CHAPTER VII

ORGANIC REAGENTS IN INORGANIC AND ORGANIC CHEMISTRY

VII,1. DIMETHYLGLYOXIME

Methyl ethyl ketone is allowed to react with *n*-butyl or *iso*-amyl nitrite in the presence of hydrochloric acid to yield diacetyl monoxime (nitrosomethyl ethyl ketone) :

$$CH_3COCH_2CH_3 + C_4H_9{}^{\alpha}ONO \longrightarrow CH_3COC(=NOH)CH_3 + C_4H_9{}^{\alpha}OH$$

The diacetyl monoxime condenses readily with hydroxylamine hydrochloride or sulphate with the formation of dimethylglyoxime (diacetyl dioxime) :

$$\begin{matrix} CH_3CO \\ | \\ CH_3C{=}NOH \end{matrix} + H_2NOH \longrightarrow \begin{matrix} CH_3C{=}NOH \\ | \\ CH_3C{=}NOH \end{matrix} + H_2O$$

In a 500 ml. three-necked flask, supported on a water bath and provided with a dropping funnel, a mechanical stirrer and a thermometer, place 72 g. (90 ml.) of redistilled methyl ethyl ketone (dried over anhydrous magnesium or copper sulphate). Start the stirrer, introduce 3 ml. of concentrated hydrochloric acid and warm the liquid to 40°. Then add 100 g. (112 ml.) of *n*-butyl nitrite (b.p. 76–79°) or 112 g. (129 ml.) of *iso*-amyl nitrite (b.p. 96–99°) (Section **III,53**) slowly, maintaining the temperature at 40–50° ; the mixture must be stirred vigorously. Heat is generated in the reaction so that cooling may now be required. Continue the stirring, without cooling, for 30 minutes after all the nitrite has been added. The reaction mixture now consists of a solution of diacetyl monoxime in *n*-butyl or *iso*-amyl alcohol. To remove any unused ketone, treat the mixture with a cold solution of 45 g. of sodium hydroxide in 100 ml. of water and stir for 20–30 minutes. Transfer the reaction mixture to a separatory funnel and extract the reddish-brown solution twice with 50 ml. portions of ether : the alcohol may be recovered, if desired, by fractionation of the ethereal extracts. Keep the aqueous layer ; it contains the sodium salt of diacetyl monoxime. Prepare a solution of 70 g. of hydroxylamine hydrochloride $\{NH_2OH,HCl\}$ or of 82 g. of hydroxylamine sulphate $\{(NH_2OH)_2,H_2SO_4\}$ in about three times its weight of water, and add sodium hydroxide solution until the solution is neutral to litmus. Place the aqueous solution of the sodium salt of diacetyl monoxime in a 1 litre bolt-head flask and add the hydroxylamine solution with stirring. Heat the mixture on a water bath for about 45 minutes. Filter off the precipitated dimethylglyoxime (1) whilst the solution is still hot, wash it with hot water, and drain well. Recrystallise the crude product from about 10 times its weight of rectified spirit. The yield of pure dimethylglyoxime (a white, crystalline solid, m.p. 240°) is 55 g.

Note.

(1) If the product is coloured, dissolve it in 2*N* sodium hydroxide solution on a water bath. Filter the hot almost saturated solution, and to the hot filtrate add a

concentrated solution of ammonium chloride in excess of the amount required to precipitate all the dimethylglyoxime, *i.e.*, employ an amount greater than the equivalent of the sodium hydroxide used. Filter at once with suction, and wash with boiling water. Recrystallise the white product from rectified spirit.

VII,2. SEMICARBAZIDE HYDROCHLORIDE

Hydrazine sulphate reacts with sodium cyanate in the presence of sodium carbonate to give semicarbazide, which remains in solution :

$$2NH_2NH_2,H_2SO_4 + Na_2CO_3 \longrightarrow (NH_2NH_2)_2H_2SO_4 + Na_2SO_4 + H_2CO_3$$

$$(NH_2NH_2)_2H_2SO_4 + 2NaCNO \longrightarrow 2H_2NCONHNH_2 + Na_2SO_4$$

Small amounts of the insoluble hydrazodicarbonamide may also be formed :

$$H_2NCONHNH_2 + HCNO \longrightarrow H_2NCONHNHCONH_2$$

To isolate the semicarbazide hydrochloride, the filtered reaction mixture is treated with excess of acetone and the resulting acetone semicarbazone is decomposed with concentrated hydrochloric acid.

