 ml. conical flask and run in 7·0 g. (5·8 ml.) of benzoyl chloride. Stopper the flask and shake vigorously until the odour of benzoyl chloride has disappeared (10–15 minutes). Filter off the solid product on a Buchner funnel and wash it with a little cold water. Recrystallise it from about 60 ml. of methylated spirit (use the apparatus of Fig. *II*, *13*, 7) but without guard tube. Filter off the crystals which separate and dry them upon filter paper in the air. The yield of pure β-naphthyl benzoate, m.p. 110°, is 11 g.

IV,182. ETHYL α-NAPHTHOATE

In a 1·5-litre three-necked flask prepare a solution of α-naphthyl magnesium bromide from 12·2 g. of magnesium turnings as detailed under *α-Naphthoic Acid*, Section **IV,163**, *Method 2* ; add just sufficient sodium-dried benzene to form a homogeneous solution. Transfer the Grignard reagent to a separatory funnel and place 88·5 g. (91 ml.) of pure diethyl carbonate (1) and 50 ml. of sodium-dried ether in the three-necked flask. Stir and add the α-naphthyl magnesium bromide as rapidly as the refluxing of the solution will permit. Continue the stirring for a further 30 minutes and allow the reaction mixture to stand overnight. Then pour the reaction mixture, with frequent shaking, into a 2·5 litre flask containing 750 g. of crushed ice. Dissolve the basic magnesium bromide by adding gradually 72·5 ml. of cold 30 per cent. sulphuric acid (15 ml. of concentrated sulphuric acid and 60 ml. of water). Separate the upper layer and extract the aqueous layer with 50 ml. of ether. Concentrate the extracts to about 200 ml. by distilling the solvent from a water bath. Wash the residue with two 20 ml. portions of 5 per cent. sodium carbonate solution (2), and dry with 10 g. of anhydrous magnesium sulphate or calcium sulphate. Remove the solvent (Fig. *II*, *13*, 4) and distil the residual liquid : collect the fraction b.p. 290–310° as crude ethyl α-naphthoate. Redistil from a Claisen flask with fractionating side arm (Figs. *II*, *24*, 2–5) and collect the pure ester at 143–145°/3 mm. The yield is 70 g.

Notes.

(1) To purify commercial diethyl carbonate wash 100 ml. of the compound with 20 ml. of 10 per cent. sodium carbonate solution, then with 20 ml. of saturated calcium chloride solution, and finally with 30 ml. of water. Dry the ester by allowing it to stand for 2 hours over 5 g. of anhydrous calcium chloride (prolonged contact results in combination of the ester with the salt), distil and collect pure diethyl carbonate at 125–126°.

(2) Upon acidifying the alkaline washings, about 1 g. of α-naphthoic acid may be isolated.

IV,183. REACTIONS AND CHARACTERISATION OF AROMATIC ESTERS

Aromatic esters usually burn with a smoky flame, possess reasonably high boiling points, and are (particularly esters of phenols) sometimes crystalline solids. Phenyl esters usually give phenol upon distillation with soda lime (see Section **IV,175** for general details).

The experimental details already given for the detection and characterisation of aliphatic esters (determination of saponification equivalents ; hydrolysis : Section **III,106**) apply equally to aromatic esters. A slight modification in the procedure for isolating the products of hydrolysis is necessary for phenolic (or phenyl) esters since the alkaline solution will contain both the alkali phenate and the alkali salt of the organic acid : upon acidification, both the phenol and the acid will be liberated. Two methods may be used for **separating the phenol and the acid :**

1. Acidify the cold alkaline reaction mixture with dilute sulphuric acid (use litmus or Congo red paper) and extract both the acid and the phenol with ether. Remove the acid by washing the ethereal extract with saturated sodium bicarbonate solution until effervescence ceases ; retain the aqueous washings. Upon evaporating the ether, the phenol remains ; it may be identified (*a*) by its action upon ferric chloride solution, (*b*) the formation of a crystalline derivative with bromine water, and (*c*) by any of the methods given in Section **IV,114**. Acidify the aqueous washings with dilute sulphuric acid whilst stirring steadily, and investigate the organic acid (Sections **III,85** and **IV,175**).

2. Add dilute sulphuric acid, with stirring, to the cold alkaline solution until the solution is acid to litmus or Congo red paper and the acid, if a solid, commences to separate as a faint permanent precipitate. Now add dilute sodium carbonate solution until the solution is alkaline (litmus paper) and any precipitate has completely redissolved. Extract the clear solution twice with ether : evaporate or distil the ether from the ethereal solution on a water bath (*CAUTION :* no flames may be near) and identify the residual phenol as under *1.* Remove the dissolved ether from the aqueous solution by boiling, acidify with dilute sulphuric acid and identify the organic acid present (see Sections **III,85** and **IV,175**).

The student is recommended to carry out **the hydrolysis of phenyl benzoate.** Place a mixture of 2 g. of phenyl benzoate (Section IV,181) and 25 ml. of 10 per cent. aqueous sodium hydroxide solution in a 100 ml. flask fitted with a reflux condenser. Boil until the ester has completely disappeared (about 1 hour). If any unchanged ester volatilises in the steam and crystallises in the condenser, pour about 5 ml. of 10 per cent. sodium hydroxide solution down the condenser in order to return the ester to the flask. Cool the clear solution in ice and, when cold, add dilute sulphuric acid with stirring until a faint but permanent precipitate is formed : test with litmus or Congo red paper to ensure that the solution is acidic. Then add dilute sodium carbonate solution with vigorous stirring until the precipitate just redissolves and the solution is alkaline to litmus paper. Extract the solution twice with ether, dry the combined ethereal extracts with anhydrous magnesium sulphate or potassium carbonate and distil off most of the ether. Pour the remainder while still hot into an evaporating or crystallising dish ; the phenol will crystallise when all the ether has evaporated. Prepare a crystalline derivative of the phenol. Acidify the aqueous solution from the ether extraction with dilute sulphuric acid, filter off the benzoic acid with suction, wash with water, and recrystallise from boiling water. Confirm the identity of the acid by a mixed m.p. determination.

Table **IV,183** summarises the physical properties of a few selected aromatic esters.

TABLE IV,183. AROMATIC ESTERS

	B.P.	M.P.	$d_{4°}^{20°}$	$n_D^{20°}$
Methyl benzoate	199°	—	1·089	1·517
Ethyl benzoate	212	—	1·047	1·505
n-Propyl benzoate	230	—	1·023	1·500
iso-Propyl benzoate	218	—	1·015	1·491
n-Butyl benzoate	248	—	1·005	1·497
iso-Butyl benzoate	242	—	0·997	—
n-Amyl benzoate	137°/15	—	—	—
iso-Amyl benzoate	262	—	0·986	1·495
Methyl phenylacetate	215	—	1·068	1·507
Ethyl phenylacetate	228	—	1·033	1·497
n-Propyl phenylacetate	241	—	1·010	1·493
n-Butyl phenylacetate	256	—	0·994	1·489
Methyl *o*-toluate	213	—	1·068	—
Ethyl *o*-toluate	227	—	1·034	1·508
Methyl *m*-toluate	215	—	1·061	—
Ethyl *m*-toluate	227	—	1·028	1·506
Methyl *p*-toluate	217	34°	—	—
Ethyl *p*-toluate	228	—	1·025	1·507
Methyl salicylate	223	—	1·184	1·537
Ethyl salicylate	234	—	1·125	1·522
n-Propyl salicylate	240	—	1·098	1·516
n-Butyl salicylate	260	—	1·073	1·512
Methyl *m*-hydroxybenzoate	—	70	—	—
Ethyl *m*-hydroxybenzoate	295	73	—	—
Methyl *p*-hydroxybenzoate	—	131	—	—
Ethyl *p*-hydroxybenzoate	297	116	—	—
Methyl *o*-methoxybenzoate	248	—	1·156	1·534
Ethyl *o*-methoxybenzoate	261	—	1·104	1·525
Methyl *m*-methoxybenzoate	237	—	1·131	1·522
Ethyl *m*-methoxybenzoate	251	—	1·100	1·515
Methyl anisate	255	49	—	—
Ethyl anisate	269	7	1·103	1·524
Methyl *o*-chlorobenzoate	234	—	—	1·536
Ethyl *o*-chlorobenzoate	243	—	1·190	1·522
Methyl *m*-chlorobenzoate	231	20	—	1.492
Ethyl *m*-chlorobenzoate	242	—	1·182	1·520
Methyl *p*-chlorobenzoate	—	44	—	—
Ethyl *p*-chlorobenzoate	238	—	1·181	1·524
Methyl *o*-bromobenzoate	246	—	—	—
Ethyl *o*-bromobenzoate	255	—	—	—
Methyl *m*-bromobenzoate	—	32	—	—
Ethyl *m*-bromobenzoate	259	—	—	—
Methyl *p*-bromobenzoate	—	81	—	—
Ethyl *p*-bromobenzoate	263	—	—	—
Methyl *o*-iodobenzoate	278	—	—	—
Ethyl *o*-iodobenzoate	275	—	—	—
Methyl *m*-iodobenzoate	277	54	—	—

TABLE IV,183. AROMATIC ESTERS (*continued*)

	B.P.	M.P.	$d_{4°}^{20°}$	$n_D^{20°}$
Ethyl *m*-iodobenzoate	150°/15	—	—	—
Methyl *p*-iodobenzoate	—	114°	—	—
Ethyl *p*-iodobenzoate	153°/14	—	—	—
Methyl *o*-nitrobenzoate	275	—	1·286	—
Ethyl *o*-nitrobenzoate	—	30	—	—
Methyl *m*-nitrobenzoate	279	79	—	—
Ethyl *m*-nitrobenzoate	297	47	—	—
Methyl *p*-nitrobenzoate	—	96	—	—
Ethyl *p*-nitrobenzoate	—	57	—	—
Methyl 3 : 5-dinitrobenzoate	—	108	—	—
Ethyl 3 : 5-dinitrobenzoate	—	94	—	—
Methyl 2 : 4-dinitrobenzoate	—	70	—	—
Ethyl 2 : 4-dinitrobenzoate	—	41	—	—
Methyl anthranilate	—	24	—	—
Ethyl anthranilate	267	13	1·117	1·565
Methyl *m*-aminobenzoate	—	38	—	—
Ethyl *m*-aminobenzoate	294	—	—	—
Methyl *p*-aminobenzoate	—	112	—	—
Ethyl *p*-aminobenzoate	—	92	—	—
Methyl cinnamate	261	36	—	—
Ethyl cinnamate	273	—	1·049	1·560
n-Propyl cinnamate	284	—	1·028	1·551
n-Butyl cinnamate	162°/12	—	1·013	1·544
Methyl dihydrocinnamate	232	—	1·043	1·503
Ethyl dihydrocinnamate	248	—	1·016	1·495
n-Propyl dihydrocinnamate	262	—	0·998	1·491
n-Butyl dihydrocinnamate	123°/11	—	0·984	1·489
Methyl *o*-nitrocinnamate	—	73	—	—
Ethyl *o*-nitrocinnamate	—	44	—	—
Methyl *m*-nitrocinnamate	—	124	—	—
Ethyl *m*-nitrocinnamate	—	79	—	—
Methyl *p*-nitrocinnamate	—	161	—	—
Ethyl *p*-nitrocinnamate	—	142	—	—
Methyl *o*-aminocinnamate	—	65	—	—
Ethyl *o*-aminocinnamate	—	78	—	—
Methyl *m*-aminocinnamate	—	84	—	—
Ethyl *m*-aminocinnamate	—	64	—	—
Methyl *p*-aminocinnamate	—	129	—	—
Ethyl *p*-aminocinnamate	—	69	—	—
Methyl phenoxyacetate	245	—	1·147	—
Ethyl phenoxyacetate	251	—	1·101	—
Methyl *dl*-mandelate	—	58	—	—
Ethyl *dl*-mandelate	255	37	—	—
Methyl *o*-benzoylbenzoate	352	52	—	—
Ethyl *o*-benzoylbenzoate	—	58	—	—

TABLE IV,183. AROMATIC ESTERS (*continued*)

	B.P.	M.P.	$d_{4^\circ}^{20^\circ}$	$n_D^{20^\circ}$
Methyl diphenylacetate	—	60°	—	—
Ethyl diphenylacetate	—	58	—	—
Methyl phthalate	282°	—	1·191	1·516
Ethyl phthalate	298	—	1·118	1·502
n-Propyl phthalate	130°/1	—	—	—
iso-Propyl phthalate	154°/10	—	—	—
n-Butyl phthalate	205°/20	—	—	—
Methyl *iso*-phthalate	—	68	—	—
Ethyl *iso*-phthalate	285	11	1·121	1·507
Methyl terephthalate	—	142	—	—
Ethyl terephthalate	302	44	—	—
Methyl 3-nitrophthalate	—	69	—	—
Ethyl 3-nitrophthalate	—	45	—	—
Methyl 4-nitrophthalate	—	66	—	—
Ethyl 4-nitrophthalate	—	34	—	—
Methyl α-naphthoate	—	—	—	—
Ethyl α-naphthoate	309	—	1·122	—
Methyl β-naphthoate	290	77	—	—
Ethyl β-naphthoate	304	32	—	—
Methyl diphenate	—	74	—	—
Ethyl diphenate	—	42	—	—
Methyl hexahydrobenzoate	183	—	0·990	1·451
Ethyl hexahydrobenzoate	196	—	0·962	1·448
Phenyl acetate	196	—	1·078	1·503
Phenyl propionate	211	20	1·050	—
Phenyl *n*-butyrate	228	—	1·023	—
Phenyl oxalate	190°/15	—	—	—
Phenyl succinate	330	121	—	—
Phenyl benzoate	299	68	—	—
Phenyl cinnamate	—	73	—	—
Phenyl salicylate (salol)	—	43	—	—
o-Cresyl acetate	208	—	1·045	—
o-Cresyl benzoate	307	—	—	—
m-Cresyl acetate	212	12	1·043	1·498
m-Cresyl benzoate	—	54	—	—
p-Cresyl acetate	212	—	1·050	1·500
p-Cresyl benzoate	316	72	—	—
α-Naphthyl acetate	—	49	—	—
α-Naphthyl benzoate	—	56	—	—
β-Naphthyl acetate	—	70	—	—
β-Naphthyl benzoate	—	107	—	—
Thymyl acetate	243	—	—	—
Thymyl benzoate	—	33	—	—
Catechol diacetate	—	63	—	—
Catechol dibenzoate	—	84	—	—
Resorcinol diacetate	278	—	—	—
Resorcinol dibenzoate	—	117	—	—
Hydroquinone diacetate	—	124	—	—
Hydroquinone dibenzoate	—	199	—	—

TABLE IV,183. AROMATIC ESTERS (*continued*)

	B.P.	M.P.	$d_{4°}^{20°}$	$n_D^{20°}$
Phloroglucinol triacetate	—	104°	—	—
Phloroglucinol tribenzoate	—	185	—	—
Pyrogallol triacetate	—	165	—	—
Pyrogallol tribenzoate	—	90	—	—
Benzoin acetate	—	83	—	—
Guaiacol acetate	240°	—	1·133	1·512
Carvacryl acetate	245	—	0·994	—
Eugenol acetate	282	30	—	—
Phenyl carbonate	—	80	—	—
o-Cresyl carbonate	—	60	—	—
m-Cresyl carbonate	—	111	—	—
p-Cresyl carbonate	—	115	—	—
Guaiacol carbonate	—	87	—	—
Benzyl formate	203	—	1·082	—
Benzyl acetate	214	—	1·057	1·523
Benzyl benzoate	323	21	—	—
Benzyl succinate	—	45	—	—
Benzyl salicylate	186°/10	—	1·180	1·581
α-Phenylethyl acetate	222	—	—	—
β-Phenylethyl acetate	224	—	1·059	1·512

AROMATIC ACID CHLORIDES

The chlorides of aromatic acids are prepared :—

1. By the action of phosphorus pentachloride upon the aromatic acid, for example :

$$\underset{p\text{-Nitrobenzoic acid}}{p\text{-}NO_2C_6H_4COOH} + PCl_5 \longrightarrow \underset{p\text{-Nitrobenzoyl chloride}}{p\text{-}NO_2C_6H_4COCl} + POCl_3 + HCl$$

The liquid phosphorus oxychloride, b.p. 107°, is a by-product and is removed by fractional distillation under normal pressure. Unless the b.p. of the acid chloride differs very considerably (say, $\lessgtr$ 100°) from that of the phosphorus oxychloride, the acyl halide is liable to contain traces of the latter. In such circumstances it is preferable to use thionyl chloride for the preparation of the acid chloride.

