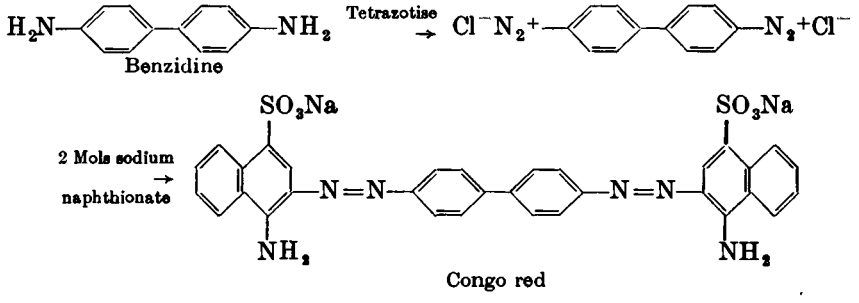
CHAPTER VIII

DYESTUFFS, INDICATORS AND RELATED COMPOUNDS

THE procedures for the preparation of a number of azo dyestuffs are described in Sections **IV,76–IV,82**; these include the indicators methyl orange and methyl red. Experimental details for the preparation of other typical dyestuffs and indicators are given in the following pages.

VIII,1. CONGO RED

This dyestuff is prepared by tetrazotising benzidine and coupling with sodium naphthionate:



Congo red

Dissolve 9·2 g. of benzidine (Section **IV,88**) in a hot mixture of 24 ml. of concentrated hydrochloric acid and 150–200 ml. of water. Cool in an ice bath to 0–5° and diazotise ("tetrazotise") by the addition of a solution of 6·9 g. of sodium nitrite (100 per cent.; if the purity is lower, the weight must be adjusted accordingly) in 50 ml. of water within 1 minute. Leave the "tetrazo" solution in ice for 5 minutes and then add it to a solution of 32 g. of sodium naphthionate (Section **IV,56**) and 40 g. of crystallised sodium acetate in 500 ml. of water. Stir well and allow the mixture to stand for 1 hour. When a sample of the liquid, upon warming with hydrochloric acid, no longer evolves nitrogen, dissolve the blue-black precipitate of the dye-acid by the gradual addition of sodium carbonate (*ca.* 20 g.), followed by stirring and warming until the temperature reaches 80°. By this time the dye should be in solution as the red sodium salt (Congo red). Filter, and just saturate (avoid an excess) the hot solution with sodium chloride and allow to cool spontaneously to room temperature. Cool in ice, filter off the Congo red at the pump (1), wash it with saturated sodium chloride solution and dry in the air. The yield is 60 g.

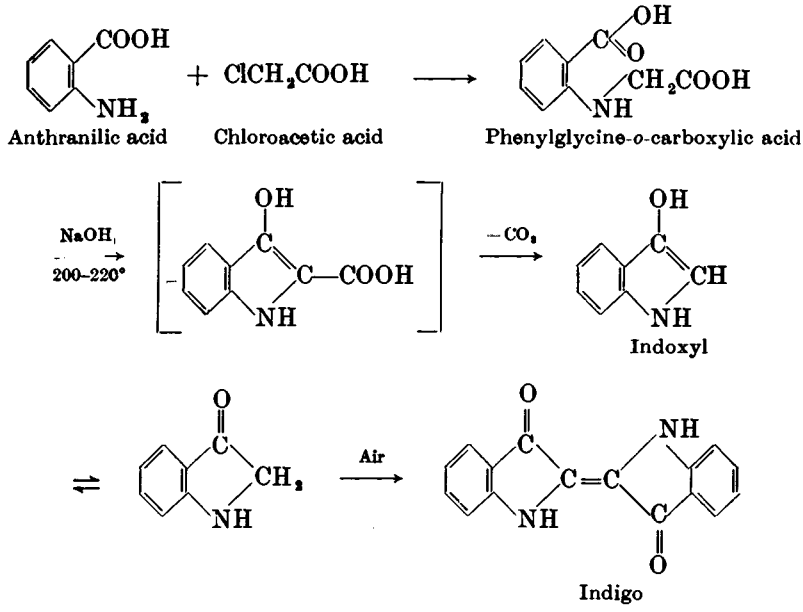
Note.

(1) If filtration is slow, the following procedure may be used. Place the fine suspension in a large evaporating dish and evaporate to dryness on a water bath. Dissolve the resulting sticky mass in the minimum volume of dilute alcohol (1 volume of water : 3 volumes of methylated spirit; about 200–250 ml.) and allow

to cool. Filter the Congo red, which is now granular, with gentle suction; and dry upon filter paper in the air. The product may contain an appreciable quantity of salt; this may be largely removed by repeating the recrystallisation from dilute alcohol.

VIII,2. INDIGO

Indigo may be prepared by the following series of reactions :—



Phenylglycine-*o*-carboxylic acid. In a 750 ml. round-bottomed flask, fitted with a reflux condenser, place 14 g. of anthranilic acid (Section **IV,170**), 10 g. of chloroacetic acid, 20 g. of anhydrous sodium carbonate and 200 ml. of water. Reflux the mixture for 3 hours, then pour into a beaker, cool, render slightly acid with concentrated hydrochloric acid, and allow to stand overnight. Filter off the crude acid and wash it with water. Recrystallise from hot water with the aid of a little decolourising carbon, and dry the acid at 100°. The yield of phenylglycine-*o*-carboxylic acid, m.p. 208°, is 12 g.

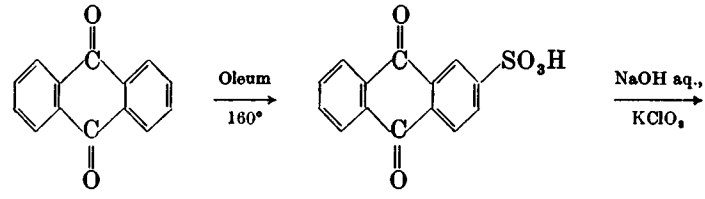
Indigo. Place a mixture of 10 g. of phenylglycine-*o*-carboxylic acid, 30 g. of sodium hydroxide pellets and 10 ml. of water in a large nickel crucible or basin. Heat the mixture to 200–210° and stir well with a thermometer protected by a copper tube (Section **IV,101**). The mass fuses and the mixture gradually assumes an orange colour. Allow the crucible to cool somewhat, and dissolve the melt in 200 ml. of water. This solution oxidises upon shaking in contact with air forming a precipitate of indigo. The conversion into indigo may be more rapidly effected (1) by acidifying with hydrochloric acid and oxidising with ferric chloride solution until no further precipitate of the dyestuff is produced. Filter off the indigo at the pump, wash it with hot water and dry. The yield is 7 g.

Note.