Dissolve 65 g. of hydrazine sulphate and 27 g. of anhydrous sodium carbonate in 250 ml. of boiling water contained in a 1 litre beaker, and cool the solution to 50–55° ; add a solution of 34 g. of pure sodium cyanate in 500 ml. of water, and allow the mixture to stand overnight. Filter off any hydrazodicarbonamide which separates and treat the filtrate with 120 g. (152 ml.) of A.R. acetone. Shake the mixture mechanically (compare Fig. *II*, *7*, 14) for 8 hours : filter off the crude acetone semicarbazone and dry it upon filter paper in the air (135 g.). A further 15 g. of the crude semicarbazone separates upon shaking for a further 6 hours. Upon evaporating the mother liquor to dryness on a water bath, the residue, after drying, weighs about 30 g. To obtain pure acetone semicarbazone, place all the crude product (180 g.) in a large modified Soxhlet apparatus (Figs. *III*, *40*, 1–2), the lower end of which is filled with glass wool, and extract during 6 hours with 200 ml. of absolute alcohol. Allow the alcoholic extract to cool, filter off the acetone semicarbazone and dry : the yield is 50 g., m.p. 186°. Concentrate the filtrate to half the original volume and add excess of ether : a further 8 g. of pure acetone semicarbazone is recovered.

To decompose the acetone semicarbazone, warm 58 g. with 50 ml. of concentrated hydrochloric acid until it *just* dissolves. Cool in ice ; the semicarbazide hydrochloride separates as a thick crystalline mass. Filter at the pump through a sintered glass funnel, and wash with a small quantity of alcohol and then with ether : dry in the air. The yield of pure semicarbazide hydrochloride, m.p. 173° (decomp.). is 35 g. A further quantity of product may be obtained either by saturating the mother liquor with hydrogen chloride or by treating it with twice its volume of alcohol and then with ether.

VII,3. DIPHENYLCARBAZIDE

Diphenylcarbazide is prepared by heating a mixture of phenylhydrazine and urea at 155° :

$$2C_6H_5NHNH_2 + CO(NH_2)_2 \longrightarrow CO(NHNHC_6H_5)_2 + 2NH_3$$

In a 500 ml. Pyrex round-bottomed flask, provided with a reflux condenser, place a mixture of 40 g. of freshly-distilled phenylhydrazine (Section IV,89) and 14 g. of urea (previously dried for 3 hours at 100°). Immerse the flask in an oil bath at 155°. After about 10 minutes the urea commences to dissolve accompanied by foaming due to evolution of ammonia : the gas evolution slackens after about 1 hour. Remove the flask from the oil bath after 135 minutes, allow it to cool for 3 minutes, and then add 250 ml. of rectified spirit to the hot golden-yellow oil ; some diphenylcarbazide will crystallise out. Heat under reflux for about 15 minutes to dissolve the diphenylcarbazide, filter through a hot water funnel or a pre-heated Buchner funnel, and cool the alcoholic solution rapidly in a bath of ice and salt. After 30 minutes, filter the white crystals at the pump, drain well, and wash twice with a little ether. Dry upon filter paper in the air. The yield of diphenylcarbazide, m.p. 171°, is 34 g. A further 7 g. may be obtained by concentrating the filtrate under reduced pressure. The compound may be recrystallised from alcohol or from glacial acetic acid.

VII,4. DIPHENYLCARBAZONE

Oxidation of diphenylcarbazide (Section VII,3) with hydrogen peroxide in the presence of alcoholic potassium hydroxide affords diphenylcarbazone :