2. By the action of thionyl chloride upon the acid (see discussion preceding Section III,86), for example :

$$\underset{\text{Benzoic acid}}{C_6H_5COOH} + SOCl_2 \longrightarrow \underset{\text{Benzoyl chloride}}{C_6H_5COCl} + SO_2 + HCl$$

It will be noted that the by-products are both gaseous. In practice, a slight excess over the theoretical quantity (20–75 per cent.) of thionyl chloride is used ; some of this is volatilised with the gaseous by-products and the remainder is easily removed by fractional distillation (thionyl chloride has b.p. 77°).

The preparation of 3 : 5-dinitrobenzoyl chloride by both the PCl_5 and $SOCl_2$ methods is described in Section III,27,*1* ; see also Section VII,22.

IV,184. *p*-NITROBENZOYL CHLORIDE

Phosphorus pentachloride method. Mix 100 g. of pure *p*-nitrobenzoic acid (Section IV,154) and 126 g. of pure phosphorus pentachloride in a 500 ml. round-bottomed flask. Fit the flask with a calcium chloride (or cotton wool) guard tube and connect the latter to a gas absorption device (*e.g.*, Fig. *II*, *8*, 1, *c*). Heat the flask on a water bath, with occasional shaking, until the reaction commences and then for a further 30 minutes or until the vigorous evolution of hydrogen chloride has almost ceased : a pale yellow homogeneous liquid is formed. Transfer the reaction mixture to a Claisen flask connected with a water-cooled condenser, and remove the phosphorus oxychloride (b.p. 107°) at ordinary pressure either by heating in an oil bath gradually to 200–220° or by heating in an air bath (Fig. *II*, *5*, 3) until the boiling point is about 150°. Allow to cool, replace the water condenser by a *short* air-cooled condenser and use a distilling flask as receiver (compare Fig. *II*, *19*, 1) ; place a bottle containing water between the receiver and the manometer (or the absorption arrangement shown in Fig. *II*, *22*, 1) in order to avoid the passage of vapours of phosphorus oxychloride or acid chloride into the pump. Distil the residual liquid under reduced pressure (1) : a small quantity of phosphorus oxychloride passes over first and the temperature rises rapidly to about 150°/20 mm. Change the receiver and collect the *p*-nitrobenzoyl chloride at 155°/20 mm. Pour the product whilst still fluid into a small wide-mouthed bottle and allow it to solidify : this prevents any moisture in the air from decomposing more than the surface

layer of acid chloride. The yield of *p*-nitrobenzoyl chloride (a yellow crystalline solid, m.p. 71°) is 105 g. and is pure enough for most purposes. A perfectly pure product, m.p. 73°, is obtained by recrystallising from carbon tetrachloride.

Note.

(1) Either an oil bath (maintained at 210–215° for a pressure of 20 mm.) or an air bath must be used. If the flask is heated with a free flame, superheating will occur leading to decomposition (sometimes violent) of the *p*-nitrobenzoyl chloride.

Thionyl chloride method. Mix 100 g. of pure *p*-nitrobenzoic acid and 125 g. (77 ml.) (1) of redistilled thionyl chloride in a 500 ml. round-bottomed flask. Fit the flask with a double surface reflux condenser carrying a calcium chloride (or cotton wool) guard tube and connect the latter to an absorption device (*e.g.*, Fig. *II*, *8*, 1, *c*). Heat the flask on a water bath with occasional shaking for 1 hour or until the evolution of hydrogen chloride and sulphur dioxide almost ceases. Allow the reaction mixture to cool, transfer it cautiously to a Claisen flask connected with a water-cooled condenser and a receiver (compare Fig. *II*, *13*, 1). Distil off the excess of thionyl chloride (b.p. 77°) slowly and continue the distillation until the temperature rises rapidly to about 120°; this will ensure that all the thionyl chloride is removed. Allow to cool, and distil the residual *p*-nitrobenzoyl chloride under diminished pressure as detailed in the *Phosphorus Pentachloride Method*. The resulting *p*-nitrobenzoyl chloride (a yellow crystalline solid) weighs 107 g. and melts at 72–73°.

Note.

(1) A large excess of thionyl chloride is recommended in order to avoid the formation of *p*-nitrobenzoic anhydride (see *Note 1* to Section IV,185).

CAUTION. The preparation of o-nitrobenzoyl chloride, o-nitrophenacetyl chloride and all o-nitroacid chlorides should not be attempted by the above methods: a violent explosion may occur upon distilling the product or when the last traces of thionyl chloride are removed "in vacuo" at 100°. Perhaps the safest method is to treat the pure acid in benzene solution with 1·1 mols of thionyl chloride and to reflux until evolution of sulphur dioxide and hydrogen chloride has ceased; the solution of the acid chloride in benzene may then be employed for most reactions.

IV,185. BENZOYL CHLORIDE

This preparation must be conducted in the fume cupboard. Fit up the apparatus shown in Fig. *III*, *28*, 1, but replace the absorption device at the top of the condenser by a calcium chloride (or cotton wool) guard tube; if it is desired to absorb the gases evolved, the guard tube may be attached to the device depicted in Fig. *II*, *8*, 1. Place 30 g. of dry powdered benzoic acid in the 150 ml. distilling (or Claisen) flask and add 36 g. (22 ml.) of redistilled thionyl chloride. Heat the flask on a boiling water bath with occasional shaking for 1 hour or until the evolution of hydrogen chloride ceases. Cool the flask, detach the condenser and fit it to the side arm for distillation: attach to the lower end of the condenser by means of a cork either a filter flask receiver (as in Fig. *II*, *13*, 1) or a small distilling flask carrying a calcium chloride (or cotton wool)

guard tube in the side arm. Have a duplicate receiver available. Distil the contents of the flask by heating carefully over a wire gauze or, better, in an air bath (Fig. *II*, *5*, 3). A small initial fraction boiling at 70–80°, consisting of unchanged thionyl chloride, passes over first, and the temperature then rises rapidly to 194°. Immediately this temperature is reached, stop the distillation, allow the condenser to drain thoroughly and remove the receiver containing the initial distillate ; introduce the duplicate receiver and continue the distillation. Collect the benzoyl chloride at 194–198° (1). The yield is 32 g. Benzoyl chloride is a colourless, highly refractive liquid with a pungent odour ; it fumes in the air and its vapour causes copious watering of the eyes.

Note.

(1) If desired, the benzoyl chloride may be distilled under reduced pressure (Fig. *II*, *20*, 1) ; the approximate b.p. may be obtained from Table II, 19.

A very small high-boiling fraction may remain in the flask : this consists largely of benzoic anhydride (b.p. 360° ; m.p. 42°) produced by the dehydrating action of the thionyl chloride upon the benzoic acid :

$$SOCl_2 + 2C_6H_5COOH \longrightarrow SO_2 + 2HCl + (C_6H_5CO)_2O$$

AROMATIC ACID ANHYDRIDES

The anhydrides of aromatic acids are prepared :—

1. By interaction of the acid chloride (1 mol) and acid (1 mol) in the presence of pyridine (2 mols) :

$$ArCOCl + C_5H_5N + ArCOOH \longrightarrow ArCO{-}O{-}COAr + C_5H_5N,HCl$$

Thus benzoic anhydride and o-chlorobenzoic anhydride (m.p. 79°) can be readily prepared by this method (compare *n*-Heptoic anhydride, Section **III,91**). It is sometimes convenient to use pyridine as the reaction medium.

In a modification the acid chloride is treated with excess of dry pyridine whereby the addition complex $ArCOCl.C_5H_5N$ is formed ; decomposition of the latter with water affords the acid anhydride :

$$2\ ArCOCl.C_5H_5N + H_2O \longrightarrow ArCO{-}O{-}COAr + 2\ C_5H_5N,HCl$$

This modification is illustrated by the preparation of *p*-chlorobenzoic anhydride from *p*-chlorobenzoyl chloride.

2. By the slow distillation of an aromatic carboxylic acid and acetic anhydride in the presence of a little phosphoric acid :

$$C_6H_5COOH + (CH_3CO)_2O \rightleftharpoons C_6H_5CO{-}O{-}COCH_3 + CH_3COOH$$
$$C_6H_5CO{-}O{-}COCH_3 + C_6H_5COOH \rightleftharpoons C_6H_5CO{-}O{-}COC_6H_5 + CH_3COOH$$

The equilibria are established comparatively slowly, hence slow distillation is essential.

IV, 186. *p*-CHLOROBENZOIC ANHYDRIDE

Place a mixture of 17·5 g. *p*-chlorobenzoyl chloride (1) and 50 ml. of dry pyridine (Section **II,47,***22*) in a loosely-stoppered 250 ml. flask and warm on a steam bath for 5 minutes. Pour the reaction mixture upon 100 g. of crushed ice and 50 ml. of concentrated hydrochloric acid. The anhydride separates out at once. When the ice has melted sufficiently, filter the mixture by suction. Wash the solid with 15 ml. of methanol and then with 15 ml. of dry benzene. The yield of crude *p*-chlorobenzoic anhydride is 14·5 g. Recrystallise from 250 ml. of dry benzene : 13 g. of the pure anhydride, m.p. 192–193°, are obtained.

(1) Prepare *p*-chlorobenzoyl chloride by refluxing and stirring 78 g. of *p*-chlorobenzoic acid (Section **IV,157**) and 100 g. of redistilled thionyl chloride until solution is complete. Distil off the excess of thionyl chloride at atmospheric pressure and then the acid chloride under reduced pressure : 70 g. of product, b.p. 119–120°/22 mm., m.p. 14–15°. are obtained.

COGNATE PREPARATION

Benzoic anhydride (*carboxylic acid - acetic anhydride method*).

Place 150 g. of benzoic acid, 150 g. (139 ml.) of acetic anhydride and 0·2 ml. of syrupy phosphoric acid in a 500 ml. bolt-head flask. Fit the latter with a two-holed stopper carrying a dropping funnel and an efficient fractionating column (compare Fig. *III*, *61*, 1) ; it is advisable to lag the latter with asbestos cloth. Set up the flask in an oil bath or in a fusible metal bath. Distil the mixture very slowly and at such a rate that the temperature of the vapour at the head of the column does

not exceed 120° (the boiling point of acetic acid is 118°). When about 25 ml. of distillate has been collected, add 25 g. (23 ml.) of acetic anhydride from the dropping funnel and continue the distillation until a further 25 ml. of liquid has been obtained. Introduce another 25 g. of acetic anhydride and continue the slow fractional distillation with the object of removing all the acetic acid and acetic anhydride (b.p. 140°); finally continue the heating until the temperature of the bath is 250–270°. Fractionally distil the residue under reduced pressure (compare Fig. *II*, *20*, 1) and collect the crude benzoic anhydride (120 g.) at 210–220°/20 mm. Dissolve this in benzene (5 ml. per 10 g.) and add just sufficient light petroleum (b.p. 40–60°) to cause a cloudiness; cool in ice, when pure benzoic anhydride, m.p. 43°, separates in colourless and odourless crystals. The first crop amounts to about one-half of the crude material taken. Remove the solvent from the mother liquor on a water bath and distil the residue; collect the fraction boiling at 210–220°/20 mm. and recrystallise as before. The total yield of pure benzoic anhydride is 95 g.

IV,187. REACTIONS AND CHARACTERISATION OF ACID CHLORIDES OF AROMATIC ACIDS

Most aromatic acid chlorides impart a strongly acid reaction when shaken with water (compare Section **III,88**). All are completely hydrolysed by boiling with solutions of caustic alkalis and yield no product volatile from the alkaline solution (compare *Esters*, Sections **III,106** and **IV,183**). They may be distinguished from acids by their facile reactions with alcohols (compare Section **III,27**), phenols (compare Section **IV,114**), and amines (compare Sections **III,123** and **IV,100**).

Acyl halides may be identified by :—hydrolysis to the corresponding acids (the latter may be further characterised as in Section **IV,175**); conversion into amides (Section **IV,191**), anilides or *p*-toluidides (Section **IV,100**); and conversion into solid esters (Section **IV,183**).

The physical properties of a few typical acid chlorides of aromatic acids are collected in Table **IV,187**). Some acid anhydrides are also included in this Table (compare Section **III,94**).