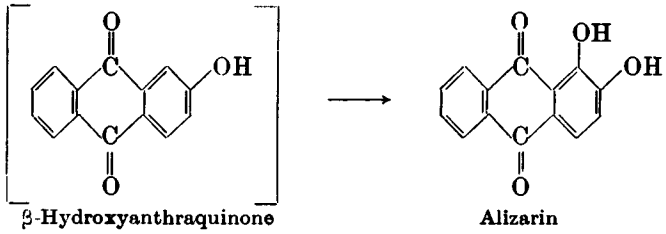
(1) The filtered solution of indoxyl may also be oxidised by placing it in a filter flask and drawing air through the solution by means of a water pump until a drop of the aqueous suspension of indigo when placed upon filter paper produces a sharply defined ring of precipitated indigo, outside which the liquid no longer becomes blue upon exposure to air.

VIII,3. ALIZARIN

Upon heating anthraquinone with fuming sulphuric acid at 160° for about 1 hour, the main product is anthraquinone-β-sulphonic acid, which is isolated as the sparingly soluble sodium salt. The latter when heated under pressure with sodium hydroxide solution and an oxidising agent (sodium or potassium chlorate) yields first the corresponding hydroxy compound : further hydroxylation occurs in the α-position through oxidation by the chlorate and 1 : 2-dihydroxyanthraquinone (alizarin) is formed.



Anthraquinone — Anthraquinone-β-sulphonic acid



β-Hydroxyanthraquinone — Alizarin

Sodium anthraquinone-β-sulphonate (" **silver salt** "). Place 50 g. of fuming sulphuric acid (40–50 per cent. SO_3) * in a 250 or 500 ml. round-bottomed flask and add 50 g. of dry, finely-powdered anthraquinone (Section **IV,145**). Fit an air condenser to the flask and heat the mixture slowly in an oil bath, with occasional shaking, so that at the end of 1 hour the temperature has reached 160°. Allow to cool and pour the warm mixture carefully into a 2 litre beaker containing 500 g. of crushed ice. Boil for about 15 minutes and filter off the unchanged anthraquinone at the pump. Neutralise the hot filtrate with sodium hydroxide and allow to cool, when the greater part of the sodium anthraquinone-β-sulphonate separates as silvery glistening plates (" silver salt "). Filter these with suction and dry upon filter paper or upon a porous plate. A second crop of crystals may be isolated by concentration of the filtrate to half the original volume. The yield is 40–45 g.

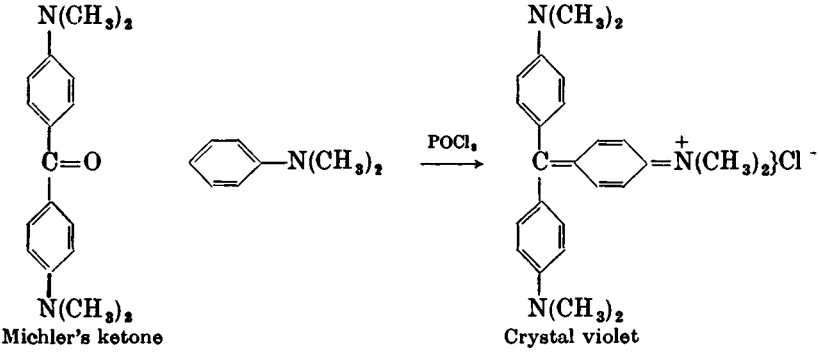
Alizarin. Dissolve successively in 75 ml. of water 6 g. of potassium chlorate, 20 g. of sodium anthraquinone-β-sulphonate and 75 g. of sodium hydroxide. Transfer the mixture to a 500 ml. autoclave (compare Section **VI,4**) and heat for 20 hours at 170°. After cooling, scrape out

* The solid acid is removed from the stock bottle by cautiously melting it in an air bath.

the violet coloured mass and extract it three or four times with 100 ml. portions of boiling water. Acidify the filtered extract with hydrochloric acid. When cold, filter the orange precipitate of alizarin at the pump, wash it thoroughly with cold water, and dry at 100°. The yield of alizarin is 14 g. It may be purified by recrystallisation from glacial acetic acid or by sublimation. The pure compound has m.p. 289°.

VIII,4. CRYSTAL VIOLET

Crystal violet is an example of a triphenylmethane dye. Its preparation in the laboratory may be illustrated by the condensation of 4 : 4′-tetramethyldiaminobenzophenone (Michler's ketone) and dimethylaniline in the presence of phosphorus oxychloride :



Michler's ketone — Crystal violet

Michler's ketone is prepared industrially by the interaction of phosgene ($COCl_2$) and dimethylaniline.

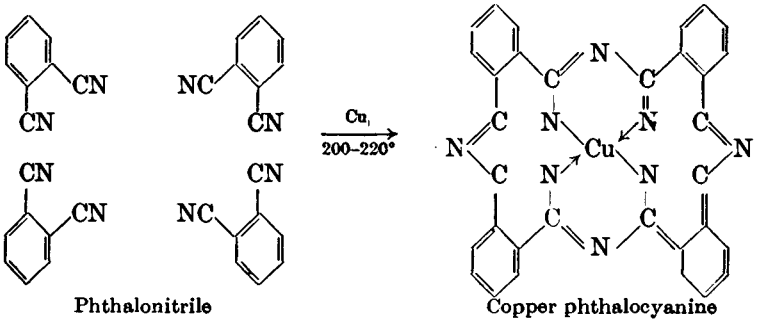
In a 1 litre round-bottomed flask, provided with an air condenser, place a mixture of 25 g. (26 ml.) of pure dimethylaniline, 10 g. of Michler's ketone (4 : 4′-tetramethyldiaminobenzophenone) and 10 g. (6 ml.) of phosphorus oxychloride. Heat on a boiling water bath for 5 hours. Add about 150 ml. of water and sufficient sodium hydroxide solution to render the solution alkaline. Calculate the quantity of sodium hydroxide required upon the basis of the hydrolysis product derived from the phosphorus oxychloride :

$$POCl_3 + 3H_2O \longrightarrow H_3PO_4 + 3HCl$$

Pass steam into the mixture (Fig. *II*, *40*, 1) until no more drops of unattacked dimethylaniline pass over into the receiver. Allow to cool and filter the reddish precipitate of the " colour base " at the pump and wash it with water. Transfer the precipitate to a large beaker and boil it with a mixture of 5 ml. of concentrated hydrochloric acid and 1 litre of water. Filter the hot solution and set the filtrate aside for crystallisation to take place. Treat the residue with successive portions of fresh dilute hydrochloric acid until it has almost entirely dissolved. On cooling and standing, the crystal violet separates in green crystals ; filter these with suction. Treat the combined filtrates, whilst stirring, with finely-powdered sodium chloride until precipitation is complete and the liquid is just saturated ; collect the precipitate in a filter. The crystal violet may be recrystallised from a little water, and dried upon filter paper in the air. The yield is 12 g.