$$CO(NHNHC_6H_5)_2 + H_2O_2 \longrightarrow C_6H_5NHNHCON{=}NC_6H_5 + 2H_2O$$

Place 24 g. of diphenylcarbazide and 200 ml. of rectified spirit in a 1 litre bolt-head flask equipped with a mechanical stirrer. Heat the solution until the solid dissolves, and to the hot vigorously stirred solution add 20 g. of potassium hydroxide pellets in one lot, followed by 20 ml. of " 10-volume " hydrogen peroxide. Vigorous stirring is essential to prevent the blood-red solution foaming over. The potassium salt of the carbazone slowly separates. Allow the mixture to stand for 5 minutes and then add, with stirring, 2*N* sulphuric acid until the resulting orange-coloured suspension is acid to litmus (about 250 ml. are required). Transfer the suspension to a 3 litre beaker, and add 1500 ml. of water to dissolve the potassium sulphate. Cool, filter the orange diphenylcarbazone at the pump, wash well with water, and dry at about 50°. The yield of crude product, m.p. 150° (decomp.), is 17 g. Recrystallise from about 75 ml. of rectified spirit : 12 g. of pure diphenylcarbazone (orange crystals, m.p. 156–158° with decomposition) are obtained.

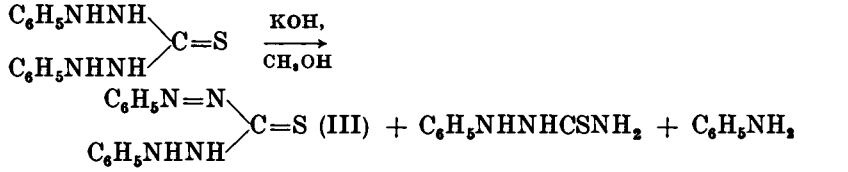
VII,5. DITHIZONE (DIPHENYLTHIOCARBAZONE)

Phenylhydrazine condenses with carbon disulphide to yield the phenylhydrazine salt of β-phenyldithiocarbazic acid (I), which on heating at 96–98° until the first evolution of ammonia is detectable affords diphenylthiocarbazide (II) :

$$2C_6H_5NHNH_2 + CS_2 \longrightarrow C_6H_5NHNH{-}\overset{\overset{S}{\|}}{C}{-}SH.NH_2NHC_6H_5 \text{ (I)}$$

$$\xrightarrow{\text{Heat}} \begin{matrix} C_6H_5NHNH \\ C_6H_5NHNH \end{matrix}\!\!>\!C{=}S \text{ (II)} + H_2S$$

Upon heating diphenylthiocarbazide with methyl alcoholic potassium hydroxide dithizone (or diphenylthiocarbazone) (III) is produced :



Equip a 500 ml. three-necked flask with a dropping funnel, a mechanical stirrer and a reflux condenser. Place a solution of 72 g. (65 ml.) of redistilled phenylhydrazine (Section IV,89) (*CAUTION :* poisonous) in 300 ml. of ether in the flask, stir vigorously, and add 33 g. (26 ml.) of A.R. carbon disulphide slowly during about 30 minutes. A precipitate is formed immediately upon the addition of the carbon disulphide, the mixture becomes warm and the temperature soon approaches the boiling point ; maintain the temperature just below the b.p. by cooling with ice water if necessary. When the addition is complete, stir for a further 30 minutes, then filter the precipitate at the pump, wash it with about 25 ml. of ether, and spread it upon filter paper for 20 minutes to permit of the evaporation of the ether. The yield of the salt (I) is 92 g.

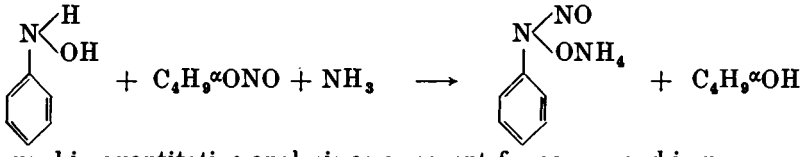
Transfer the salt to a 600 ml. beaker or 500 ml. wide-mouthed conical flask and heat on a boiling water bath (temperature 96–99°) with continuous stirring by hand using a heavy glass rod flattened at the bottom. After about 10 minutes, the substance softens and begins to decompose with the evolution of hydrogen sulphide ; after 20–30 minutes ammonia is evolved. When the ammonia is first detected by its odour, immediately remove the vessel containing the reaction mixture (green or brown in colour) from the water bath to a bath of cold water for 1 minute, and then immerse it in finely-crushed ice. (Unless the mixture is immediately cooled after removal from the water bath, the product may decompose violently after 10–15 minutes.) Then add 75 ml. of alcohol and warm gently to loosen the mass ; stir until the precipitate becomes granular. Allow to stand for 1 hour, filter at the pump and wash with 25 ml. of alcohol. The yield of crude, white diphenylthiocarbazide (II) is 60 g.