TABLE IV,187. ACID CHLORIDES AND ACID ANHYDRIDES OF AROMATIC ACIDS

Acid Chloride	B.P.	M.P.
Benzoyl	197°	—
o-Toluyl	212	—
m-Toluyl	219	—
p-Toluyl	227	—
o-Nitrobenzoyl	148°/9 mm.	20°
m-Nitrobenzoyl	—	35
p-Nitrobenzoyl	—	75
3 : 5-Dinitrobenzoyl	196°/11 mm.	70
2 : 4-Dinitrobenzoyl	—	46
o-Chlorobenzoyl	236	—
m-Chlorobenzoyl	225	—
p-Chlorobenzoyl	222	16
o-Methoxybenzoyl	254	—
m-Methoxybenzoyl	244	—
Anisoyl	145°/14 mm.	22
Phenylacetyl	210	—
Cinnamoyl	131°/11 mm.	36
Diphenylcarbamyl	—	85
s-Phthaloyl	281	14
3-Nitrophthaloyl	—	77
α-Naphthoyl	163°/10	26
β-Naphthoyl	305	53

Anhydride	B.P.	M.P.
Benzoic	360°	42°
o-Toluic	—	39
m-Toluic	—	71
p-Toluic	—	95
o-Nitrobenzoic	—	135
m-Nitrobenzoic	—	163
p-Nitrobenzoic	—	190
3 : 5-Dinitrobenzoic	—	109
2 : 4-Dinitrobenzoic	—	160
o-Chlorobenzoic	—	79
m-Chlorobenzoic	—	95
p-Chlorobenzoic	—	194
Anisic	—	99
Phenylacetic	—	72
Cinnamic	—	136
Phthalic	—	132
3-Nitrophthalic	—	164
4-Nitrophthalic	—	119
Tetrachlorophthalic	—	255
Tetrabromophthalic	—	280
1 : 8-Naphthalic	—	274
Diphenic	—	217
d-Camphoric	270	220

AROMATIC ACID AMIDES

Aromatic acid amides may be prepared :—

1. By the action of concentrated ammonia solution upon the appropriate acid chloride, for example :

$$\underset{\text{Benzoyl chloride}}{C_6H_5COCl} + NH_3 \longrightarrow \underset{\text{Benzamide}}{C_6H_5CONH_2} + HCl\ (\longrightarrow NH_4Cl)$$

2. By the action of an alkaline solution of hydrogen peroxide upon the corresponding nitrile, for example :

$$\underset{o\text{-Tolunitrile}}{2\,o\text{-}CH_3C_6H_4CN} + 2H_2O_2 \longrightarrow \underset{o\text{-Toluamide}}{2\,o\text{-}CH_3C_6H_4CONH_2} + O_2$$

Acid amides possess weakly amphoteric properties ; salts such as

$$C_6H_5CONH_2,HCl \quad \text{and} \quad C_6H_5CONHNa$$

are formed at low temperatures (to avoid hydrolysis), but are difficult to isolate. The mercury derivatives can, however, usually be readily prepared because they crystallise well and mercuric oxide is too weakly basic to cause hydrolysis of the amide, for example :

$$\underset{\text{Benzamide}}{2\,C_6H_5CONH_2} + HgO \longrightarrow \underset{\text{Mercury benzamide}}{(C_6H_5CONH)_2Hg} + H_2O$$

3. By the action of concentrated hydrochloric acid at about 40° upon arylacetonitriles ; hydrolysis is arrested at the arylacetamide stage (see Section IV,160 for the preparation of phenylacetamide by this method) :

$$\underset{\text{Benzyl cyanide}}{C_6H_5CH_2CN} + H_2O \rightarrow \underset{\text{Phenylacetamide}}{C_6H_5CH_2CONH_2}$$

IV,188. BENZAMIDE

Place 50 ml. of concentrated ammonia solution (sp. gr. 0·88) in a 200 ml. conical flask (1) and cool in ice. Add 12·1 g. (10·0 ml.) of redistilled benzoyl chloride (Section IV,185) drop by drop from a separatory funnel whilst shaking the flask frequently. Filter off the precipitated benzamide, wash with a little cold water, and recrystallise from hot water (about 50 ml.) ; dry upon filter paper in the air (2). The yield of pure benzamide, m.p. 129°, is 9 g.

Notes.

(1) An alternative procedure, which does not require ice cooling, is to add all the 10 ml. of benzoyl chloride rapidly to a mixture of 50 ml. of concentrated ammonia solution and 50 ml. of water contained in a 200 ml. conical flask, stopper securely and shake vigorously for about 15 minutes. Heat is evolved so that the stopper should be held down tightly. After 30 minutes the benzamide is filtered off and worked up as above.

(2) The benzamide should not be dried in the steam oven, since it will undergo partial decomposition at 100° into benzonitrile and thus give an impure product of low m.p.

IV,189. MERCURY BENZAMIDE

To 100 ml. of rectified spirit in a 250 ml. round-bottomed flask add 8 g. of benzamide and 10 g. of finely-powdered mercuric oxide. Boil under reflux for 30 minutes and filter the hot solution through a fluted filter paper to remove unreacted mercuric oxide. If the first portion of

the filtrate is somewhat turbid, return it to the filter ; the remainder will pass through as a clear filtrate. Cool the latter in ice ; colourless crystals of mercury benzamide separate. Filter at the pump, wash with a little cold alcohol, drain and dry in the air. The yield of mercury benzamide, m.p. 222–223°, is 3·5 g. It may be recrystallised from hot rectified spirit.

IV,190. *o*-TOLUAMIDE

Place 44 g. of *o*-tolunitrile (Section IV,66), 150 ml. of " 100-volume " (30 per cent.) hydrogen peroxide (1), 200 ml. of rectified spirit (2) and 15 ml. of 25 per cent. sodium hydroxide solution in a 1 litre round-bottomed flask. Oxygen is soon evolved and the mixture becomes warm. Maintain the temperature inside the flask at 40–50° by external cooling ; if the temperature is permitted to rise much above 50°, the evolution of oxygen may become so rapid as to cause the mixture to foam out of the flask. The exothermic reaction is complete after about 1 hour. Maintain the temperature of the mixture at 50° by external heating for a further 3 hours. While still warm, add 5 per cent. sulphuric acid until exactly neutral to litmus and distil in steam (Fig. *II*, *40*, 1) until 500 ml. of distillate are collected : heat the flask with a small flame after most of the alcohol has passed over. Pour the residue, which should have a volume of about 300 ml., into a 600 ml. beaker, and cool to about 20°. Filter off the crystals at the pump, transfer them to a glass mortar, and grind to a paste with 50 ml. of cold water, filter with suction and wash on the filter with a further 50 ml. of cold water. Dry in the air upon filter paper. The yield of *o*-toluamide (white crystals), m.p. 141°, is 46 g. It may be recrystallised from hot water (1 g. per 10 ml.), but the m.p. is unchanged.

Notes.

(1) Difficultly hydrolysable nitriles, such as *o*-tolunitrile, require 30 per cent hydrogen peroxide. For most nitriles, however, both aromatic and aliphatic, an equivalent amount of 6–12 per cent. hydrogen peroxide gives more satisfactory results ; the above procedure must, however, be modified, according to the solubility of the nitriles and amides.

(2) This volume of rectified spirit is required to produce a homogeneous solution.

IV,191. REACTIONS AND CHARACTERISATION OF PRIMARY AROMATIC AMIDES

Primary aromatic amides are crystalline solids with definite melting points. Upon boiling with 10–20 per cent. sodium or potassium hydroxide solution, they are hydrolysed with the evolution of ammonia (vapour turns red litmus paper blue and mercurous nitrate paper black) and the formation of the alkali metal salt of the acid :

$$RCONH_2 + NaOH \longrightarrow RCOONa + NH_3$$

The acid is liberated upon acidification. Hydrolysis may also be effected (but less readily and usually not quite so satisfactorily) by boiling with dilute hydrochloric acid (1 : 1) or 20 per cent. sulphuric acid :

$$RCONH_2 + H_2O + HCl \longrightarrow RCOOH + NH_4Cl$$

The **hydrolysis by alkali** is illustrated by the following experimental details for benzamide. Place 3 g. of benzamide and 50 ml. of 10 per cent. sodium hydroxide solution in a 150 ml. conical or round-bottomed flask equipped with a reflux condenser. Boil the mixture gently for 30 minutes; ammonia is freely evolved. Detach the condenser and continue the boiling in the open flask for 3–4 minutes to expel the residual ammonia. Cool the solution in ice, and add concentrated hydrochloric acid until the mixture is strongly acidic; benzoic acid separates immediately. Leave the mixture in ice until cold, filter at the pump, wash with a little cold water and drain well. Recrystallise the benzoic acid from hot water. Determine the m.p., and confirm its identity by a mixed m.p. test.

The characterisation of a primary aromatic amide is based upon its own m.p. and the identification of the acid (see Section **IV,175**) produced on hydrolysis. A crystalline derivative may be prepared directly with xanthhydrol (for experimental details, see Section **III,110**, *1*).

The melting points of a few selected primary aromatic amides (together with those of the xanthylamides, where known) are collected in Table **IV,191**. A more detailed list will be found in the column headed *Amides* in **Table IV,175** (*Aromatic Carboxylic Acids*).

TABLE IV,191. PRIMARY AROMATIC AMIDES

Amide	M.P.	Xanthylamide
Benzamide	129°	224°
o-Nitrobenzamide	175	—
m-Nitrobenzamide	142	—
p-Nitrobenzamide	201	232
o-Toluamide	143	200
m-Toluamide	95	—
p-Toluamide	159	225
Phenylacetamide	157	196
Salicylamide	139	—
m-Hydroxybenzamide	167	—
p-Hydroxybenzamide	162	—
Phenylurea	147	225
o-Tolylurea	191	228
m-Tolylurea	142	—
p-Tolylurea	183	—
asym.-Diphenylurea	189	180
α-Phenylpropionamide	92	158
β-Phenylpropionamide	105	189
Benzylurea	149	—
p-Phenetylurea (Dulcin)	173	—
Phthalimide	235	177
Hydrobenzamide	110	—

IV,192. REACTIONS AND CHARACTERISATION OF SUBSTITUTED AROMATIC AMIDES (AROMATIC ACYLATED BASES)

This group comprises substances of the type RCONHR′ and RCONR′R″, *i.e.*, substituted amides of the aromatic series. They are all well-defined crystalline solids, sparingly soluble in cold but, often, appreciably soluble in hot water and moderately soluble in ether ; they are generally neutral or feebly basic in reaction.

Upon warming with 10–20 per cent. sodium or potassium hydroxide solution, no ammonia is evolved (distinction from primary amides). The base, however, is usually liberated upon **fusion with soda lime** (see experimental details in Section **IV,175**) and at the same time the acyl group yields a hydrocarbon. Thus benz-*p*-toluidide affords *p*-toluidine and benzene.

Carry out a preliminary soda lime fusion test to determine whether the base is liberated under these conditions ; if it is, repeat the experiment with 1 g. of the substance. Identify the base (amine) by its m.p. (if a solid) and the preparation of a solid derivative (Section **IV,100**).

Hydrolysis of the original compound will confirm its identity. Boil 0·5–1·0 g. of the original substance with 10–20 ml. of concentrated hydrochloric acid under reflux for 2 hours :

$$RCONHR' + H_2O + HCl \longrightarrow RCOOH + R'NH_3^+Cl^-$$

The solution will then contain the free acid and the hydrochloride of the base ; either of these may separate if sparingly soluble. If a solid crystallises from the cold solution, filter, test with sodium bicarbonate solution {compare Section **III,85**, (i)} and compare the m.p. with that of the original compound. If it is a hydrolysis product, examine it separately. Otherwise, render the filtrate alkaline with sodium hydroxide solution and extract the base with ether ; if the presence of the unchanged acyl compound is suspected, extract the base with weak acid. Identify the base in the usual manner (see Section **IV,100**). The acid will be present as the sodium salt in the alkaline extract and may be identified as described in Section **IV,175**.

Benzanilide and similar compounds are very slowly hydrolysed by concentrated hydrochloric acid ; hydrolysis is quite rapid with 60–70 per cent. sulphuric acid (for experimental details, see Section **IV,52**). In the preliminary experiment boil 0·5–1·0 g. of the compound with 10–20 ml. of dilute sulphuric acid (1 : 1 by volume) under reflux for 20–30 minutes. Dilute with 10 ml. of water and filter off any acid which may be precipitated ; if the carboxylic acid is liquid and volatile, distil it directly from the reaction mixture. Render the residue alkaline and isolate the base as above.

The melting points of some typical substituted aromatic amides are collected in Table **IV,192**. Other examples will be found in the appropriate columns of Tables **IV,100A** and **B** (*Primary and Secondary Aromatic Amines*) and of Table **IV,175** (*Aromatic Carboxylic Acids*).