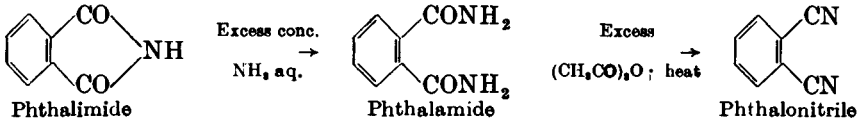
VIII,5. COPPER PHTHALOCYANINE (MONASTRAL BLUE)

The pure pigment may be obtained by heating phthalonitrile (4 mols) and copper bronze (1 atom) at 200–220° :



Phthalonitrile — Copper phthalocyanine

Phthalonitrile may be prepared by the following series of reactions from phthalimide :—



Phthalimide — Phthalamide — Phthalonitrile

Phthalamide. Mix 200 g. of phthalimide (Section **IV,169**) with 600 ml. of concentrated ammonia solution in a 1 litre beaker and stir mechanically for 24 hours. Filter off the micro-crystalline cake of phthalamide and dry at 100°. The yield is 200 g., m.p. 220° (decomp.).

Phthalonitrile. In a 1 litre round-bottomed flask, provided with a reflux condenser, place 100 g. of phthalamide and 350 ml. of acetic anhydride. Reflux for 5–6 hours. Add the reaction product whilst still hot cautiously to 700 ml. of boiling water ; this decomposes the excess of acetic anhydride. Cool in ice, and then render the reaction mixture alkaline with sodium hydroxide solution. Filter off the precipitated crystals at the pump, wash with water, and dry at 100°. The yield of the crude nitrile is 70 g. After one or two recrystallisations from benzene, the m.p. should be 141°—that of pure phthalonitrile. It is usually best to distil the crude nitrile under reduced pressure (Figs. *II*, *19*, 3–4) : the distillate has m.p. 137–138°, and the m.p. is raised to 141° after one recrystallisation from benzene.

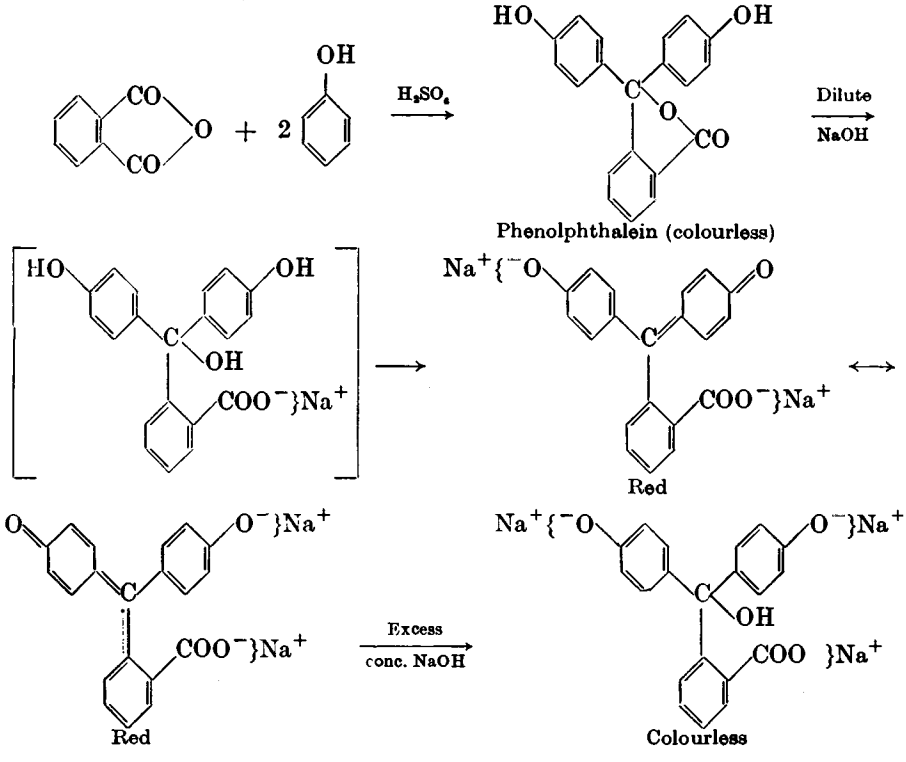
Copper phthalocyanine (Monastral blue). In a wide glass tube place 12·8 of phthalonitrile and 1·59 g. of copper bronze. Heat, with stirring by means of a thermometer, in an oil bath. A green colour first forms at 190° and the mass becomes pasty at 220°. Maintain the bath temperature at 220° for 15 minutes : the internal temperature rises rapidly and at times exceeds that of the bath by 40–50° and stirring becomes impossible. Allow the mass to cool slightly and grind it with alcohol. Boil the finely-ground product repeatedly with alcohol until the washings are colourless and contain no phthalonitrile ; then dry at 100°. The yield of crude copper phthalocyanine, which contains a little uncombined copper bronze, is 10 g. To remove the copper, dust 10 g. of the finely-powdered, crude product into 100 g. (55 ml.) of concentrated sulphuric acid with mechanical stirring. Allow to stand for 1 hour,

filter the solution through a sintered glass funnel, wash with concentrated sulphuric acid, and pour the combined filtrate and washings in a thin stream and with stirring on to 100 g. of finely-crushed ice. Allow the flocculent blue precipitate to coalesce for 2–3 hours, filter at the pump and wash with boiling water. Finally, boil the pigment with alcohol, filter and dry at 100°. The recovery of pure pigment is about 90 per cent.

The reaction between phthalonitrile and copper also takes place readily in boiling quinoline or α-methylnaphthalene : the pigment is precipitated as fast as it is formed as a crystalline product. It is separated from the excess of copper by shaking with alcohol, when the metal sinks and the pigment, which remains in suspension, can be poured off ; the process may be repeated to give the pure compound.

VIII,6. PHENOLPHTHALEIN

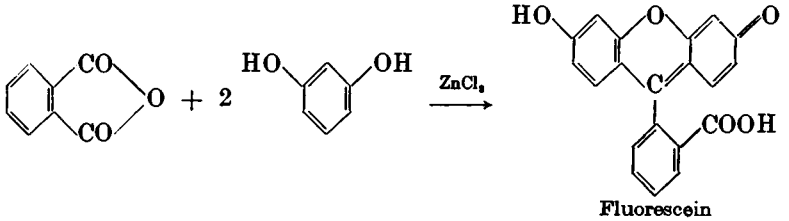
Phenol condenses with phthalic anhydride in the presence of concentrated sulphuric acid or anhydrous zinc chloride to yield the colourless phenolphthalein as the main product. When dilute caustic alkali is added to an alcoholic solution of phenolphthalein, an intense red colouration is produced. The alkali opens the lactone ring in phenolphthalein and forms a salt at one phenolic group. The reaction may be represented in steps, with the formation of a hypothetical unstable intermediate that changes to a coloured ion. The colour is probably due to resonance which places the negative charge on either of the two equivalent oxygen atoms. With excess of concentrated caustic alkali, the first red colour disappears ; this is due to the production of the carbinol and attendant salt formation, rendering resonance impossible. The various reactions may be represented as follows :