Dissolve 30 g. of potassium hydroxide pellets in 300 ml. of methyl alcohol in a 500 ml. round-bottomed flask, add the crude diphenylthiocarbazide, and fit a reflux condenser. Immerse the flask in a boiling water bath, and from the moment that the solution commences to boil, reflux the mixture for exactly 5 minutes : if the refluxing is prolonged beyond this period, the yield of product is decreased. Cool the resulting solution in ice water and filter by gravity (glass wool). Treat the red filtrate with ice-cold *N* sulphuric acid, stirring vigorously with a mechanical stirrer, until the solution is just acid to Congo red paper (about 500 ml. are required : at the end point the mother liquor is colourless). Filter the blue-black precipitate at the pump and wash it with 25 ml. of cold water. (Take care in handling the precipitate or suspensions of it since it dyes the skin black and other materials pink ; if any of it is spilled or splashed, remove it at once since the compound dries to a light fine powder which is readily scattered.) Dissolve the crude dithizone in 250 ml. of 5 per cent. sodium hydroxide solution, filter with suction, cool the filtrate in ice and

immediately acidify it with ice-cold *N* sulphuric acid until it is just acid to Congo red paper (about 325 ml. are required). Filter the precipitate at the pump ; transfer it to a 1 litre beaker and stir with about 900 ml. of water. Filter the mixture and repeat the washing process until the washings are free from sulphate. Finally suck the precipitate as dry as possible on the Buchner funnel, and dry upon clock glasses in the oven at 40°. The yield of dithizone is 75 g. The pure compound is completely soluble in chloroform and decomposes sharply at a temperature between 165° and 169°.

VII,6. CUPFERRON

Cupferron, the ammonium salt of the *N*-nitroso derivative of phenylhydroxylamine, is prepared by passing ammonia gas into an ethereal solution of phenylhydroxylamine and *n*-butyl nitrite :

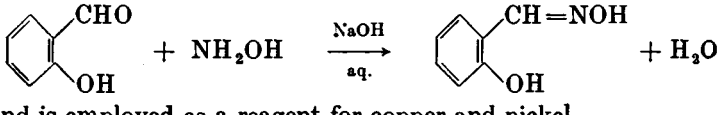


It is used in quantitative analysis as a reagent for copper and iron.

Weigh the moist phenylhydroxylamine obtained from 100 g. of nitrobenzene by the procedure described in Section **IV,83** and dissolve it in 450 ml. of ether ; weigh the ether-insoluble material (water and sodium chloride). The difference between the two weighings is the weight of phenylhydroxylamine in solution. Filter the ether solution through a dry fluted filter paper into a 500 ml. bolt-head flask, which is fitted with a mechanical stirrer and is immersed in an ice-salt bath. When the temperature has fallen to 0°, pass a rapid stream of dry ammonia from a cylinder into the solution. After 15 minutes, add the theoretical quantity of freshly-distilled *n*-butyl nitrite (Section **III,53**) (9·5 g. of $Bu^{\alpha}NO_2$ for every 10 g. of C_6H_5NHOH) slowly through a dropping funnel whilst passing a rapid stream of ammonia into the solution ; it is essential that the ammonia is always present in excess. Maintain the temperature of the reaction mixture below 10°. After the *n*-butyl nitrite has been added, stir the reaction mixture for an additional 10 minutes to complete the reaction. Filter off the cupferron and wash it several times with small volumes of ether. Spread the product upon sheets of filter paper until the ether has volatilised. Store it in tightly-stoppered bottles containing a little ammonium carbonate in a filter paper bag or thimble. The yield is about 85 per cent. of the theoretical based upon the weight of phenylhydroxylamine used.

VII,7. SALICYLALDOXIME

This substance is readily obtained by the interaction of salicylaldehyde with hydroxylamine hydrochloride in the presence of alkali :



The compound is employed as a reagent for copper and nickel.

Method 1. Dissolve 25·0 g. of salicylaldehyde (Section **IV,122**) in 215 ml. of 2*N* sodium hydroxide solution, add 12·05 g. of hydroxylamine hydrochloride, and warm the mixture for 30 minutes on a water bath. Acidify with acetic acid and cool in ice ; the salicylaldoxime separates as a congealed oil. Recrystallise from chloroform - light petroleum (b.p. 40–60°). The yield of salicylaldoxime (colourless crystals, m.p. 57°) is 5 g.