TABLE IV,192. SUBSTITUTED AROMATIC AMIDES

Amide	M.P.	Amide	M.P.
Formanilide	50°	*m*-Methoxyacetanilide	80°
Acetanilide	114	*p*-Methoxyacetanilide	130
Propionanilide	106	2 : 4-Dimethylacetanilide	133
n-Butyranilide	96	2 - 5-Dimethylacetanilide	142
iso-Butyranilide	105	*N*-Ethyl-*p*-nitroacetanilide	118
n-Valeranilide	63		
iso-Valeranilide	110	Acetyl-*o*-toluidine	112
n-Caproanilide	95	Acetyl-*m*-toluidine	66
Oenanthoanilide	71	Acetyl-*p*-toluidine	154
Caprylanilide	57		
Pelargoanilide	57	Acetyl-*o*-anisidine	88
Caprianilide	70	Acetyl-*m*-anisidine	80
Lauranilide	78	Acetyl-*p*-anisidine	130
Palmitanilide	91	Acetyl-*o*-phenetidine	79
Stearanilide	94	Acetyl-*m*-phenetidine	96
Lactanilide	59	Acetyl-*p*-phenetidine (or phenacetin)	137
Furoanilide	124	Acetyl-α-naphthylamine	160
Acetoacetanilide	85	Acetyl-β-naphthylamine	134
Oxanilide	246		
Malonanilide	225	*NN'*-Diacetyl-*o*-phenylenediamine	186
Succinanilide	230	*NN'*-Diacetyl-*m*-phenylenediamine	191
Adipanilide	239	*NN'*-Diacetyl-*p*-phenylenediamine	304
Sebacanilide	202		
		Benzoyl-*o*-toluidine	144
Cinnamanilide	153	Benzoyl-*m*-toluidine	125
Benzanilide	162	Benzoyl-*p*-toluidine	158
o-Nitrobenzanilide	155	Benzoyl-*o*-anisidine	60
m-Nitrobenzanilide	154	Benzoyl-*m*-anisidine	—
p-Nitrobenzanilide	211	Benzoyl-*p*-anisidine	154
o-Toluanilide	125	Benzoyl-*o*-phenetidine	104
m-Toluanilide	126	Benzoyl-*m*-phenetidine	103
p-Toluanilide	148	Benzoyl-*p*-phenetidine	173
Anisanilide	169	Benzoyl-α-naphthylamine	161
		Benzoyl-β-naphthylamine	162
α-Naphthanilide	163		
β-Naphthanilide	171	*NN'*-Dibenzoyl-*o*-phenylenediamine	301
		NN'-Dibenzoyl-*m*-phenylenediamine	240
Acetanilide	114	*NN'*-Dibenzoyl-*p*-phenylenediamine	>300
N-Methylacetanilide	103		
N-Ethylacetanilide	54		
N-*n*-Propylacetanilide	50	Acetyl-*N*-methyl-*o* toluidine	56
o-Chloroacetanilide	88	Acetyl-*N*-methyl-*m*-toluidine	66
m-Chloroacetanilide	79	Acetyl-*N*-methyl-*p*-toluidine	83
p-Chloroacetanilide	179	Acetyl-*N*-methyl-α-naphthylamine	94
o-Bromoacetanilide	99	Acetyl-*N*-methyl-β-naphthylamine	51
m-Bromoacetanilide	88		
p-Bromoacetanilide	167	*N*-Formyldiphenylamine	74
o-Iodoacetanilide	110	*N*-Acetyldiphenylamine	101
m-Iodoacetanilide	119		
p-Iodoacetanilide	184	Saccharin	220
o-Aminoacetanilide	132	Phthalimide	235
m-Aminoacetanilide	88	Carbanilide	238
p-Aminoacetanilide	163	Diphenylguanidine	147
o-Nitroacetanilide	94	Benzoylpiperidine	48
m-Nitroacetanilide	155		
p-Nitroacetanilide	216	*N*-Phenylurethane (or Ethyl *N*-phenylcarbamate)	53
o-Hydroxyacetanilide	209	Ethyl oxanilate	67
m-Hydroxyacetanilide	149		
p-Hydroxyacetanilide	168		
o-Methoxyacetanilide	88	Ethyl oxamate	114

AROMATIC NITRILES

Aromatic nitriles may be prepared :—

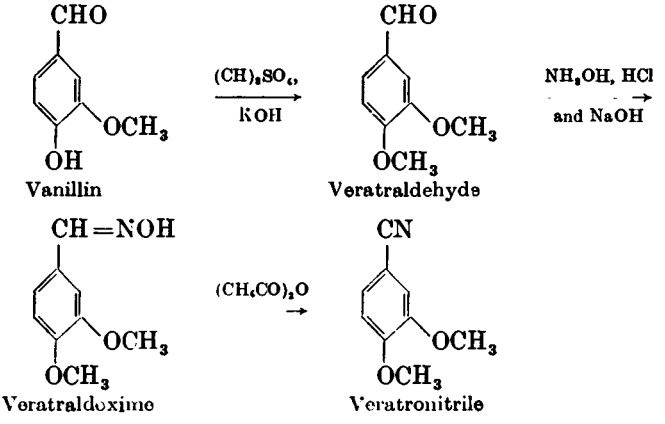
1. From amines by the diazo reaction (see discussion preceding Section IV,59 : *p*-tolunitrile and benzonitrile from *p*-toluidine and aniline respectively, Section IV,66).

2. By dehydration of aromatic amides with phosphorus pentoxide, for example :

$$\underset{\text{Benzamide}}{C_6H_5CONH_2} \xrightarrow{P_2O_5} \underset{\text{Benzonitrile}}{C_6H_5CN}$$

3. By heating halogenated benzenes or naphthalenes with cuprous cyanide, for example, α-naphthonitrile from α-bromonaphthalene and cuprous cyanide (Section IV,163).

4. From aldehydes by conversion into the oximes, followed by removal of the elements of water by the action of acetic anhydride, for example :



The readily-available vanillin is employed in the starting material in this preparation.

IV,193. BENZONITRILE

Place 45 g. of benzamide (Section IV,188) and 80 g. of phosphorus pentoxide in a 250 ml. Claisen flask (for exact experimental details on the handling and weighing out of phosphoric oxide, see under *Acetamide*, Section III,111). Mix well. Arrange for distillation (Fig. *II*, *19*, 1 or Fig. *II*, *20*, 1) under reduced pressure ; use a water pump with an air leak in the system so that a pressure of about 100 mm. is attained. Heat the flask with a free flame until no more liquid distils : the nitrile will pass over at 126–130°/100 mm. Wash the distillate with a little sodium carbonate solution, then with water, and dry over anhydrous calcium chloride or magnesium sulphate. Distil under normal pressure (Fig. *II*, *13*, 2 or *II*, *13*, 6) from a 50 ml. flask : the benzonitrile passes over as a colourless liquid at 188–189° (compare Section IV,66). The yield is 28 g.

IV,194. VERATRONITRILE

Veratraldehyde (methyl vanillin). Place 152 g. of a good sample of commercial vanillin, m.p. 81–82°, in a 1 litre three-necked flask (or Pyrex wide-mouthed bottle), equipped with a reflux condenser, a mechanical stirrer, and two separatory funnels (one of these may be supported in the top of the reflux condenser by means of a grooved cork). Melt the vanillin by warming on a water bath and stir vigorously. Charge one funnel with a solution of 82 g. of pure potassium hydroxide in 120 ml. of water and the other funnel with 160 g. (120 ml.) of purified dimethyl sulphate (1) (*CAUTION:* conduct all operations with dimethyl sulphate in the fume cupboard). Run in the potassium hydroxide solution at the rate of two drops a second, and 20 seconds after this has started add the dimethyl sulphate at the same rate. Stop the external heating after a few minutes; the mixture continues to reflux gently from the heat of the reaction. The reaction mixture should be pale reddish-brown since this colour indicates that it is alkaline; should the colour change to green, an acid reaction is indicated and this condition should be corrected by slightly increasing the rate of addition of the alkali. When half to three-quarters of the reagents have been added, the reaction mixture becomes turbid and separates into two layers. As soon as all the reagents have been run in (about 20 minutes), pour the yellow reaction mixture into a large porcelain basin and allow to cool without disturbance, preferably overnight. Filter the hard crystalline mass of veratraldehyde, grind it in a glass mortar with 300 ml. of ice-cold water, filter at the pump and dry in a vacuum desiccator. The yield of veratraldehyde, m.p. 43–44°, is 160 g. This product is sufficiently pure for most purposes; it can be purified without appreciable loss by distillation under reduced pressure, b.p. 158°/8 mm.; m.p. 46°. The aldehyde is easily oxidised in the air and should therefore be kept in a tightly stoppered bottle.

Note.

(1) **Dimethyl sulphate may be purified (*a*) by allowing it to stand over anhydrous potassium carbonate until it is neutral to Congo red paper, or (*b*) by washing, just before use, with an equal volume of ice water, followed by one-third of its volume of cold, saturated sodium bicarbonate solution.**

Veratronitrile. Dissolve 83 g. of veratraldehyde in 200 ml. of warm rectified spirit in a 1 litre bolt-head flask, and add a warm solution of 42 g. of hydroxylamine hydrochloride in 50 ml. of water. Mix thoroughly and run in a solution of 30 g. of sodium hydroxide in 40 ml. of water. Allow the mixture to stand for 2·5 hours, add 250 g. of crushed ice, and saturate the solution with carbon dioxide. The aldoxime separates as an oil: allow the mixture to stand for 12–24 hours in an ice chest or refrigerator when the oil will solidify. Filter off the crystalline aldoxime at the pump, wash well with cold water, and dry in the air upon filter paper. The yield of **veratraldoxime** is 88 g.

Into a 250 ml. Pyrex round-bottomed flask, provided with a ground-in glass air condenser, place 88 g. of veratraldoxime and 100 g. (92·5 ml.) of redistilled acetic anhydride. Heat cautiously. Immediately the vigorous reaction commences, remove the flame. When the reaction

subsides, boil the solution gently for 20 minutes, and then pour it carefully with stirring into 300 ml. of cold water. Continue the stirring and cool in ice. Filter off the almost colourless crystals of veratronitrile and dry in the air. The resulting nitrile (60 g.) is quite pure and melts at 67°.

IV,195. REACTIONS AND CHARACTERISATION OF AROMATIC NITRILES

Aromatic nitriles are generally liquids or low melting point solids, and usually have characteristic odours. They give no ammonia with aqueous sodium hydroxide solution in the cold, are hydrolysed by boiling aqueous alkali but more slowly than primary amides :

$$RCN + NaOH + H_2O \longrightarrow RCOONa + NH_3$$

When distilled with soda lime (Section **IV,175**), nitriles yield some ammonia, but pass over, in part, unchanged. They are identified by the b.p. and by hydrolysis to, and characterisation of, the corresponding acid.

Hydrolysis may be effected with 10–20 per cent. sodium hydroxide solution (see p-*Tolunitrile* and *Benzonitrile* in Section **IV,66**) or with 10 per cent. methyl alcoholic sodium hydroxide. For difficult cases, *e.g.*, α-*Naphthonitrile* (Section **IV,163**), a mixture of 50 per cent. sulphuric acid and glacial acetic acid may be used. In alkaline hydrolysis the boiling is continued until no more ammonia is evolved. In acid hydrolysis 2–3 hours boiling is usually sufficient : the reaction product is poured into water, and the organic acid is separated from any unchanged nitrile or from amide by means of sodium carbonate solution. The resulting acid is identified as detailed in Section **IV,175**.

Nitriles may often be hydrolysed (hydrated) to the amides ($RCN \longrightarrow RCONH_2$) by concentrated sulphuric acid or by concentrated hydrochloric acid, usually in the cold or at 40° (see Sections **III,115** and **IV,160**). The resulting amide is, of course, a useful derivative.

The physical properties of some typical aromatic nitriles are collected in Table **IV,195**.

TABLE IV,195. AROMATIC NITRILES

Nitrile	B.P.	M.P.
Benzonitrile	191°	—
o-Tolunitrile	205	—
m-Tolunitrile	212	—
p-Tolunitrile	218	29°
o-Chlorobenzonitrile	232	43
m-Chlorobenzonitrile	—	41
p-Chlorobenzonitrile	223	96
o-Bromobenzonitrile	252	53
m-Bromobenzonitrile	225	38
p-Bromobenzonitrile	236	113
o-Iodobenzonitrile	—	55
o-Nitrobenzonitrile	—	111
m-Nitrobenzonitrile	—	118
p-Nitrobenzonitrile	—	149
Phenylacetonitrile	234	—
p-Nitrophenylacetonitrile	—	116
α-Phenylpropionitrile	232	—
β-Phenylpropionitrile	261	—
dl-Mandelonitrile	170d	—
α-Naphthonitrile	299	36
β-Naphthonitrile	306	66
Cinnamonitrile	255	20
Phthalonitrile	—	141

SOME AROMATIC PEROXIDES AND PER-ACIDS

Organic peroxides may be prepared :—

1. By the interaction of an acyl chloride with hydrogen peroxide in the presence of alkali ($H_2O_2 + 2NaOH \equiv Na_2O_2$), for example :

$$\underset{\text{Benzoyl chloride}}{2C_6H_5COCl} + Na_2O_2 \longrightarrow \underset{\text{Benzoyl peroxide}}{(C_6H_5CO)_2O_2} + 2NaCl$$

2. By the reaction between a solution of an acyl halide in a dry organic solvent, such as toluene, with a cold solution of sodium peroxide, for example :

$$\underset{p\text{-Nitrobenzoyl chloride}}{2p\text{-}O_2NC_6H_4COCl} + Na_2O_2 \longrightarrow \underset{p\text{-Nitrobenzoyl peroxide}}{[p\text{-}O_2NC_6H_4CO]_2O_2} + 2NaCl$$

The preparation of **organic per-acids** is illustrated by :—

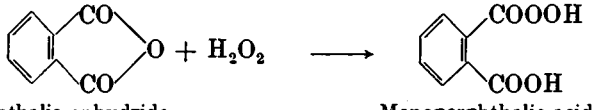
Perbenzoic acid. Treatment of a cold sodium methoxide solution with a solution of pure benzoyl peroxide in chloroform affords methyl benzoate and a solution of the sodium salt of perbenzoic acid :

$$(C_6H_5CO)_2O_2 + CH_3ONa \longrightarrow C_6H_5COOONa + C_6H_5COOCH_3$$

The methyl benzoate is removed by extraction with chloroform, and upon cautious acidification of the aqueous layer perbenzoic acid is liberated ; the latter is extracted with chloroform and is usually preserved as a solution in this solvent :

$$C_6H_5COOONa + H_2SO_4 \longrightarrow \underset{\text{Perbenzoic acid}}{C_6H_5COOOH} + NaHSO_4$$

Monoperphthalic acid. This is obtained by adding finely-powdered phthalic anhydride to a well-stirred solution of 30 per cent. hydrogen peroxide in alkali at −10° ; the solution is acidified and the per-acid is extracted with ether :



Phthalic anhydride — Monoperphthalic acid

IV,196. BENZOYL PEROXIDE

Immerse a 600 ml. beaker, containing 50 ml. of "40-volume" hydrogen peroxide and equipped with a mechanical stirrer, in an ice bath. Support two dropping funnels, containing respectively 30 ml. of 4*N* sodium hydroxide solution and 30 g. (25 ml.) of redistilled benzoyl chloride (Section **IV,185**), with their stems inside the beaker. Add the two reagents alternately a few drops at a time, taking care that the temperature does not rise above 5–8° and that the solution is maintained faintly alkaline throughout. When all the reagents have been added, stir the solution for a further half an hour ; by this time the odour of the benzoyl chloride should have disappeared. Filter off the flocculent precipitate at the pump, wash it with a little cold water, and dry upon filter paper. The yield of benzoyl peroxide is 12 g. It may be purified by dissolving in chloroform *at room temperature* and adding twice the volume of methyl alcohol. It should *not* be recrystallised from hot chloroform as serious explosion may result. The compound melts at 106° with decomposition. Like all organic peroxides, benzoyl peroxide should be handled with care.

To **determine the exact peroxide content** of benzoyl peroxide (and of other organic peroxides) the following procedure may be employed. Place about 0·05 g. of the sample of peroxide in a glass-stoppered conical flask: add 5–10 ml. of acetic anhydride (A.R. or other pure grade) and 1 g. of powdered sodium iodide. Swirl the mixture to dissolve the sodium iodide and allow the solution to stand for 5–20 minutes. Add 50–75 ml. of water, shake the mixture vigorously for about 30 seconds, and titrate the liberated iodine with standard sodium thiosulphate solution using starch as indicator.