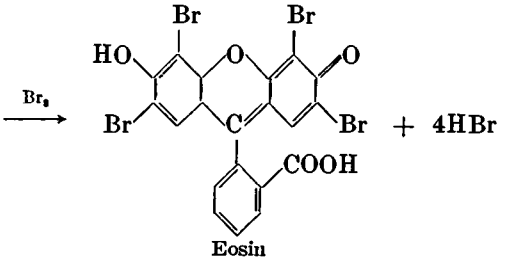
To a mixture of pure phenol and 25 g. of phthalic anhydride contained in a 250 ml. round-bottomed flask, add 20 g. (11 ml.) of concentrated sulphuric acid. Heat the flask in an oil bath at 115–120° for 9 hours. Then pour the reaction mixture whilst still hot into 1 litre of hot water contained in a 2 litre beaker, and boil until the odour of phenol has disappeared; add water to replace that lost by evaporation. When cold, filter the yellow, granular precipitate at the pump and wash it with water. Dissolve the solid in dilute sodium hydroxide solution, filter from the undissolved residue (the by-products of the reaction). Acidify the filtrate with dilute acetic acid and a few drops of dilute hydrochloric acid, and allow to stand overnight. The crude phenolphthalein separates as a pale yellow, sandy powder; filter and dry. Purify the crude product by dissolving it in six times its weight of absolute alcohol, add decolourising carbon and reflux on a water bath for 1 hour. Filter the hot solution through a preheated Buchner funnel, wash the residue with 2 parts by weight of boiling absolute alcohol and concentrate the combined filtrate and washings to two-thirds of its bulk on a water bath. Dilute the cooled solution with eight times the weight of cold water (it will become turbid), stir the mixture well and, after standing for a few seconds, filter through a wet filter to remove the resinous oil which separates. Heat the filtrate on a water bath to evaporate most of the alcohol; the turbidity disappears and the phenolphthalein separates out in the form of a white powder. Filter this off and dry. The yield of pure phenolphthalein, m.p. 256–258°, is 18 g.

VIII,7. FLUORESCEIN AND EOSIN

Fluorescein is obtained by condensing phthalic anhydride (1 mol) with resorcinol (2 mols) in the presence of anhydrous zinc chloride. The tetrabromo derivative, readily prepared by the addition of the calculated quantity of bromine, is eosin.



Fluorescein



Eosin

Dibromofluorescein is prepared by treating fluorescein in 80 per cent. acetic acid solution with the theoretical quantity of bromine.

Fluorescein. Grind together in a mortar 15 g. of phthalic anhydride and 22 g. of resorcinol, and transfer the mixture to a 350 or 500 ml. conical flask. Support the flask in an oil bath and heat to 180° (internal temperature). While the oil bath is being heated, weigh out rapidly 7 g. of anhydrous zinc chloride, immediately grind it to a coarse powder in a mortar and place it in a stoppered tube. (The zinc chloride should not be exposed to the air longer than is absolutely necessary; if the contents of the stock bottle appear moist, dry a 10–15 g. portion by fusing it in a porcelain dish.) Add the zinc chloride in small portions, with stirring by means of a thermometer, to the mixture in the flask. Continue the heating at 180° with stirring at intervals of 2–3 minutes until the solution becomes so viscous that further stirring is not practicable (45–90 minutes). The resulting dark red mass consists largely of a mixture of fluorescein and zinc chloride together with basic zinc salts. Allow the oil bath to cool to about 90°, and add 200 ml. of water and 10 ml. of concentrated hydrochloric acid to the reaction mixture, and then raise the temperature of the oil bath until the water boils. Stir the mixture from time to time when the temperature of the oil rises above 110°: great care should be taken to prevent the dilute acid from boiling over. Continue the boiling until the reaction mixture has disintegrated and all the zinc salts have dissolved. Filter the insoluble residue of fluorescein at the pump, grind it with water in a mortar, and filter again. Dry at 100°. The yield is 30 g. This product is pure enough for the preparation of eosin.

The fluorescein may be purified by dissolving it in dilute sodium hydroxide solution, filtering if necessary, precipitating with dilute hydrochloric acid (1 : 1), filtering, washing and drying.

Eosin (Tetrabromofluorescein). Place 16·5 g. of powdered fluorescein and 80 ml. of rectified (or methylated) spirit in a 250 ml. flask. Support a small dropping funnel, containing 36 g. (12 ml.) of bromine, above the flask: make sure that the stopcock of the funnel is well lubricated before charging the latter with bromine. Add the bromine dropwise during about 20 minutes. When half the bromine has been introduced, and the fluorescein has been converted into dibromofluorescein, all the solid material disappears temporarily since the dibromo derivative is soluble in alcohol: with further addition of bromine the tetrabromofluorescein (sparingly soluble in alcohol) separates out. Allow the reaction mixture to stand for 2 hours, filter off the eosin at the pump, wash it with alcohol, and dry at 100°. The yield of eosin (orange-coloured powder) is 25 g.

Sodium salt of eosin. Grind together in a mortar 12 g. of eosin with 2 g. of anhydrous sodium carbonate. Transfer the mixture to a 250 ml. conical flask, moisten it with 10 ml. of rectified spirit, add 10 ml. of water and warm on a water bath, with stirring, until the evolution of carbon dioxide ceases. Add 50 ml. of ethyl alcohol, heat to boiling, and filter the hot solution through a fluted filter paper (supported in a short-stemmed funnel) into a beaker, and allow to stand overnight. Filter off the brownish-red crystals of sodium eosin, wash with a little alcohol, and dry. The yield is 10 g.

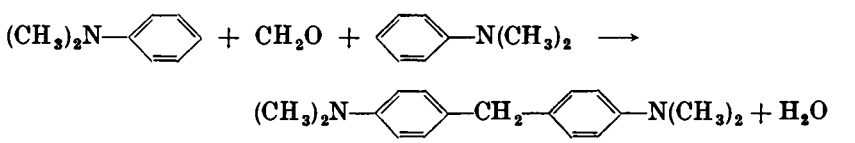
Dibromofluorescein. To a suspension of 33 g. of fluorescein in 125 ml. of 80 per cent. acetic acid, warmed to 80° and stirred mechanically,

add a solution of 32 g. (10 ml.) of bromine in 100 ml. of 80 per cent. acetic acid. Continue the stirring for 2 hours at 80°, filter at the pump, and wash with alcohol, followed by ether. The product weighs 50 g., and is almost pure dibromofluorescein hydrobromide. Wash thoroughly with hot water, and thus obtain pure dibromofluorescein, m.p. 285°. The compound is a deep red, micro-crystalline powder and crystallises from 30 per cent. alcohol in red plates.