Method 2. Dissolve 20·0 g. of salicylaldehyde in 30 ml. of rectified spirit, add a solution of 15 g. of hydroxylamine hydrochloride in 10 ml. of water, and render the mixture just alkaline with 10 per cent. sodium carbonate solution whilst cooling in ice. Allow to stand overnight. Acidify with acetic acid, distil off the alcohol under reduced pressure (water pump), dilute with twice the volume of water, and extract with two 50 ml. portions of ether. Dry the ethereal extract with anhydrous sodium or magnesium sulphate, distil off most of the ether, and allow the residue to crystallise. Recrystallise from chloroform - light petroleum (b.p. 40–60°). The yield of salicylaldoxime, m.p. 57°, is 12 g.

VII,8. α-BENZOINOXIME

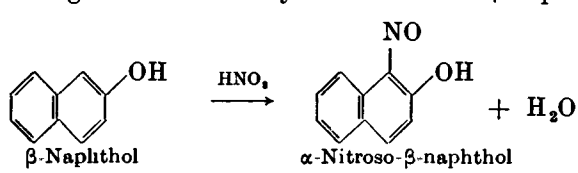
Benzoin condenses with hydroxylamine hydrochloride in the presence of alkali to give α-benzoinoxime (" cupron ") as the main product :

$$C_6H_5CHOHCOC_6H_5 + NH_2OH \longrightarrow C_6H_5CHOHC(=NOH)C_6H_5 + H_2O$$

In a 250 ml. bolt-head flask, fitted with a reflux condenser, place a mixture of 10 g. of benzoin (Section **IV,125**) and 20 g. (25 ml.) of rectified spirit together with an aqueous solution of 8·0 g. of hydroxylamine hydrochloride which has previously been neutralised with 4·4 g. of sodium hydroxide. Reflux for 60 minutes. Add water to precipitate the benzoinoxime, and cool in an ice bath. Filter the solid with suction at the pump, wash it with water, and recrystallise from dilute alcohol. Alternatively, the dry solid may be recrystallised from ether. The yield of pure α-benzoinoxime, m.p. 151°, is 5 g.

VII,9. α-NITROSO-β-NAPHTHOL

Treatment of a solution of sodium nitrite and the sodium salt of β-naphthol with sulphuric acid gives an excellent yield of α-nitroso-β-naphthol :



β-Naphthol α-Nitroso-β-naphthol

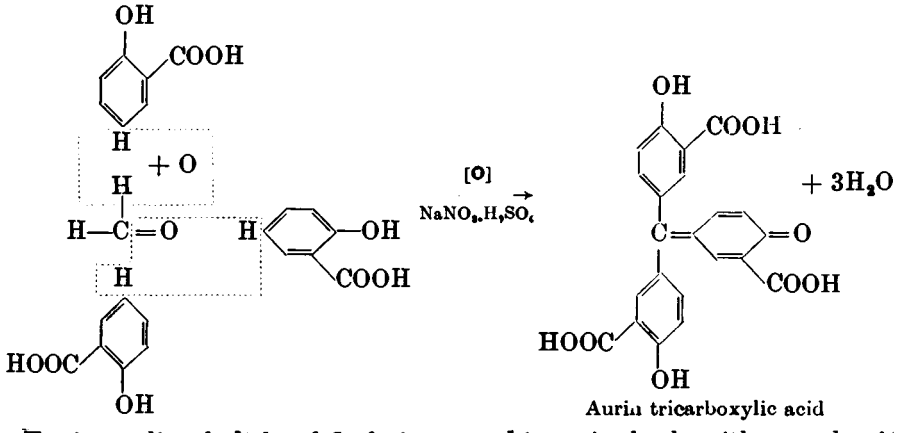
Dissolve 100 g. of β-naphthol (Section **IV,102**) in a warm solution of 28 g. of sodium hydroxide in 1200 ml. of water contained in a 2·5 litre round-bottomed or bolt-head flask fitted with a mechanical stirrer. Cool the solution to 0° in a bath of ice and salt, and add 50 g. of powdered sodium nitrite. Start the stirrer and add, by means of a separatory funnel supported above the flask, 220 g. (166·5 ml.) of sulphuric acid (sp. gr. 1·32) at such a rate that the whole is added during 90 minutes