When polymers or other water-soluble substances are present in the sample, it is advantageous to add a small amount of chloroform to the initial reaction mixture; after the subsequent addition of water, a two-phase system results which may be titrated in the usual way to a starch end point or by observing the disappearance of the iodine colour in the chloroform layer.

IV,197. *p*-NITROBENZOYL PEROXIDE

Immerse a 600 ml. beaker containing 100 ml. of water in a bath of crushed ice. Provide an efficient mechanical stirrer and a thermometer for recording the temperature of the solution. When the temperature of the water has fallen to 0–5°, add 10 g. of sodium peroxide (*CAUTION*). Support a dropping funnel, charged with a solution of 37 g. of *p*-nitrobenzoyl chloride (Section **IV,184**) in 100 ml. of dry toluene, over the beaker. Add this solution dropwise over a period of about 30 minutes whilst stirring vigorously. Continue the stirring for a further 90 minutes, then filter off the precipitate at the pump, and wash it with 200 ml. of cold water. Dry in the air. The yields of *p*-nitrobenzoyl peroxide, m.p. 155–156° (decomp.), is 28 g. Purify by dissolving *as rapidly as possible* in 500 ml. of dry toluene which has been preheated to 80–85°; immediately the solid is completely dissolved (about 2 minutes stirring is required), filter through a preheated Buchner funnel and cool the filtrate at once in a bath of crushed ice; 25 g. of very pale yellow needles, m.p. 156° (decomp.) are obtained.

IV,198. PERBENZOIC ACID (BENZOYL HYDROGEN PEROXIDE)

Place 5·2 g. of sodium in a 500 ml. dry conical flask provided with a reflux condenser, and add 100 ml. of absolute methyl alcohol; slight cooling may be necessary to moderate the vigour of the reaction. Cool the resulting solution of sodium methoxide to — 5° in a freezing mixture of ice and salt: remove the condenser. Add a solution of 50 g. of freshly recrystallised benzoyl peroxide (Section **IV,196**) (1) in 200 ml. of chloroform, with shaking and cooling, at such a rate that the temperature does not rise above 0°. Keep the mixture in the ice-salt bath for 5 minutes with continuous shaking; it turns milky but no precipitate appears. Transfer the reaction mixture to a 1 litre separatory funnel and extract the sodium perbenzoate with 500 ml. of water containing much crushed ice. [It is essential that the preparation be carried out as rapidly as possible and the temperature kept as near 0° as feasible, especially before the free acid is liberated from the sodium salt.] Separate the chloroform layer, and extract the aqueous layer twice with 100 ml.

portions of cold chloroform to remove the methyl benzoate. Liberate the perbenzoic acid from the aqueous solution by the addition of 225 ml. of ice-cold *N* sulphuric acid and extract it from solution with three 100 ml. portions of cold chloroform. Dry the moist chloroform solution (about 308 ml.) with a little anhydrous sodium or magnesium sulphate, and keep it in an ice box or a refrigerator until required (2) ; it contains about 24 g. of perbenzoic acid.

To determine the exact perbenzoic acid content of the solution, proceed as follows. Dissolve 1·5 g. of sodium iodide in 50 ml. of water in a 250 ml. reagent bottle and add about 5 ml. of glacial acetic acid and 5 ml. of chloroform. Introduce a known weight or volume of the chloroform solution of perbenzoic acid and shake vigorously. Titrate the liberated iodine with standard 0·1*N* sodium thiosulphate solution in the usual manner.

$$1 \text{ Ml. of } 0{\cdot}1N \text{ } Na_2S_2O_3 \equiv 0{\cdot}0069 \text{ g. of perbenzoic acid}$$

To obtain crystalline perbenzoic acid, dry the moist chloroform solution with a little anhydrous sodium or magnesium sulphate for an hour, filter, and wash the desiccant with a little dry chloroform. Remove the chloroform under reduced pressure at the ordinary temperature whilst carbon dioxide is introduced through a capillary tube. Dry the white or pale yellow residue for several hours at 30–35° under 10 mm. pressure. The yield of crystalline perbenzoic acid, m.p. about 42°, which is contaminated with a little benzoic acid, is 22 g. It is moderately stable when kept in the dark in a cold place ; it is very soluble in chloroform, ethyl acetate and ether, but only slightly soluble in cold water and in cold light petroleum.

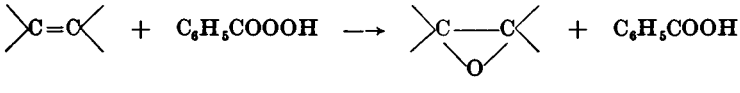
Notes.

(1) It is essential to use freshly recrystallised benzoyl peroxide. The commercial material usually gives poor results. Commercial benzoyl peroxide may be recrystallised from a small amount of hot chloroform, or by dissolving in chloroform and precipitating with absolute methyl alcohol.

The m.p. is not always a safe criterion of purity. Benzoyl peroxide may be analysed as follows : Dissolve about 0·5 g., accurately weighed, of benzoyl peroxide in 15 ml. of chloroform in a 350 ml. conical flask. Cool to − 5°, and add 25 ml. of 0·1*N* sodium methoxide solution at once with cooling and shaking. After 5 minutes at − 5°, add 100 ml. of iced water, 5 ml. of 10 per cent. sulphuric acid, and 2 g. of potassium iodide in 20 ml. of 10 per cent. sulphuric acid in the order mentioned with vigorous stirring. Titrate the liberated iodine with standard 0·1*N* sodium thiosulphate solution.

$$1 \text{ Ml. of } 0{\cdot}1N \text{ } Na_2S_2O_3 \equiv 0{\cdot}0121 \text{ g. of benzoyl peroxide.}$$

(2) Perbenzoic acid is used for the conversion of ethylenic compounds into oxides :



The number of ethylenic linkages in a given compound can be established with accuracy by quantitative titration with perbenzoic acid. A solution of the substance and excess of perbenzoic acid in chloroform is allowed to stand for several hours at a low temperature and the amount of unreacted perbenzoic acid in solution is determined : a blank experiment is run simultaneously.

Owing to the greater stability and the easier preparation, monoperphthalic acid is generally preferred to benzoic acid.

IV,199. MONOPERPHTHALIC ACID

Cool a 500 ml. round-bottomed flask containing 125 ml. of 15 per cent. sodium hydroxide solution, and equipped with a mechanical stirrer, in a bath of ice and salt. When the temperature has fallen to — 10°, add in one portion 57·5 g. (52·5 ml.) of " 100 volume " (or 30 per cent.) hydrogen peroxide which has previously been cooled to — 10°. The temperature rises owing to the heat of the reaction. When the temperature has again dropped to — 10°, add, whilst stirring *vigorously*, 37·5 g. of pure phthalic anhydride (1) (finely-powdered to pass a 40-mesh sieve) as quickly as possible. Immediately the anhydride has dissolved (2), add 125 ml. of 20 per cent. sulphuric acid which has previously been cooled to — 10°. Filter the solution through a plug of glass wool in a funnel into a 1-litre separatory funnel: extract with ether (once with 250 ml., then three times with 125 ml. portions). Shake the combined ether extracts with three 75 ml. portions of 40 per cent. ammonium sulphate solution and dry for 24 hours, preferably in an ice chest or refrigerator, over 25 g. of anhydrous sodium or magnesium sulphate. The ether solution, which contains 30 g. of monoperphthalic acid (3), may be used for the conversion of unsaturated compounds into oxides (see under *Perbenzoic Acid*, Section **IV,198**, *Note 2*). If ether is not a suitable solvent for the oxidation reactions in which the per-acid is to be used, the monoperphthalic acid may be dissolved in dry chloroform or in peroxide-free dioxan after the removal of the ether (see below).

To prepare **crystalline monoperphthalic acid**, place the thoroughly dry ethereal solution (4) in a distilling flask equipped with a capillary tube connected with a calcium chloride or cotton wool drying tube, and attach the flask to a water pump. Evaporate the ether without the application of heat (ice will form on the flask) to a thin syrup (about 150 ml.). Transfer the syrup to an evaporating dish, rinse the flask with a little anhydrous ether, and add the rinsings to the syrup. Evaporate the remainder of the ether in a vacuum desiccator over concentrated sulphuric acid: about 30 g. of monoperphthalic acid, m.p. 110° (decomp.), is obtained.

Notes.

(1) If it is suspected that phthalic acid is present in the phthalic anhydride, the latter may be dissolved in chloroform; the phthalic acid is insoluble in this solvent.

(2) The whole success of the preparation depends upon reducing the time interval between the addition of the phthalic anhydride and the acidification of the reaction mixture to a minimum; vigorous stirring will assist the initial dissolution, but prolonged stirring leads to excessive evolution of oxygen. The more rapidly the anhydride dissolves, the smaller the oxygen evolution, and the better the yield of monoperphthalic acid.

(3) To determine the per-acid content, add 30 ml. of 20 per cent. potassium iodide solution to 2·0 ml. of the solution and, after 10 minutes, titrate the liberated iodine with standard 0·05*N* sodium thiosulphate solution (compare *Perbenzoic Acid*, Section **IV,198**, *Note 1*).

(4) The results are unsatisfactory unless the drying is very thorough; only 1 per cent. of water in the ether solution will destroy all the per-acid.

AROMATIC ALCOHOLS

Aromatic alcohols (derivatives of carbinol HCH_2OH) may be prepared (compare *Aliphatic Alcohols*, discussion preceding Section III,14) :

1. By the Cannizzaro reaction. This consists in the action of a concentrated aqueous solution of sodium or potassium hydroxide upon an aldehyde (see detailed discussion before Section IV,123), for example :

$$\underset{\text{Benzaldehyde}}{2C_6H_5CHO} + KOH \longrightarrow \underset{\text{Potassium benzoate}}{C_6H_5COOK} + \underset{\text{Benzyl alcohol}}{C_6H_5CH_2OH}$$

Only half of the aldehyde is reduced to the alcohol, the other half being oxidised to the acid. By using a slight excess (say, 1·3 mols) of aqueous formaldehyde, practically the whole of the aromatic aldehyde is converted into the alcohol : the formaldehyde is simultaneously oxidised to formic acid. This is sometimes termed a **crossed Cannizzaro reaction.** The example given is :

$$\underset{p\text{-Tolualdehyde}}{p\text{-}CH_3C_6H_4CHO} + \underset{\text{Formaldehyde}}{HCHO} + KOH \longrightarrow \underset{p\text{-Tolyl carbinol}}{p\text{-}CH_3C_6H_4CH_2OH} + \underset{\text{Potassium formate}}{HCOOK}$$

Benzaldehyde and veratraldehyde (Section IV,194) may be similarly converted into the corresponding alcohols.

Aromatic primary alcohols differ from aliphatic primary alcohols in that they react with concentrated hydrochloric acid in the cold to yield the corresponding chlorides, for example :

$$\underset{\text{Benzyl alcohol}}{C_6H_5CH_2OH} + HCl \longrightarrow \underset{\text{Benzyl chloride}}{C_6H_5CH_2Cl} + H_2O$$

2. Reduction of ketones, *e.g.*, with zinc powder and alcoholic sodium hydroxide leads to secondary alcohols, for example :

$$\underset{\text{Benzophenone}}{C_6H_5COC_6H_5} + 2H \longrightarrow \underset{\text{Benzhydrol}}{C_6H_5CH(OH)C_6H_5}$$

3. By the action of a Grignard reagent upon an ester or a ketone, for example :

$$\underset{\text{Phenyl magnesium bromide}}{2C_6H_5MgBr} + \underset{\text{Ethyl benzoate}}{C_6H_5COOC_2H_5} \longrightarrow (C_6H_5)_3COMgBr + MgBrOC_2H_5$$

$$(C_6H_5)_3COMgBr + H_2O \longrightarrow \underset{\text{Triphenylcarbinol}}{(C_6H_5)_3COH} + MgBrOH$$

A little diphenyl is formed as a by-product in the reaction :

$$C_6H_5MgBr + C_6H_5Br \longrightarrow C_6H_5{-}C_6H_5 + MgBr_2$$

$$C_6H_5MgBr + \underset{\text{Benzophenone}}{(C_6H_5)_2CO} \longrightarrow (C_6H_5)_3COMgBr \xrightarrow{H_2O} \underset{\text{Triphenylcarbinol}}{(C_6H_5)_3COH}$$

Triphenylchloromethane $(C_6H_5)_3CCl$ is readily hydrolysed by warm water to triphenylcarbinol, thus providing an alternative method for the preparation of the latter. The former is conveniently obtained by the reaction between carbon tetrachloride and benzene in the presence of anhydrous aluminium chloride :

$$3C_6H_6 + CCl_4 + AlCl_3 \longrightarrow (C_6H_5)_3CCl.AlCl_3 + 3HCl$$

$$(C_6H_5)_3CCl.AlCl_3 + xH_2O \longrightarrow (C_6H_5)_3CCl + AlCl_3{,}xH_2O$$

4. By the reduction of aromatic esters with sodium and absolute ethyl alcohol, for example :

$$\underset{\text{Ethyl phenylacetate}}{C_6H_5CH_2COOC_2H_5} + 4H \longrightarrow \underset{\beta\text{-Phenylethyl alcohol}}{C_6H_5CH_2CH_2OH} + C_2H_5OH$$

IV,200. *p*-TOLYL CARBINOL (*p*-METHYL BENZYL ALCOHOL)

Equip a 1 litre three-necked flask with a reflux condenser, a mercury-sealed mechanical stirrer, a dropping funnel and a thermometer ; the bulb of the thermometer should reach almost to the bottom of the flask. Place 170 g. of commercial potassium hydroxide pellets (about 85 per cent. KOH) and 250 ml. of methyl alcohol (acetone-free) in the flask and set the stirrer in motion. Most of the alkali dissolves in a few minutes and the temperature rises considerably. Immerse the flask in a large cold-water bath and, when the temperature has fallen to 60–65°, add a mixture of 120 g. (118 ml.) of *p*-tolualdehyde (Section **IV,118**) and 100 ml. (*ca.* 1·3 mols) of formalin at such a rate (during about 15 minutes) that the internal temperature remains at 60–70° : maintain the internal temperature at 60–70° for a further 3 hours. Replace the reflux condenser by a condenser set for downward distillation, and distil off the methyl alcohol, while stirring, until the temperature reaches about 100°. Add 300 ml. of water to the warm residue, cool the mixture and separate the resulting two layers at once ; if the upper layer is allowed to stand, it will solidify. Extract the aqueous layer with four 50 ml. portions of benzene. Wash the combined oil and benzene extracts with five 25 ml. portions of water to remove the potassium *o*-toluate ; extract the combined washings with 25 ml. of benzene and add the benzene layer to the washed extract. Dry the benzene solution by shaking with a few grams of anhydrous magnesium sulphate and distil off the benzene (Fig. *II*, *13*, 4 but with Claisen flask) until the temperature rises to 90°. Finally distil under reduced pressure (Fig. *II*, *19*, 1) and collect the *p*-tolyl carbinol at 116–118°/20 mm. (1). The product solidifies in the receiver to a mass (110 g.) of oily crystals, m.p. 54–55°. Recrystallise from an equal weight of technical heptane (b.p. 90–100°) ; 88 g. of pure *p*-tolyl carbinol, m.p. 61°, are obtained.