It may be converted into dibromofluorescein diacetate as follows. Reflux a mixture of 10 g. of dibromofluorescein, 40 ml. of redistilled acetic anhydride and 1 drop of concentrated sulphuric acid for 1 hour, pour into water, filter, wash, and dry: the resulting diacetate (95 per cent. yield) has m.p. 210°. Upon recrystallisation from acetic anhydride or nitrobenzene, the pure diacetate (colourless or pale yellow plates), m.p. 211°, is obtained. Hydrolysis with alcoholic sulphuric acid gives a quantitative yield of pure dibromofluorescein, m.p. 285°.

VIII,8. *pp'*-TETRAMETHYLDIAMINODIPHENYLMETHANE

This compound, also termed "**tetramethyl base**" is prepared by the condensation of dimethylaniline (2 mols) with formaldehyde (1·2 mols) in the presence of a little sulphanilic acid:

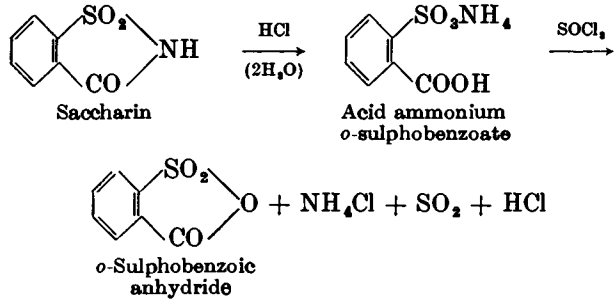


In a 500 ml. three-necked flask, fitted with a reflux condenser and mechanical stirrer, place 121 g. (126·5 ml.) of dimethylaniline, 45 g. of 40 per cent. formaldehyde solution and 0·5 g. of sulphanilic acid. Heat the mixture under reflux with vigorous stirring for 8 hours. No visible change in the reaction mixture occurs. After 8 hours, remove a test portion of the pale yellow emulsion with a pipette or dropper and allow it to cool. The oil should solidify completely and upon boiling it should not smell appreciably of dimethylaniline; if this is not the case, heat for a longer period. When the reaction is complete, steam distil (Fig. *II*, *41*, 1) the mixture until no more formaldehyde and dimethylaniline passes over; only a few drops of dimethylaniline should distil. As soon as the distillate is free from dimethylaniline, pour the residue into excess of cold water when the base immediately solidifies. Decant the water and wash the crystalline solid thoroughly with water to remove the residual formaldehyde. Finally melt the solid under water and allow it to solidify. A hard yellowish-white crystalline cake of crude base, m.p. 80–90°, is obtained in almost quantitative yield. Recrystallise from 250 ml. of alcohol; the recovery of pure *pp'*-tetramethyldiaminodiphenylmethane, m.p. 89–90°, is about 90 per cent.

VIII,9. *o*-SULPHOBENZOIC ANHYDRIDE

Hydrolysis of saccharin (o-sulphobenzoic imide) (Section IV, 209) with dilute hydrochloric acid yields acid ammonium *o*-sulphobenzoate, which upon

heating with thionyl chloride in benzene solution affords o-sulphobenzoic anhydride :



Saccharin — Acid ammonium o-sulphobenzoate — o-Sulphobenzoic anhydride

Acid ammonium o-sulphobenzoate. In a 1 litre three-necked flask, fitted with a mechanical stirrer and a reflux condenser, place 19 g. of *o*-sulphobenzoic imide (" saccharin insoluble "), 17 ml. of concentrated hydrochloric acid and 60 ml. of distilled water. Boil the mixture over a free flame with continual stirring until all the solid dissolves (2·5–3 hours); some foaming may occur during the first few minutes of boiling. Then add another 19 g. of *o*-sulphobenzoic imide and heat the mixture again as before until a clear solution results (about 1·5 hours). Continue the heating for a further hour, pour the solution into a 600 ml. beaker and allow to cool. Filter off the crystals which separate at the pump, wash as free as possible from hydrochloric acid with ice-cold distilled water, and dry in the air. The yield is 40 g. A further small quantity may be isolated by concentrating the mother liquor and washings on a water bath under reduced pressure. The product is sufficiently pure for conversion into *o*-sulphobenzoic anhydride. If perfectly pure acid ammonium *o*-sulphobenzoate is required, it may be recrystallised from an equal weight of distilled water.

o-Sulphobenzoic anhydride. Place 40 g. of finely-powdered acid ammonium *o*-sulphobenzoate and 40 ml. of sodium-dried A.R. benzene in a dry 500 ml. three-necked flask, fitted with a separatory funnel, mechanical stirrer and double surface condenser. Add, with stirring, 64 g. (39 ml.) of redistilled thionyl chloride. Attach the upper end of the condenser by means of a bent glass tube to a gas absorption trap (Fig. *II*, *8*, 1, *c*). Warm the mixture gently on a water bath, with stirring, for 3–4 hours or until the evolution of gas slackens; if the reaction becomes very vigorous, interrupt the heating for a short time. Add a further 80 ml. of sodium-dried benzene, reflux for 1 hour, and filter the hot suspension through a sintered glass funnel (*FUME CUPBOARD*: presence of thionyl chloride). Extract the solid material, consisting largely of ammonium chloride, with two 20 ml. portions of hot, dry benzene. Cool the combined filtrate and washings contained in a 250 ml. distilling flask in an ice bath; most of the sulphobenzoic anhydride crystallises out. Decant the benzene mother liquor from the crystals (1). Attach a condenser and filter flask receiver (compare Fig. *II*, *13*, 1), distil the residual excess of solvent, and finally heat until the solid has just melted; remove any adhering solvent by *slightly* reducing the pressure. pour the clear liquid residue into a porcelain basin and allow it to cool

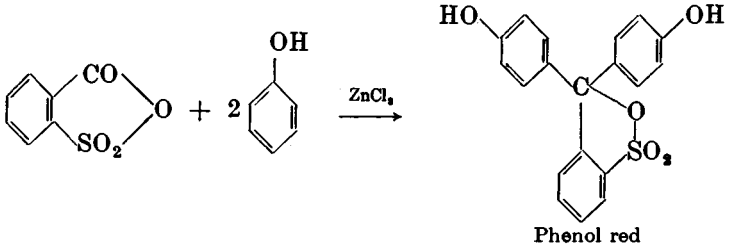
in a desiccator over calcium chloride. The yield of *o*-sulphobenzoic anhydride, m.p. 122–123°, is 24 g. The compound is sensitive to moist air, which converts it into the free acid ; it should be kept in a desiccator or in a bottle fitted with a solid rubber stopper. The above crude product is quite satisfactory for the preparation of sulphonephthaleins. The pure compound, m.p. 128°, may be obtained by recrystallisation from dry benzene.

Note.