and the temperature is kept at 0° : add crushed ice (about 200 g. in all) from time to time in order to maintain the temperature at 0°. The solution should react acid to Congo red paper after all the sulphuric acid has been introduced. Stir the mixture for an additional hour ; keep the temperature at 0°. Filter off the α-nitroso-β-naphthol at the pump and wash it thoroughly with water. Dry the pale yellow product upon filter paper in the air for four days ; the colour changes to dark brown and the α-nitroso-β-naphthol, m.p. 97°, weighs 130 g. It contains about 10 per cent. of its weight of moisture, but is otherwise almost pure. The moisture may be removed by leaving the air-dried compound in a desiccator for 24 hours ; it then weighs 115 g. and melts at 106°.

If α-nitroso-β-naphthol is required in the crystalline condition, recrystallise it from light petroleum, b.p. 60–80° (7·5 ml. per gram) ; the recovery is almost quantitative, m.p. 106°.

VII,10. AMMONIUM SALT OF AURIN TRICARBOXYLIC ACID (" ALUMINON ")

Formaldehyde condenses with salicylic acid in the presence of nitrite-containing sulphuric acid to give aurin tricarboxylic acid ; this is converted by ammonia solution into the ammonium salt, which is employed as a reagent for aluminium (" **aluminon** ") :



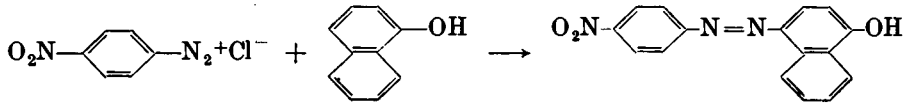
Aurin tricarboxylic acid

Equip a 1 litre bolt-head flask, immersed in an ice bath, with a mechanical stirrer. Place 70 ml. of concentrated sulphuric acid in the flask and add 10 g. of solid sodium nitrite in small portions with vigorous stirring at such a rate that only a very small amount of oxides of nitrogen are evolved. Then introduce, during 15 minutes, 20 g. of powdered salicylic acid. Continue the stirring at 20° until all the solid dissolves : a homogeneous, light red to brown, very viscid solution is obtained. Cool to 0° in a bath of ice and salt, add 5 ml. of formalin (35–40 per cent. formaldehyde) slowly and with very vigorous stirring and at such a rate that the temperature does not rise above 5–10°. The reaction is complete a few minutes after all the formalin has been introduced. Stir vigorously and add about 100 g. of finely-crushed ice, followed by 500 ml. of ice water ; if frothing occurs, add a few drops of ether. Stop the stirring when the

aurin tricarboxylic acid has been disintegrated into small pieces, wash the solid several times with cold water by decantation, and then filter at the pump. Whilst the solid is still on the filter paper in the Buchner funnel, dissolve it in dilute ammonia solution (1 volume of concentrated ammonia solution to 1 volume of water). Evaporate the filtrate to dryness on a water bath. The resulting ammonium salt of aurin tricarboxylic acid (a pale yellowish-brown, glassy solid) weighs 21 g.

VII,11. *p*-NITROBENZENE-AZO-α-NAPHTHOL

p-Nitrobenzenediazonium chloride couples with an alkaline solution of α-naphthol to give *p*-nitrobenzene-azo-α-naphthol :



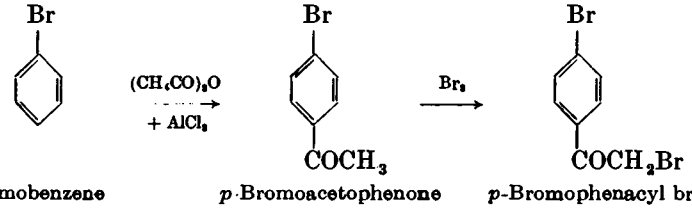
The substance is employed under the name of "**Magneson II**" as a test for magnesium.