Note.

(1) The b.p. at atmospheric pressure is 217°.

Cognate Preparation

Benzyl alcohol. This alcohol, b.p. 205·5°, may be similarly prepared from benzaldehyde in approximately the same yield (compare Section **IV,123.**)

IV,201. BENZHYDROL (DIPHENYLCARBINOL)

In a 700 ml. bolt-head flask, equipped with a reflux condenser and a mechanical stirrer, place 50 g. of benzophenone (Section **IV,139**), 500 ml. of rectified spirit, 50 g. of sodium hydroxide and 50 g. of zinc powder. Stir

the mixture ; the temperature slowly rises to about 70°. After 3 hours, when the temperature has commenced to fall, filter the reaction mixture with suction and wash the residue twice with 25 ml. portions of hot alcohol. Do not allow the residual zinc powder to become dry as it is inflammable. Pour the filtrate into 2 litres of ice water acidified with 100 ml. of concentrated hydrochloric acid. The benzhydrol separates as a white crystalline mass. Filter at the pump and dry in the air. The yield of crude benzhydrol, m.p. 65°, is 49 g. Recrystallise from 50 ml. of hot alcohol and cool in a freezing mixture of ice and salt. Collect the colourless crystals and dry in the air ; 36 g. of pure diphenylcarbinol, m.p. 68°, are obtained. Precipitate the mother liquor with water to recover the residual benzhydrol, and recrystallise this from a small quantity of hot alcohol.

IV,202. TRIPHENYLCARBINOL

Procedure for advanced students. Place 15·5 g. of dry magnesium turnings in a 1 litre three-necked flask fitted with a dropping funnel, mercury-sealed mechanical stirrer and a double surface reflux condenser. Place a solution of 15 g. (10 ml.) of dry bromobenzene (Section **IV,18**) in 35 ml. of sodium dried ether (Section II,**47**, *1*) in the dropping funnel. Provide both the latter and the reflux condenser with calcium chloride (or cotton wool) guard tubes in order to prevent the entrance of moisture into the reaction mixture. Run in the bromobenzene solution on to the magnesium and warm gently on a water bath until the reaction becomes vigorous. If no reaction ensues, add a small crystal of iodine to start the reaction ; the use of iodine is generally unnecessary if the reagents and the apparatus are thoroughly dry. As soon as the reaction is moderately vigorous, immerse the flask in a bath of cold water. Start the stirrer and add a solution of 75·5 g. (50·5 ml.) of dry bromobenzene in 200 ml. of sodium-dried ether at such a rate as to cause vigorous refluxing (during about 1 hour) ; when all the bromobenzene solution has been introduced, stir the mixture for 20–30 minutes, *i.e.*, until most (or all) of the magnesium has dissolved.

To the resulting Grignard reagent (phenyl magnesium bromide) cooled in a cold water bath, add a solution of 37·5 g. (36 ml.) of dry ethyl benzoate (Section **IV,176**) in 100 ml. of dry benzene (either sodium-dried or dried with anhydrous magnesium or calcium sulphate) at such a rate that the mixture refluxes gently (about 1 hour). Then reflux the mixture for 1 hour on a water bath. Cool in a freezing mixture of ice and salt and pour it slowly, with constant stirring, into a mixture of 750 g. of crushed ice and 25 ml. of concentrated sulphuric acid. Continue the stirring until all the solid dissolves ; it may be necessary to add 25 g. of solid ammonium chloride to facilitate the decomposition of the magnesium complex, and also a little more benzene to dissolve all the product. When all the solids have passed into solution, separate the benzene layer and wash it successively with 100 ml. of water, 100 ml. of 5 per cent. sodium bicarbonate solution and 100 ml. of water. Remove the benzene as completely as possible from a 1 litre round-bottomed flask : steam distil the residue (Fig. *II*, *40*, 1) in order to separate unchanged bromo-

benzene and diphenyl (by-product). Filter the cold residue in the flask at the pump, wash it with water and dry. The resulting crude triphenylcarbinol weighs 62 g. Recrystallise it from carbon tetrachloride (4 ml. per gram of solid): the first crop of crystals, after drying in air to remove the solvent of crystallisation, weighs 56 g. and melts at 162°. Treat the mother liquid with 1 g. of decolourising carbon, concentrate to one-quarter of the original volume and cool in ice: a further 3 g. of pure triphenylcarbinol is obtained.

In an **alternative method of preparation**, benzophenone is used. Prepare the Grignard reagent from 13·5 g. of magnesium turnings as above, cool in cold water, and add a solution of 91 g. of benzophenone (Section **IV,139**) in 200 ml. of dry benzene at such a rate that the mixture refluxes gently. Reflux the mixture for 60 minutes, and isolate the triphenylcarbinol in the manner described above. The yield is of the same order.

Procedure for elementary students. Fit a 500 ml. round-bottomed or bolt-head flask with a two-way adapter carrying a separatory funnel and a reflux (preferably double surface) condenser (Fig. *II*, *13*, 9). If an adapter is not available, fit the reflux condenser directly into the flask and mount the separatory funnel into the top of the condenser by means of a grooved cork. Make certain that all the apparatus, including the corks, is perfectly dry before the preparation is attempted. Place 2·7 g. of dry magnesium turnings, 15 ml. of sodium-dried ether (Section **II,47**, *1*) and a minute crystal of iodine in the flask. Prepare a solution of 18 g. of dry bromobenzene (Section **IV,18**) in 50 ml. of anhydrous ether in a small corked conical flask. Pour about 10 ml. of this solution into the separatory funnel and add it to the contents of the flask. Await the beginning of the reaction (slight boiling of the ether). If no reaction commences within 3 minutes, warm the flask gently in a bath of warm water until the reaction starts; remove the water bath. When the reaction has started (*but not before*), add the remainder of the bromobenzene solution from the separatory funnel in small portions, *i.e.*, at such a rate that the ether refluxes gently without external heating. After all the halide has been added, replace the separatory funnel by a calcium chloride or cotton wool guard tube (1) and reflux the mixture *gently* on a water bath for 30–40 minutes in order to complete the reaction: most of the magnesium should then have disappeared.

Remove the flask containing the Grignard reagent and cool it to room temperature or below by immersion in a bath of cold water or ice water. Replace the guard tube by a separatory funnel (1) containing a solution of 7·5 g. (7·2 ml.) of dry ethyl benzoate (Section **IV,163**) in 20 ml. of anhydrous ether. Run this solution dropwise into the Grignard reagent and thoroughly mix the solutions by shaking from time to time; cool the flask occasionally if the boiling is very vigorous. Finally reflux gently on a water bath for 15–30 minutes. Cool the contents of the flask and pour cautiously into a mixture of 150 g. of crushed ice and 5 ml. of concentrated sulphuric acid contained in a large flask or beaker. Stir so that the magnesium compound is completely decomposed and the triphenylcarbinol, etc., dissolves in the ether: the addition of a further small quantity of technical ether may be necessary to effect the solution

of the solid. Transfer to a separatory funnel, run off the lower layer, and shake the ethereal solution twice with 30 ml. portions of 10 per cent. sulphuric acid (to remove magnesium salts completely), once with water, and finally with 25 ml. of water containing 0·5 g. of sodium bisulphite (to remove the iodine used to start the reaction). Return the ether to the (washed) 500 ml. flask and distil off the ether on a water bath ; take the customary precautions against fire. Add 50–75 ml. of water to the residue and fit the flask for steam distillation (Fig. *II*, *40*, 1). Steam distil until no further oil (unchanged reactants and diphenyl) passes over. Upon cooling the flask, the residue solidifies. Filter the solid at the pump and dry it between several layers of filter papers. Recrystallise the crude but colourless triphenylcarbinol (12 g.) from rectified (or methylated) spirit or from carbon tetrachloride (4 ml. per gram of solid) ; dry the recrystallised product in the air. The yield of pure triphenylcarbinol, m.p. 162°, is 10 g.

Note.

(1) If the apparatus of Fig. *II*, *13*, 9 is used, there is, of course, no need to remove the guard tube from the top of the condenser.

IV,203. TRIPHENYLCHLOROMETHANE *

Place 200 g. (228 ml.) of sodium-dried A.R. benzene and 80 g. (47 ml.) of dry, pure carbon tetrachloride in a 500 ml. three-necked flask, equipped with a reflux condenser attached to a trap (Fig. *II*, *8*, 1, *c*) for the absorption of the hydrogen chloride, a mercury-sealed mechanical stirrer, and a device for the addition of a solid (see Figs. *II*, *7*, 12, *c* or *d*) ; charge the last-named with 60 g. of finely-powdered, anhydrous aluminium chloride. Cool the flask in an ice bath, and add the aluminium chloride in small portions to the contents of the flask at such a rate that the reaction mixture does not reflux during the addition (about 1·5 hours). Remove the ice bath 15 minutes after all the solid has been introduced, and allow the reaction to proceed without further cooling. When heat is no longer evolved, reflux the mixture until the evolution of hydrogen chloride subsides (*ca.* 2 hours) ; then allow to cool to room temperature. Pour the cold reaction product in a thin stream on to a mixture of 300 g. of crushed ice and 300 ml. of concentrated hydrochloric acid ; stir vigorously. Separate the benzene layer and extract the aqueous layer with a little benzene ; wash the combined extracts once with 200 ml. of cold concentrated hydrochloric acid. Dry the benzene solution by leaving for at least two hours over 25 g. of anhydrous calcium chloride (or anhydrous magnesium sulphate). Distil off the benzene (Fig. *II*, *13*, 4 but with Claisen flask fitted with a thermometer) until the temperature reaches about 100°. Transfer the warm residue, with the aid of a little dry benzene, to a 200 ml. conical flask, cool to about 40°, add 3–4 ml. of acetyl chloride (1) and heat the mixture nearly to the boiling point. Shake the solution vigorously whilst cooling rapidly to room temperature and then cool in ice for 2 hours. Filter the solid triphenylchloromethane on a sintered glass funnel with suction, crush the crystals with a large glass stopper, wash with three 30 ml. portions of light petroleum, b.p. 60–80°

* Sometimes termed *Trityl chloride.*

(free from aromatic hydrocarbons). Dry in a vacuum desiccator over paraffin wax shavings or silica gel to remove the solvent. The resulting pale greenish-yellow crystals of triphenylchloromethane melt at 111–112° and weigh 90 g. Store the product in a well-stoppered (or in a "screw-topped") bottle sealed with paraffin wax; this is necessary since triphenylchloromethane is slowly hydrolysed to triphenylcarbinol by the moisture of the air (2).

Notes.

(1) The acetyl chloride converts any triphenylcarbinol which may be present into triphenylchloromethane:

$$(C_6H_5)_3COH + CH_3COCl \longrightarrow (C_6H_5)_3CCl + CH_3COOH$$

(2) The partially hydrolysed product may be purified by recrystallisation from one-third its weight of pure benzene containing 10–20 per cent. of acetyl chloride, and washing the crystals with light petroleum (b.p. 60–80°) to which a little acetyl chloride has been added.

To prepare triphenylcarbinol from triphenylchloromethane, boil the latter with excess of water for 10 minutes. Filter off the resulting triphenylcarbinol, dry between filter papers, and recrystallise from carbon tetrachloride or alcohol; m.p. 162°. The yield is almost quantitative.

IV,204. β-PHENYLETHYL ALCOHOL

Equip a 3 litre three-necked flask with a separatory funnel, a mercury-sealed mechanical stirrer and a long reflux condenser with an inner tube 2–2·5 cm. in diameter: use a short length of wide-bore rubber "pressure tubing" for fitting the condenser into the flask. Place 42 g. of clean sodium and 120 ml. of sodium-dried toluene in the flask and heat the latter in an oil bath until the sodium has melted. Start the stirrer; when the sodium is finely divided, remove the oil bath and allow the mixture to cool. Continue the stirring during the cooling in order to keep the sodium in the finely divided form. When the mixture has cooled to about 60°, add a solution of 50 g. of ethyl phenylacetate (Section **IV,179**) in 150 g. (190 ml.) of "super-dry" ethyl alcohol (Section **II,47,5**) as rapidly as possible without allowing the reaction to get out of control. Then add a further 200 g. (253 ml.) of "super-dry" alcohol. When the reaction has subsided, heat the flask in a water bath until the sodium is completely dissolved. Distil off the alcohol and toluene under reduced pressure (compare Fig. *II*, *37*, 1). Dilute the residue with water and extract the phenylethyl alcohol with ether or benzene, dry the extract with anhydrous magnesium sulphate, remove the solvent, and distil the residual oil under reduced pressure. Collect the β-phenylethyl alcohol at 116–118°/25 mm. The yield is 25 g.

The alcohol may be purified by conversion into the calcium chloride addition compound. Treat it with anhydrous calcium chloride; much heat is evolved and the addition compound is formed. After several hours, remove any oil which has not reacted by washing with petroleum ether (b.p. 60–80°). Decompose the solid with ice water, separate the alcohol, dry and distil.

IV,205. REACTIONS AND CHARACTERISATION OF AROMATIC ALCOHOLS

Aromatic alcohols are insoluble in water and usually burn with a smoky flame. Their boiling points are comparatively high ; some are solids at the ordinary temperature. Many may be oxidised by cautious addition of dilute nitric acid to the corresponding aldehyde ; upon neutralistion of the excess of acid, the aldehyde may be isolated by ether extraction or steam distillation, and then identified as detailed under *Aromatic Aldehydes*, Section **IV,135.**

Most aromatic alcohols exhibit the majority of the reactions given under *Aliphatic Alcohols*, Section **III,27**, and may be converted into crystalline derivatives as there described.

Table **IV,205**, contains the melting points of the derivatives of a number of commonly-occurring aromatic alcohols.