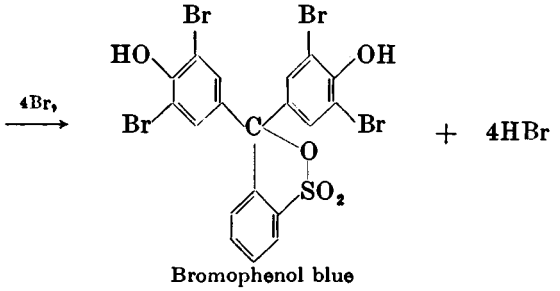
(1) A further small quantity may be recovered from the mother liquors by removing the solvent at atmospheric pressure and distilling the residue under reduced pressure : the anhydride passes over at 184–186°/18 mm.

VIII,10. SULPHONEPHTHALEINS

By condensing o-sulphobenzoic anhydride with phenol in the presence of anhydrous zinc chloride, phenolsulphonephthalein (**phenol red**) is formed. Tetrabromination of the latter affords tetrabromophenolsulphonephthalein (**bromophenol blue**) :

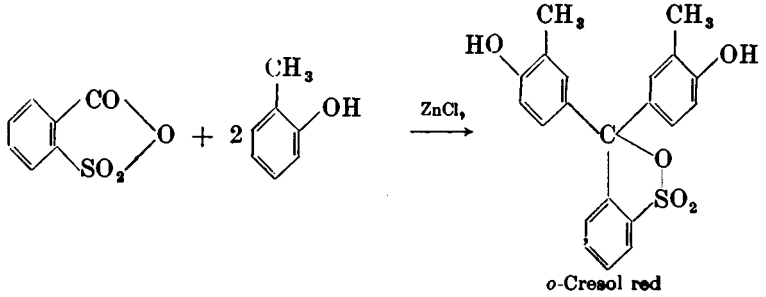


Phenol red

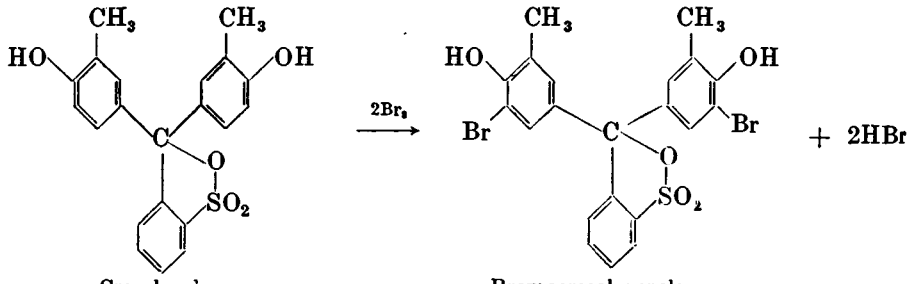


Bromophenol blue

Similarly o-sulphobenzoic anhydride and o-cresol yields o-cresolsulphonephthalein (***o*-cresol red**) ; dibromination of the last-named gives dibromo-o-sulphonephthalein (**bromocresol purple**) :



o-Cresol red



o-Cresol red — Bromocresol purple

Phenolsulphonephthalein (phenol red). Mix 10 g. of *o*-sulphobenzoic anhydride (Section **VIII,9**), 14 g. of pure phenol and 10 g. of freshly fused zinc chloride in a small conical flask. Place a glass rod in the flask and heat gently over a flame to melt the phenol. Then heat the flask containing the well-stirred mixture in an oil bath at 135–140° for 4 hours. Stir from time to time, but more frequently during the first hour ; if the mixture froths unduly, remove the flask from the bath, cool and then resume the heating. When the reaction is complete, add 50 ml. of water, allow the water to boil and stir to disintegrate the product. Filter the crude dye with suction and wash it well with hot water. Dissolve the residue in the minimum volume of warm (60°) 20 per cent. sodium hydroxide solution, filter, and just acidify the filtrate with warm dilute hydrochloric acid (1 : 1). Filter the warm solution, wash with water, and dry upon filter paper. The yield of phenol red (a brilliant red powder) is 11 g.

Tetrabromophenolsulphonephthalein (bromophenol blue). Suspend 5 g. of phenolsulphonephthalein in 40 ml. of glacial acetic acid. Heat the acid almost to boiling and add dropwise a solution of 5 ml. of bromine in 20 ml. of glacial acetic acid whilst keeping the original mixture just below the boiling point. Evolution of hydrogen bromide commences immediately the bromine is introduced. The phenolsulphonephthalein gradually dissolves and an almost colourless precipitate of the tetrabromo derivative gradually separates. Filter with suction, wash with glacial acetic acid to remove the excess of bromine, and finally with benzene. Dry upon filter paper in the air and preserve in a tightly stoppered bottle. The yield is 7·5 g. The product may be crystallised from acetone-glacial acetic acid and melts at 270–271° (decomp.).

***o*-Cresolsulphonephthalein (*o*-cresol red).** Proceed as for *Phenol Red*, but use a mixture of 10 g. of *o*-sulphobenzoic anhydride, 12 g. of pure *o*-cresol, 8 g. of freshly fused zinc chloride and heat for 4 hours at 115–120°. Add 50 ml. of water and 5 ml. of dilute hydrochloric acid (1 : 1), boil and disintegrate the melt. Filter and wash with a little warm water. Dry the residue on a water bath, powder, and triturate with a mixture of 20 ml. of benzene and 20 ml. of ether in order to remove the excess of *o*-cresol. Filter, wash with ether, and dry upon filter paper. The yield is 11 g. The compound may be recrystallised from glacial acetic acid.

Dibromo-*o*-cresolsulphonephthalein (bromocresol purple). Dissolve 5 g. of *o*-cresolsulphonephthalein in 50 ml. of glacial acetic acid, heat to boiling under reflux, add slowly a solution of 2 ml. of bromine in

20 ml. of glacial acetic acid, and boil gently for 1 hour. Allow to cool, filter off the bromocresol purple, wash with a little glacial acetic acid, followed by a little benzene, and dry. The yield is 4 g.

VIII,11. *N*-PHENYLANTHRANILIC ACID

N-Phenylanthranilic acid may be prepared by the action of aniline upon *o*-chlorobenzoic acid in the presence of anhydrous potassium carbonate and a little copper oxide :

$$o\text{-}ClC_6H_4COOH + C_6H_5NH_2 \xrightarrow[\text{then HCl}]{K_2CO_3,\ CuO;} o\text{-}C_6H_5NHC_6H_4COOH$$

The compound is employed *inter alia* as an indicator in titrations with potassium dichromate and ceric sulphate solutions.