Dissolve 5·0 g. of *p*-nitroaniline (Section **IV,51**) in a warm mixture of 13 ml. of concentrated hydrochloric acid and 13 ml. of water contained in a 250 ml. beaker. Place the beaker in an ice-salt bath and cool to 0–5° whilst stirring vigorously ; *p*-nitroaniline hydrochloride will separate in a finely-divided crystalline form. Add a cold solution of 3·7 g. of sodium nitrite in 8 ml. of water slowly and with stirring to an end point with potassium iodide - starch paper : do not allow the temperature of the solution to rise above 8°. Dissolve 5·2 g. of α-naphthol in a solution of 7 g. of sodium hydroxide in 25 ml. of water, cool in ice and add the diazotised solution slowly and with stirring. Then add concentrated hydrochloric acid slowly and with vigorous stirring to the cold mixture until it is strongly acid to Congo red paper. The colour will change from violet to dark red-brown. Filter with *gentle suction*, wash with water until free from acid, and dry upon filter paper in the air. The yield is 21 g.

p-Nitrobenzene-azo-resorcinol ("**Magneson I**") may be similarly prepared by substituting resorcinol for α-naphthol ; it may be recrystallised from methyl alcohol and melts at 199–200°.

VII,12. *p*-BROMOPHENACYL BROMIDE

This substance is conveniently obtained by treating *p*-bromoacetophenone (Section **IV,138**) with the calculated quantity of bromine dissolved in glacial acetic acid :

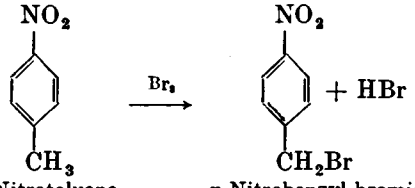


Bromobenzene *p*-Bromoacetophenone *p*-Bromophenacyl bromide

Place a solution of 50 g. of *p*-bromoacetophenone (Section IV,138) in 100 ml. of glacial acetic acid in a 500 ml. flask. Add very slowly (about 30 minutes) from a dropping funnel 40 g. (12·5 ml.) of bromine : shake the mixture vigorously during the addition and keep the temperature below 20°. *p*-Bromophenacyl bromide commences to separate as needles after about half of the bromine has been introduced. When the addition is complete, cool the mixture in ice water, filter the crude product at the pump, and wash it with 50 per cent. alcohol until colourless (about 100 ml. are required). Recrystallise from rectified (or methylated) spirit (*ca.* 400 ml.). The yield of pure *p*-bromophenacyl bromide (colourless needles, m.p. 109°) is 50 g.

VII,13. *p*-NITROBENZYL BROMIDE

Bromination of *p*-nitrotoluene yields *p*-nitrobenzyl bromide :



p-Nitrotoluene *p*-Nitrobenzyl bromide

Place 150 g. of *p*-nitrotoluene, m.p. 51–52°, in a 500 ml. three-necked flask, fitted with a reflux condenser, a liquid-sealed mechanical stirrer, and a separatory funnel with stem reaching nearly to the bottom of the flask. Attach a gas absorption trap (Fig. *II*, *8*, 1, *c*) to the top of the condenser. Heat the flask in an oil bath at 145–150° and add 184 g. (59 ml.) of bromine during 2 hours (1). Continue the stirring for an additional 10 minutes after all the bromine has been added. Pour the contents of the flask whilst still liquid (*CAUTION*) (2) into a 2·5 litre round-bottomed flask containing 2 litres of hot light petroleum, b.p. 80–100°, and 8 g. of decolourising carbon. Attach a reflux condenser to the flask, heat it on an electric hot plate until the material dissolves, boil for 10 minutes, and filter rapidly through a pre-heated Buchner funnel. Cool the filtrate to 20°, filter the crystals with suction, press well and wash with two 25 ml. portions of cold light petroleum. The crude *p*-nitrobenzyl bromide, m.p. 95–97° (150 g.) is sufficiently pure for many purposes. Purify by dissolving in 1500–1700 ml. of light petroleum, b.p. 80–100°, boil with 8 g. of decolourising carbon, and filter through a pre-heated Buchner or sintered glass funnel. Cool the filtrate in ice, filter at the pump, drain well, and wash with two 15 ml. portions of cold light petroleum. The yield of pure *p*-nitrobenzyl bromide (pale yellow crystals, m.p. 98–99°) is 135 g.

Notes.

(1) Improved yields may be obtained by exposing the flask to the light of two 300-watt tungsten lamps during the bromination.