TABLE IV,205. **AROMATIC ALCOHOLS**

Alcohol	B.P.	M.P.	3 : 5-Dinitrobenzoate	*p*-Nitrobenzoate	Phenylurethane	α-Naphthylurethane	Hydrogen 3-nitrophthalate	Other Derivatives
Benzyl	205°	—	113°	86°	76°	134°	176°	—
β-Phenylethyl	220	—	108	63	80	119	123	—
Methylphenyl carbinol (1)	203	20°	94	43	92	106	—	—
Ethylphenyl carbinol (2)	219	—	—	60	—	102	—	—
n-Propylphenyl carbinol (3)	118°/18	16	—	58	—	99	—	—
n-Butylphenyl carbinol (4)	137°/21	—	—	—	75	—	—	—
Diphenyl carbinol (5)	298	69	142	—	140	136	—	Acetyl, 42°
γ-Phenyl-*n*-propyl (6)	237	—	92	46	48	—	117	—
Triphenyl carbinol	380	165	—	—	—	—	—	Acetyl, 88; triphenylmethane, 92
o-Nitrobenzyl	270	74	—	—	—	—	—	Benzoyl, 102
m-Nitrobenzyl	—	27	—	—	—	—	—	Benzoyl, 72
p-Nitrobenzyl	185°/12	93	—	—	—	—	—	Benzoyl, 95; acetyl, 78
o-Aminobenzyl	—	82	—	—	—	—	—	*N*-Acetyl, 114; picrate, 110
m-Aminobenzyl	—	97	—	—	—	—	—	*N*-Acetyl, 107; dibenzoyl, 114
p-Aminobenzyl	—	65	—	—	—	—	—	Diacetyl, 188
o-Chlorobenzyl	230	74	—	94	—	—	—	—
m-Chlorobenzyl	234	—	—	—	—	—	—	—
p-Chlorobenzyl	235	75	—	—	—	—	—	—
o-Bromobenzyl	—	80	—	—	—	—	—	*o*-Bromobenzoic acid, 150 ($KMnO_4$)
m-Bromobenzyl	254	—	—	—	—	—	—	—
p-Bromobenzyl	—	77	—	—	—	—	—	Acetyl, 23
o-Iodobenzyl	—	90	—	—	—	—	—	—
m-Iodobenzyl	165°/16	—	—	—	—	—	—	—
p-Iodobenzyl	—	72	—	—	—	—	—	—
o-Hydroxybenzyl (7)	—	87	—	—	—	—	—	Benzoyl, 60
m-Hydroxybenzyl	—	73	—	—	—	—	—	Acetyl, 84; diacetyl, 75

TABLE IV,205. AROMATIC ALCOHOLS (*continued*)

Alcohol	B.P.	M.P.	3 : 5-Dinitrobenzoate	*p*-Nitrobenzoate	Phenylurethane	α-Naphthylurethane	Hydrogen 3-nitrophthalate	Other Derivatives
p-Hydroxybenzyl . .	—	125°	—	—	—	—	—	—
o-Methoxybenzyl . .	249°	—	—	—	—	136°	—	Benzoyl, 59°
m-Methoxybenzyl . .	252	—	—	—	—	—	—	—
p-Methoxybenzyl (8) . .	259	25	—	—	93°	—	—	Benzoyl, 38; anisic acid, 184
o-Tolyl carbinol (9) . .	219	36	—	—	79	—	—	*o*-Toluic acid, 104
m-Tolyl carbinol . .	217	—	—	—	—	116	—	—
p-Tolyl carbinol . .	217	60	—	—	79	—	—	—
Cinnamyl	257	33	121°	78°	91	114	—	—
Piperonyl (10) . . .	—	58	—	—	102	—	—	Benzoyl, 66
Benzoin	—	137	—	123	165	140	—	Acetyl, 83; benzoyl, 125; semicarbazone, 206d; 2 : 4-dinitrophenylhydrazone, 234

(1) α-Phenylethyl alcohol or α-Methylbenzyl alcohol.
(2) α-Ethylbenzyl alcohol.
(3) α-Phenyl-*n*-butyl alcohol or α-Propylbenzyl alcohol.
(4) α-Phenyl-*n*-amyl alcohol.
(5) Benzhydrol.
(6) Hydrocinnamyl alcohol.
(7) Saligenin.
(8) Anisyl alcohol.
(9) 2-Methylbenzyl alcohol.
(10) 3 : 4-Methylenedioxybenzyl alcohol.

COMPOUNDS DERIVED FROM AROMATIC SULPHONIC ACIDS

Aryl sulphonic acids, either free or in the form of their sodium or potassium salts, are converted into the acid chlorides by reaction with phosphorus pentachloride or phosphorus oxychloride, for example :

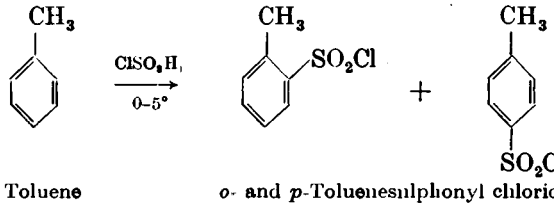
$$\underset{\text{Na benzenesulphonate}}{3C_6H_5SO_2ONa} + PCl_5 \xrightarrow{170\text{–}180^\circ} \underset{\text{Benzenesulphonyl chloride}}{3C_6H_5SO_2Cl} + NaPO_3 + 2NaCl$$

$$2C_6H_5SO_2ONa + POCl_3 \xrightarrow{170\text{–}180^\circ} 2C_6H_5SO_2Cl + NaPO_3 + NaCl$$

$$\underset{\text{Na } p\text{-toluenesulphonate}}{3p\text{-}CH_3C_6H_4SO_2ONa} + PCl_5 \xrightarrow{170\text{–}180^\circ} \underset{\text{chloride (m.p. 69°)}}{3p\text{-}CH_3C_6H_4SO_2Cl} + NaPO_3 + 2NaCl$$

The **aryl sulphonyl chlorides** may also be obtained from the aromatic hydrocarbon and chlorosulphonic acid, for example :

$$C_6H_6 + 2ClSO_3H \xrightarrow[20\text{–}25^\circ]{\text{3 Equivalents.}} C_6H_5SO_2Cl + H_2SO_4 + HCl$$



Toluene — *o*- and *p*-Toluenesulphonyl chlorides

The mixture of o- and *p*-toluenesulphonyl chlorides produced from toluene may be separated by cooling to − 10° to − 20° when most of the *p*-isomer, which is a solid, m.p. 69°, separates out. Both isomers may be easily converted (*e.g.*, by treatment with solid ammonium carbonate or with concentrated ammonia solution) into the corresponding highly crystalline sulphonamides which may be employed for interesting syntheses.

Dichloramine-T and chloramine-T. When *p*-toluenesulphonamide is dissolved in *excess* of sodium (or calcium) hypochlorite solution, it is converted into the soluble salt of the *N*-monochloro derivative :

$$p\text{-}CH_3C_6H_4SO_2NH_2 + NaOCl \longrightarrow \{p\text{-}CH_3C_6H_4SO_2NCl\}^-Na^+ + H_2O$$

Upon the addition of a weak acid (*e.g.*, acetic acid), it reacts with the liberated hypochlorous acid giving *NN*-dichloro-*p*-toluenesulphonamide (dichloramine-T) which, being insoluble in water, crystallises rapidly :

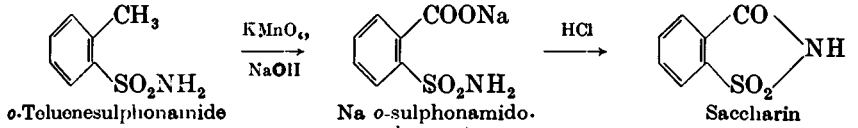
$$\{p\text{-}CH_3C_6H_4SO_2NCl\}^-Na^+ + HOCl + CH_3COOH \longrightarrow \underset{\text{Dichloramine-T}}{p\text{-}CH_3C_6H_4SO_2NCl_2} + CH_3COONa + H_2O$$

When the dichloramine-T is heated with sodium hydroxide solution, the reverse change occurs and sodium *N*-chloro-*p*-toluenesulphonamide (chloramine-T) crystallises out on cooling at a suitable concentration :

$$p\text{-}CH_3C_6H_4SO_2NCl_2 + 2NaOH \longrightarrow \underset{\text{Chloramine-T}}{\{p\text{-}CH_3C_6H_4SO_2NCl\}^-Na^+} + NaOCl + H_2O$$

Both chloramine-T and dichloramine-T slowly liberate hypochlorous acid in contact with water and are therefore employed as antiseptics : the former is employed in the form of a dilute (*e.g.*, 0·2 per cent.) aqueous solution, and the latter (which is insoluble in water) as a solution in an organic solvent, such as a chlorinated paraffin.

Saccharin (imide of o-sulphobenzoic acid). Upon oxidising o-toluenesulphonamide with potassium permanganate in alkaline solution, the sodium salt of o-sulphonamidobenzoic acid is formed, which upon acidifying with concentrated hydrochloric acid or warming passes spontaneously into the cyclic imide of o-sulphobenzoic acid or saccharin :



o-Toluenesulphonamide — Na *o*-sulphonamidobenzoate — Saccharin

Saccharin itself is sparingly soluble in cold water, but the imino hydrogen is acidic and the compound forms a water-soluble sodium salt. The latter is about 500 times as sweet as cane sugar.

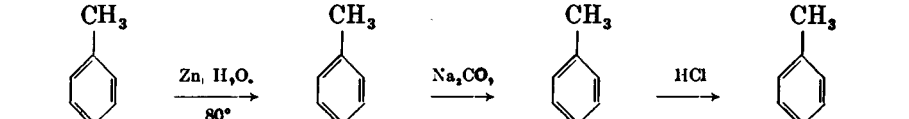
The use of benzenesulphonyl chloride or of *p*-toluenesulphonyl chloride in the separation and identification of amines is described in Section IV,100.

Esters of *p*-toluenesulphonic acid, which are of great value as alkylating agents, may be prepared by interaction of *p*-toluenesulphonyl chloride and the alcohol in the presence of sodium hydroxide solution or of pyridine, for example :

$$p\text{-}CH_3C_6H_4SO_2Cl + C_4H_9^{\alpha}OH + NaOH \longrightarrow p\text{-}CH_3C_6H_4SO_2OC_4H_9^{\alpha} + NaCl + H_2O$$

n-Butyl alcohol — *n*-Butyl *p*-toluenesulphonate

One method of preparing **sulphinic acids** has already been described (diazo reaction, Section IV,65). Reduction of a sulphonyl chloride with zinc powder and water affords the zinc salt of the sulphinic acid, converted by sodium carbonate to the sodium salt (in which form it is conveniently isolated), and by hydrochloric acid into the somewhat unstable sulphinic acid, for example :



p-Toluenesulphonyl chloride — Na *p*-toluene sulphinate — *p*-Toluenesulphinic acid

Thiophenols (or aryl mercaptans) are obtained by more vigorous reduction of sulphonyl chlorides (or of sulphinic acids), for example with zinc and dilute sulphuric acid, and are isolated by steam distillation :

$$C_6H_5SO_2Cl + 6H \xrightarrow[0^\circ]{Zn,\ H_2SO_4} C_6H_5SH + HCl + 2H_2O$$

Benzenesulphonyl chloride — Thiophenol

IV,206. BENZENESULPHONYL CHLORIDE

Method 1. Equip a 1 litre three-necked flask (or bolt-head flask) with a separatory funnel, a mechanical stirrer (Fig. *II*, *7*, 10), a thermometer (with bulb within 2 cm. of the bottom) and an exit tube leading to a gas absorption device (Fig. *II*, *8*, 1, *c*). Place 700 g. (400 ml.) of chlorosulphonic acid in the flask and add slowly, with stirring, 156 g. (176 ml.) of pure benzene (1); maintain the temperature between 20° and 25° by immersing the flask in cold water, if necessary. After the addition is complete (about 2·5 hours), stir the mixture for 1 hour, and then pour it on to 1500 g. of crushed ice. Add 200 ml. of carbon tetrachloride, stir, and separate the oil as soon as possible (otherwise appreciable hydrolysis occurs); extract the aqueous layer with 100 ml. of carbon tetrachloride. Wash the combined extracts with dilute sodium carbonate solution, distil off most of the solvent under atmospheric pressure (2), and distil the residue under reduced pressure. Collect the benzenesulphonyl chloride at 118–120°/15 mm.; it solidifies to a colourless solid, m.p. 13–14°, when cooled in ice. The yield is 270 g. A small amount (10–20 g.) of diphenylsulphone, b.p. 225°/10 mm., m.p. 128°, remains in the flask.

Notes.

(1) A 50 per cent. excess of chlorosulphonic acid is used; a smaller excess leads to increased formation of diphenylsulphone ($C_6H_5SO_2C_6H_5$) at the expense of the sulphonyl chloride.

(2) Any water present will distil with the carbon tetrachloride; the hydrolysis of the chloride is thus avoided.

Method 2. Place 90 g. of sodium benzenesulphonate (Section IV,29) (previously dried at 130–140° for 3 hours) and 50 g. of powdered phosphorus pentachloride (1) in a 500 ml. round-bottomed flask furnished with a reflux condenser; heat the mixture in an oil bath at 170–180° for 12–15 hours. Every 3 hours remove the flask from the oil bath, allow to cool for 15–20 minutes, stopper and shake thoroughly until the mass becomes pasty. At the end of the heating period, allow the reaction mixture to cool. Pour on to 1 kilo of crushed ice. Extract the crude benzenesulphonyl chloride with 150 ml. of carbon tetrachloride and the aqueous layer with 75 ml. of the same solvent. Remove the solvent under atmospheric pressure and proceed as in *Method 1.* The yield is about 170 g., but depends upon the purity of the original sodium benzenesulphonate.

Note.

(1) Alternatively a mixture of 90 g. of sodium benzenesulphonate and 60 g. (36 ml.) of phosphorus oxychloride may be used. The experimental procedure is identical with that for phosphorus pentachloride, but the yield is slightly better.