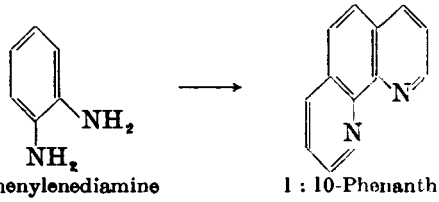
In a 1 litre round-bottomed flask, equipped with an air condenser, place a mixture of 44 g. of *o*-chlorobenzoic acid (Section **IV,157**) (1), 156 g. (153 ml.) of redistilled aniline, 41 g. of anhydrous potassium carbonate and 1 g. of cupric oxide. Reflux the mixture in an oil bath for 2 hours. Allow to cool. Remove the excess of aniline by steam distillation and add 20 g. of decolourising carbon to the brown residual solution. Boil the mixture for 15 minutes, and filter at the pump. Add the filtrate with stirring to a mixture of 30 ml. of concentrated hydrochloric acid and 60 ml. of water, and allow to cool. Filter off the precipitated acid with suction, and dry to constant weight upon filter paper in the air. The yield of *N*-phenylanthranilic acid, m.p. 181–182° (capillary tube placed in preheated bath at 170°), is 50 g. This acid is pure enough for most purposes. It may be recrystallised as follows : dissolve 5 g. of the acid in either 25 ml. of alcohol or in 10 ml. of acetic acid, and add 5 ml. of hot water ; m.p. 182–183°.

Note.

(1) Commercial *o*-chlorobenzoic acid may be purified in the following manner. Dissolve 60 g. of the technical acid in 200 ml. of hot water containing 20 g. of sodium carbonate, add 10 g. of decolourising carbon, boil for 15 minutes, and filter at the pump. Add the filtrate with stirring to 31 ml. of concentrated hydrochloric acid diluted with an equal volume of water. Collect the purified acid with suction, wash it with a little cold water, and dry at 100°.

VIII,12. 1 : 10-PHENANTHROLINE

This important oxidation-reduction indicator is readily prepared by a double Skraup reaction (compare Section V,1) upon o-phenylenediamine :



o-Phenylenediamine 1 : 10-Phenanthroline

In view of the high reactivity and sensitivity to oxidation of o-phenylenediamine, the normal experimental conditions of the Skraup reaction are modified : the condensation is carried out in the presence of glycerol, arsenic acid *solution* and dilute sulphuric acid.

In a 2 litre round-bottomed flask, equipped with a reflux condenser, place 20 g. of *o*-phenylenediamine (Section **IV,92**), 108 g. of glycerol, 100 ml. of arsenic acid solution (1) and 400 ml. of dilute sulphuric acid (2). Reflux the mixture for 3·5 hours, and allow to cool. Transfer to a 3 litre beaker, dilute with an equal volume of water, render alkaline with concentrated ammonia solution, sp. gr. 0·88 (about 1050 ml. are required), and allow to stand overnight. Remove the tar by filtration through a fluted filter paper. Transfer the tar plus filter paper to a 500 ml. round-bottomed flask and reflux it for 20 minutes with 200 ml. of benzene. Remove the benzene layer and repeat the extraction with 100–200 ml. portions of benzene until the extracts are colourless : the total volume of benzene required is about 800 ml. Extract the dark aqueous filtrate with four or five 250 ml. portions of hot benzene. Combine all the benzene extracts in a 3 litre round-bottomed flask, and distil off the benzene on a water bath. Transfer the viscid, tarry residue to a small beaker or evaporating dish, evaporate as much benzene as possible on a water bath, and then cool in ice. The product sets to a dark solid mass of crude 1 : 10-(or *o*-)phenanthroline weighing 19 g. Reflux the crude *o*-phenanthroline for 5 minutes with 100 ml. of benzene and 2 g. of decolourising carbon, filter through a hot water funnel, and allow the benzene solution to cool. Collect the pale brown *o*-phenanthroline (4 g.) which separates, and dry it upon filter paper in the air ; this is the monohydrate and melts at 108–110°. Evaporate the mother liquor to dryness and recrystallise the residue twice from 30 ml. of moist boiling benzene : a further 6 g. of pure *o*-phenanthroline monohydrate is isolated. The compound may also be recrystallised from benzene - light petroleum (b.p. 40–60°), but this medium yields a somewhat more coloured product.

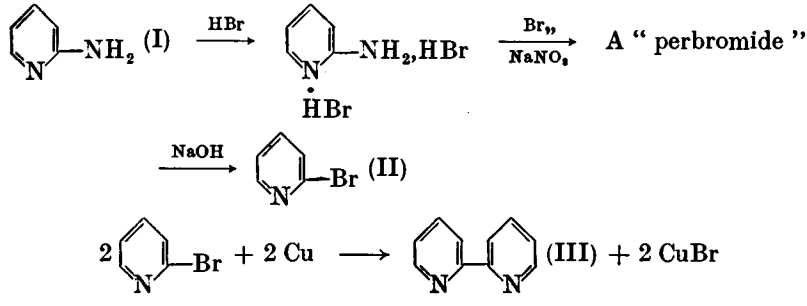
Notes.

(1) The arsenic acid solution is prepared by dissolving 123 g. of arsenic pentoxide in 104 ml. of water ; 100 ml. of the cold solution are used in the experiment.

(2) The dilute sulphuric acid is prepared by adding 240 ml. of concentrated sulphuric acid slowly and with stirring to 200 ml. of water ; 400 ml. of the cold, diluted acid are employed in the preparation.

VIII,13. 2 : 2′-DIPYRIDYL

2-Aminopyridine (I) is converted by diazotisation in the presence of bromine and concentrated hydrobromic acid into 2-bromopyridine (II) ; the latter upon treatment with copper powder in the presence of *p*-cymene yields 2 : 2′-dipyridyl (III).

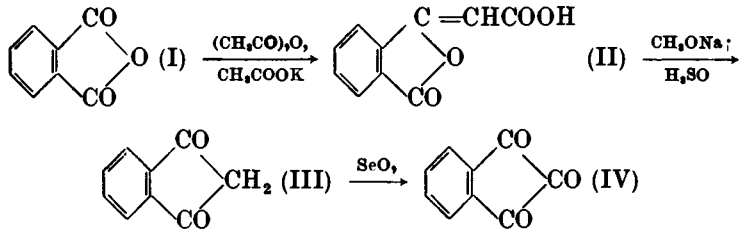


2-Bromopyridine. Place 395 ml. of 48 per cent. hydrobromic acid in a 3-litre three-necked flask, fitted with a dropping funnel, mechanical stirrer and low temperature thermometer. Cool to 10–15° in an ice-salt bath and add 75 g. of 2-aminopyridine (Section **IX,10**) over a period of about 10 minutes. Whilst maintaining the temperature at 0° or lower, add 375 g. (120 ml.) of bromine dropwise with stirring. The reaction mixture thickens during the addition of the first half of the bromine (*ca.* 30 minutes) owing to the formation of a yellow-orange " perbromide " ; the second half may then be introduced more rapidly (*ca.* 15 minutes). Now add a solution of 140 g. of A.R. sodium nitrite in 200 ml. of water dropwise over a period of 2 hours whilst keeping the temperature at 0° or lower. Continue the stirring for 30 minutes ; then run in a solution of 300 g. of sodium hydroxide in 300 ml. of water at such a rate that the temperature does not rise above 20–25°. Extract the reaction mixture with four 125 ml. portions of ether, dry the ethereal extracts for 1 hour over 50 g. of potassium hydroxide pellets, remove the ether on a steam bath, and distil the residue from a Claisen flask with fractionating side arm (Fig. *II, 24,* 2–5) under reduced pressure. Collect the 2-bromopyridine at 74–75°/13 mm. ; the yield is 115 g. The b.p. at atmospheric pressure is 193–195°.

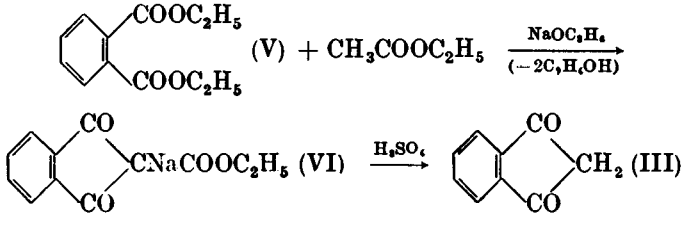
2 - 2′-Dipyridyl. In a 1-litre three-necked flask, equipped with a reflux condenser and mechanical stirrer, place 21 g. of copper powder and 200 ml. of *p*-cymene (b.p. 176–177°). Whilst refluxing the mixture gently with stirring, add 104 g. of 2-bromopyridine dropwise over a period of 1 hour ; add three additional portions of 21 g. each of copper powder (through the otherwise closed third neck) during this period. Continue the heating with stirring for a further 2·5 hours, cool, acidify with dilute hydrochloric acid, and separate the *p*-cymene by steam distillation. Render the residual solution strongly alkaline with concentrated sodium hydroxide solution and steam distil again until the distillate gives only a pale red colouration with ferrous sulphate solution. Saturate the steam distillate with sodium chloride and extract repeatedly with ether ; it is best to use a continuous extractor (Fig. *II, 44,* 2). Dry the ethereal extracts over anhydrous potassium carbonate, remove the ether by distillation through an efficient fractionating column (2 : 2′-dipyridyl is slightly volatile in ether vapour), and distil the residue under reduced pressure. Collect the 2 : 2′-dipyridyl (31·5 g.) at 147°/16 mm. ; it solidifies on cooling, m.p. 69–70°.

VIII,14. NINHYDRIN (INDANE-1 : 2 : 3-TRIONE HYDRATE)

Ninhydrin (also named 1 : 2 : 3-triketoindane or 1 : 2 : 3-triketohydrindene hydrate) is prepared most simply from the inexpensive phthalic anhydride (I). The latter is condensed with acetic anhydride in the presence of potassium acetate to give phthalylacetic acid (II) ; reaction of the latter with sodium methoxide in methanol yields 1 : 3-indanedionecarboxylic acid, which is decomposed upon warming with dilute hydrochloric or sulphuric acid to indane-1 : 3-dione (or 1 : 3-diketohydrindene) (III). Selenium dioxide oxidation of (III) affords indane-1 : 2 : 3-trione hydrate (ninhydrin) (IV).



1 : 3-Indanedione (III) may also be prepared by condensation of diethyl phthalate (V) with ethyl acetate in the presence of sodium ethoxide; the resulting sodium 1 : 3-indanedione-2-carboxylic ester (VI) upon warming with sulphuric acid yields (III).



Phthalylacetic acid. Heat a mixture of 30 g. of phthalic anhydride, 40 ml. of acetic anhydride and 5 g. of potassium acetate under reflux in an oil bath at 155–165° for 15 minutes. Pour the reaction mixture into ice-cold water, collect the yellow precipitate by suction filtration, wash it three times with 25 ml. of water and once with 10 ml. of 50 per cent. ethanol. Dry the product at 100°; the yield of crude phthalylacetic acid is 20 g. Recrystallise from hot methanol; yellow needles, m.p. 245–246°, are obtained.

Indane-1 : 3-dione (1 : 3-diketohydrindene). *Method A.* To a solution of sodium methoxide, prepared from 6·1 g. of sodium and 200 ml. of anhydrous methanol, add 15 g. of phthalylacetic acid and allow to stand for 1 hour at room temperature; collect the yellow precipitate by suction filtration. Mix the yellow solid with 150 ml. of 10 per cent. sulphuric acid, heat on a steam bath until no more carbon dioxide is evolved (15–20 minutes), filter the hot solution and allow to cool. Collect the yellow crystals by filtration at the pump, wash with a little water and dry at 100°. The yield of crude 1 : 3-indanedione, m.p. 125–126°, is 7 g. Recrystallise from light petroleum, b.p. 80–100°, and thus obtain the pure product, m.p. 129–130°.

Method B. Place 125 g. (106·5 ml.) of diethyl phthalate and 25 g. of " molecular " sodium (sodium " sand "; see Section **II,50,***6*) in a 500 ml. round-bottomed flask fitted with a reflux condenser and dropping funnel. Heat the flask on a steam bath and add a mixture of 122·5 g. (136 ml.) of dry ethyl acetate and 2·5 ml. of absolute ethanol over a period of 90 minutes. Continue the heating for 6 hours, cool and add 50 ml. of ether. Filter the sodium salt (VI) on a sintered glass funnel and wash it with the minimum volume of ether. Dissolve the sodium salt (96 g.) in 1400 ml. of hot water in a 3-litre beaker, cool the solution to 70°, stir vigorously and add 100 ml. of sulphuric acid (3 parts of concentrated acid to 1 part of

water). Cool the mixture to 15° in an ice bath, collect the 1 : 3-indanedione by suction filtration, wash with a little water and dry at 100°; the yield is 58 g. Recrystallisation from a dioxan-benzene mixture by the addition of light petroleum (b.p. 80–100°) gives the pure compound, m.p. 130°.

Indane-1 : 2 : 3-trione hydrate (ninhydrin). In a 500 ml. three-necked flask, fitted with a reflux condenser and mechanical stirrer, place 11 g. of resublimed selenium dioxide dissolved in 240 ml. of dioxan and 5 ml. of water. Heat the stirred solution to 60–70°, remove the source of heat, add 15 g. of crude 1 : 3-indanedione and reflux the resulting mixture for 6 hours. A solid separates during this period. Filter the mixture, transfer the filtrate to a distilling flask and distil off about 180 ml. of dioxan; then add 100 ml. of water, boil the solution to coagulate the red tarry precipitate and remove it by filtration. Concentrate the filtrate to about 50 ml. and filter. Boil the filtrate with 0·2–0·3 g. of decolourising carbon, filter again, concentrate to 20–25 ml. and keep at room temperature. Collect the crystals of crude ninhydrin by suction filtration, and recrystallise from hot water with the addition of a little decolourising carbon, if necessary. The yield of colourless ninhydrin is 6 g.; the crystals turn red between 125° and 130° and melt at 242–243°.