IV,207. *p*-TOLUENESULPHONYL CHLORIDE

Method 1. In a 750 ml. three-necked flask or wide-mouthed glass bottle, equipped with a dropping funnel, a mechanical stirrer (Fig. *II*, *7*, 10) a thermometer (with bulb within 2 cm. of the bottom) and an outlet tube leading to a gas absorption device (Fig. *II*, *8*, 1, *c*), place 400 g. (228 ml.) of chlorosulphonic acid and cool to 0° in a freezing mixture of ice and

salt. Introduce 100 g. (115 ml.) of pure dry toluene from the dropping funnel dropwise at such a rate that the temperature of the well-stirred mixture does not rise above 5°. When all the toluene has been added (about 3 hours), stir the reaction mixture for 4 hours, and then allow to stand overnight in the freezing mixture. Pour the liquid on to 1 kilo of crushed ice, separate the aqueous solution from the oily layer (mixture of *o*- and *p*-toluenesulphonyl chlorides) and wash the latter several times by decantation with cold water. To separate the *ortho* and *para* isomers, cool the oil at — 10° to — 20° (*e.g.*, with ice and calcium chloride) for several hours; the almost pure *p*-toluenesulphonyl chloride will crystallise out. Filter at the pump upon a sintered glass funnel. The crude *p*-toluenesulphonyl chloride (30 g.) may be purified by recrystallisation from light petroleum (b.p. 40–60°) and then melts at 69°. The filtrate consists largely of **o-toluenesulphonyl chloride**: it may be obtained pure by dissolving it in carbon tetrachloride, removing the solvent and fractionating under reduced pressure; it is an oil, b.p. 126°/10 mm. The yield is about 120 g.

Method 2. The procedure described under *Benzenesulphonyl Chloride, Method 2* (Section **IV,206**) may be used with suitable adjustment for the difference in molecular weights between sodium *p*-toluenesulphonate (Section **IV,30**) and sodium benzenesulphonate. When the reaction product is poured on to ice, the *p*-toluenesulphonyl chloride separates as a solid. This is filtered with suction; it may be recrystallised from light petroleum (b.p. 40–60°) and then melts at 69°.

IV,208. DICHLORAMINE-T AND CHLORAMINE-T

***p*-Toluenesulphonamide.** Grind together 10 g. of *p*-toluenesulphonyl chloride (Section **IV,207**) and 20 g. of ammonium carbonate in a mortar until a fine uniform powder is obtained. Heat the mixture in an evaporating dish on a water bath for 1–2 hours and stir the mixture frequently with a glass rod. Allow to cool and extract with a little cold water to remove the excess of ammonium salts. Recrystallise the crude *p*-toluenesulphonamide from boiling water (200–250 ml.), and dry the colourless crystals at 100°. The yield of pure product, m.p. 138°, is 9 g.

Alternatively, grind 10 g. of *p*-toluenesulphonyl chloride to a fine powder and add it to 30 ml. of concentrated ammonia solution (sp. gr. 0·88). Heat the mixture to boiling (*FUME CUPBOARD*) and cool. Filter and recrystallise the *p*-toluenesulphonamide from boiling water (add 1 g. of decolourising carbon, if necessary). The yield of pure product, m.p. 138°, is almost theoretical.

Dichloramine-T (*p*-toluenesulphondichloramide). Prepare about 200 ml. of a saturated solution of calcium hypochlorite by grinding a fresh sample of bleaching powder with water and filtering with slight suction. Dissolve 5 g. of *p*-toluenesulphonamide in as small a volume of the calcium hypochlorite solution as possible (about 150 ml.) and filter the solution if necessary. Cool in ice, and add about 50 ml. of a mixture of equal volumes of glacial acetic acid and water *slowly* and with stirring until precipitation is complete. The dichloramine-T separates out first as a fine emulsion, which rapidly forms colourless crystals. Filter the latter

at the pump, wash with a little cold water, drain and dry immediately either between pads of filter paper or upon a porous tile. The yield is 6·5 g., m.p. 81°. Upon recrystallisation from light petroleum (b.p. 60–80°) or from chloroform - light petroleum, perfectly pure dichloramine-T, m.p. 83°, is obtained with negligible loss.

Chloramine-T (sodium *N*-chloro-*p*-toluenesulphonamide). For this preparation use dichloramine-T which has been prepared as above and thoroughly drained but not necessarily dried. Heat 45 ml. of 10 per cent. sodium hydroxide solution in a beaker over a wire gauze to a temperature of about 80°, and add the dichloramine-T in small quantities, stirring the mixture gently after each addition until a clear solution is obtained. When the addition is complete, filter the hot solution if turbid, and then allow it to cool spontaneously. Filter the crystals with suction, wash with a little brine solution, and dry upon filter paper or in a desiccator over anhydrous calcium chloride. The resulting chloramine-T weighs 8 g. and is almost pure. It may be recrystallised, if desired, from twice its weight of hot water.

Chloramine-T is a salt and has no definite m.p. : upon heating it loses water of crystallisation and decomposes violently at 175–180°.

IV,209. SACCHARIN

o-Toluenesulphonamide. Place 20 g. of *o*-toluenesulphonyl chloride (Section **IV,207**) in a large evaporating dish mounted on a water bath. Add powdered ammonium carbonate cautiously with stirring until the mass is quite hard and solid and the unpleasant odour of the sulphonyl chloride has disappeared. Allow to cool, and extract with cold water to remove the excess of ammonium carbonate. Recrystallise the crude *o*-toluenesulphonamide first from hot water (add a little decolourising carbon if it is dark in colour) and then from alcohol. The yield of pure product, m.p. 154°, is 16 g.

Oxidation of *o*-toluenesulphonamide to saccharin. In a 600 ml. beaker, mounted on a wire gauze and provided with a mechanical stirrer, place 12 g. of *o*-toluenesulphonamide, 200 ml. of water and 3 g. of pure sodium hydroxide. Stir the mixture and warm to 34–40° until nearly all has passed into solution (about 30 minutes). Introduce 19 g. of finely-powdered potassium permanganate in small portions at intervals of 10–15 minutes into the well-stirred liquid. At first the permanganate is rapidly reduced, but towards the end of the reaction complete reduction of the permanganate is not attained. The addition occupies 4 hours. Continue the stirring for a further 2–3 hours, and then allow the mixture to stand overnight. Filter off the precipitated manganese dioxide at the pump and decolourise the filtrate by the addition of a little sodium bisulphite solution. Exactly neutralise the solution with dilute hydrochloric acid (use methyl orange or methyl red as external indicator). Filter off any *o*-sulphonamidobenzoic acid (and/or *o*-toluenesulphonamide) which separates at this point. Treat the filtrate with concentrated hydrochloric acid until the precipitation of the saccharin is complete. Cool, filter at the pump and wash with a little cold water. Recrystallise from hot water. The yield of pure saccharin, m.p. 228°, is 7·5 g.

IV,210. *n*-BUTYL *p*-TOLUENESULPHONATE

Equip a 1 litre three-necked flask with a separatory funnel, a mechanical stirrer and a thermometer, the bulb of which reaches within 2 cm. of the bottom. Place 72 g. (89 ml.) of *n*-butyl alcohol and 105 g. of *p*-toluenesulphonyl chloride (Section **IV,207**) (1) in the flask and 160 ml. of 20 per cent. (5*N*) sodium hydroxide solution in the separatory funnel; immerse the flask in a bath of cold water. Run in the sodium hydroxide solution, with stirring, at such a rate that the temperature does not rise above 15° (3–4 hours). Now add another portion of 105 g. of *p*-toluenesulphonyl chloride, and introduce 160 ml. of 5*N* sodium hydroxide solution slowly, keeping the temperature below 15°. Continue the stirring for 4 hours longer. Separate the oily layer and treat it with enough benzene or light petroleum (b.p. 60–80°) to cause it to float on water; then wash it well with 25 ml. of 10 per cent. sodium hydroxide solution, and dry by allowing it to stand over 10 g. of anhydrous potassium carbonate. Filter and distil off the solvent using a 250 ml. Claisen flask (compare Fig. *II*, *13*, 4). Distil the residual ester under reduced pressure (2) (oil pump) and collect the *n*-butyl *p*-toluenesulphonate at 132–133°/3 mm. The yield is 130 g.

Notes.

(1) Commercial *p*-toluenesulphonyl chloride may be purified by dissolving it in benzene, washing with 5 per cent. sodium hydroxide solution, drying by shaking with anhydrous potassium carbonate or magnesium sulphate, and distilling under reduced pressure: b.p. 146°/15 mm.; m.p. 69°. The distillation should be completed without interruption.

(2) It is best to distil under greatly reduced pressure; slight decomposition occurs even at 10 mm. pressure (b.p. 170–171°/10 mm.).

Cognate Preparations

Methyl *p*-toluenesulphonate. This, and other alkyl esters, may be prepared in a somewhat similar manner to the *n*-butyl ester with good results. Use 500 g. (632 ml.) of methyl alcohol contained in a 1 litre three-necked or bolt-head flask. Add 500 g. of powdered pure *p*-toluenesulphonyl chloride with mechanical stirring. Add from a separatory funnel 420 g. of 25 per cent. sodium hydroxide solution drop by drop: maintain the temperature of the mixture at 23–27°. When all the alkali has been introduced, test the mixture with litmus; if it is not alkaline, add more alkali until the mixture is neutral. Allow to stand for several hours: the lower layer is the ester and the upper one consists of alcohol. Separate the ester, wash it with water, then with 4 per cent. sodium carbonate solution and finally with water. Dry over a little anhydrous magnesium sulphate, and distil under reduced pressure. Collect the methyl *p*-toluenesulphonate at 161°/10 mm.; this solidifies on cooling and melts at 28°. The yield is 440 g.

***n*-Dodecyl-*p*-toluenesulphonate** (*pyridine method*). In a 500 ml. three-necked flask, equipped with a stirrer and thermometer, place 46·5 g. of *n*-dodecyl alcohol (lauryl alcohol), m.p. 22–23°, and 79 g. (81 ml.) of dry pyridine. Surround the flask by a bath sufficiently cold to lower the temperature of the mixture to 10°. Add 52·5 g. of *p*-toluenesulphonyl

chloride in portions during 20 minutes, or at such a rate that the temperature does not rise above 20°. Stir the mixture for 3 hours at a temperature below 20°, then dilute with 150 ml. of concentrated hydrochloric acid in 500 ml. of ice water. Collect the ester on a chilled Buchner funnel and suck as dry as possible. Transfer the solid to a 400 ml. beaker, add 150 ml. of methyl alcohol, and warm the mixture on a steam bath until the ester melts. Cool in a freezing mixture whilst stirring vigorously; the ester separates in a finely divided state. Collect it on a chilled funnel and allow to dry in the air, preferably below 20°. The yield of ester, m.p. 24–25°, is 78 g. Recrystallise by dissolving in 100 ml. of light petroleum, b.p. 40–60°, drying the solution over anhydrous magnesium sulphate to remove traces of water, and cool to 0°. Collect the pure *n*-dodecyl-*p*-toluenesulphonate, m.p. 29–30°, in a chilled funnel.

The pyridine procedure may be applied to the preparation of other esters; they are isolated by ether extraction. The yields are generally better than by the sodium hydroxide method.

IV,211. SODIUM *p*-TOLUENESULPHINATE

In a 3 litre wide-mouthed glass jar place 600 ml. of water: provide a stainless steel mechanical stirrer (compare Fig. *II*, 7, 6) and a wide tube for passing steam directly into the liquid. Pass dry steam into the water until the temperature reaches 70°; shut off the steam, and add 80 g. of zinc powder (90–100 per cent. pure). Stir the mixture and add 100 g. of finely-powdered *p*-toluenesulphonyl chloride by means of a porcelain spoon during about 10 minutes; the temperature rises to about 80°. Stir for a further 10 minutes and then pass steam into the mixture until the temperature is 90°. Shut off the steam, and add 50 ml. of 12*N* sodium hydroxide solution, followed by finely-powdered sodium carbonate in 10 g. portions until the mixture is strongly alkaline. Considerable frothing occurs. Filter at the pump; the filtrate has a volume of about 900 ml. Transfer the residue to a 1 litre battery jar (or glass jar), add 150 ml. of water and stir with the metal stirrer. Pass in steam until the mixture commences to froth excessively, shut off the steam and continue the stirring for 10 minutes. Filter with suction, and add the filtrate to the main solution in a large evaporating dish. Evaporate the solution to a volume of about 200 ml. or until a considerable crust forms on the edges; cool in ice water. Filter at the pump and dry the crystals upon filter or drying paper until efflorescence just commences, then place in a tightly stoppered bottle. The yield of sodium *p*-toluenesulphinate (p-$CH_3C_6H_4SO_2Na,2H_2O$) is 70 g.

To prepare the free sulphinic acid, dissolve some of the sodium salt in cold water and cautiously acidify with hydrochloric acid; avoid an excess of mineral acid since it dissolves the sulphinic acid to a certain extent. The resulting *p*-toluenesulphinic acid is difficult to dry without partial conversion into the sulphonic acid and thiolsulphonic ester ($3RSO_2H \xrightarrow{H_2O} RSO_3H + RSO_2SR$); fairly satisfactory results may be obtained by placing the sheets of filter paper in an office ledger press and exerting pressure. The m.p. is 85°.

IV,212. THIOPHENOL

This preparation must be carried out in the fume cupboard since thiophenol has an extremely unpleasant and repulsive odour ; the substance should not be allowed to come into contact with the hands or clothing since the odour clings for days.

Place 720 g. of crushed ice and 240 g. (130 ml.) of concentrated sulphuric acid in a 1500 ml. round-bottomed or bolt-head flask equipped with a mechanical stirrer. Immerse the flask in a freezing mixture of ice and salt and maintain the temperature at — 5° to 0° throughout the preparation. Start the stirrer and add 60 g. of benzenesulphonyl chloride (Section **IV,206**) in small portions over a period of half an hour. (Benzenesulphonyl chloride melts at 14° and hence it must be added slowly and with vigorous stirring in order that it may be as finely-divided as possible for maximum reactivity in the subsequent reduction.) Then add 120 g. of zinc powder (90–100 per cent. pure) as rapidly as possible without the temperature rising above 0° (about 30 minutes). Stir the mixture for a further 1·5 hours. Fit a two-holed stopper through which the mechanical stirrer (Fig. *II*, 7, 10) and a double surface reflux condenser are passed ; remove the ice-salt bath and allow the reaction mixture to warm up spontaneously, whilst continuing the stirring. Within 5 minutes or so, a rather violent reaction with the evolution of much hydrogen sets in ; it may be necessary to cool the flask momentarily in a stream of water. When the energetic reaction has subsided, warm the mixture, with vigorous stirring, over a ring burner until the solution becomes clear (4–6 hours). Steam distil the thiophenol until organic material ceases to pass over. Separate the organic layer from the distillate, dry it with anhydrous calcium chloride or magnesium sulphate, and distil. Collect the thiophenol at 166–169° ; the yield is 34 g.

Cognate Preparation

Thio-*p*-cresol (*p*-tolyl mercaptan), *p*-$CH_3C_6H_4SH$. This compound may be similarly prepared from *p*-toluenesulphonyl chloride (Section **IV,207**). The thio-*p*-cresol crystallises in the steam distillate and is collected and dried ; m.p. 43°. The b.p. under normal pressure is 194–195°.