(2) Care must be taken in manipulating the lachrymatory solutions of *p*-nitrobenzyl bromide. If the substance should come into contact with the skin, bathe the affected part with alcohol.

VII,14. *p*-PHENYLPHENACYL BROMIDE

p-Phenylphenacyl bromide may be prepared from diphenyl by the following series of reactions :—

$$\underset{\text{Diphenyl}}{C_6H_5C_6H_5} + (CH_3CO)_2O \xrightarrow{AlCl_3} \underset{p\text{-Phenylacetophenone}}{p\text{-}C_6H_5C_6H_4COCH_3} + CH_3COOH$$

$$p\text{-}C_6H_5C_6H_4COCH_3 + Br_2 \xrightarrow{CH_3COOH} \underset{p\text{-Phenylphenacyl bromide}}{p\text{-}C_6H_5C_6H_4COCH_2Br} + HBr$$

p-Phenylacetophenone. In a 1 litre three-necked flask, provided with a dropping funnel, a mechanical stirrer and a reflux condenser, place 60 g. of diphenyl, 118 g. of finely-powdered anhydrous aluminium chloride and 350 ml. of anhydrous carbon disulphide. Charge the dropping funnel with 42·5 g. (40 ml.) of pure acetic anhydride and close the mouth of the funnel with a calcium chloride or cotton wool guard tube. Heat the mixture on a water bath until gentle refluxing commences, and add the acetic anhydride during 1 hour ; the addition product makes its appearance as a curdy mass when about three-quarters of the anhydride has been added. Reflux the reaction mixture gently for a further hour. Allow to cool and pour the reaction product slowly and with stirring on to crushed ice to which hydrochloric acid has been added. Filter the precipitated *p*-phenylacetophenone on a Buchner funnel (1), wash repeatedly with water until free from acid, dry and distil under reduced pressure. There is usually a small fraction of low boiling point ; the main product passes over at 196–210°/18 mm. and solidifies on cooling. The yield of crude *p*-phenylacetophenone, m.p. 118°, is 66 g. Upon recrystallisation from rectified spirit, the m.p. is raised to 120–121° ; the recovery is about 80 per cent.

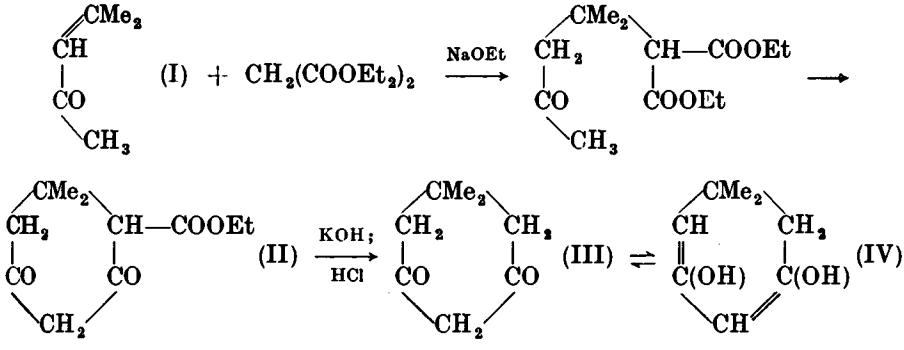
p-Phenylphenacyl bromide. Suspend 36 g. of *p*-phenylacetophenone in 200 ml. of glacial acetic acid in a 500 ml. flask, warm gently on a water bath until a clear solution results, then cool as far as possible without the formation of crystals. To this solution add 29·5 (9·5 ml.) of bromine ; do not allow the temperature to rise above 45° during the addition. The brominated product separates from the solution when about three-quarters of the bromine has been added. After 2 hours, cool the flask in a bath of ice and salt, filter the product, wash with a little cold glacial acetic acid, followed by small volumes of water until all the acid has been removed. The yield of crude material, m.p. 124·5–125·5°, is 42 g. Recrystallise from hot rectified spirit (600–700 ml.) and add a little decolourising carbon to remove the colour : pure, colourless *p*-phenylphenacyl bromide, m.p. 125·5°, is obtained.

Note.

(1) A further quantity of ketone may be isolated by evaporating the solvent from the carbon disulphide layer.

VII,15. 5 : 5-DIMETHYL-1 : 3-*CYCLO*HEXANEDIONE (DIMETHYLDIHYDRORESORCINOL)

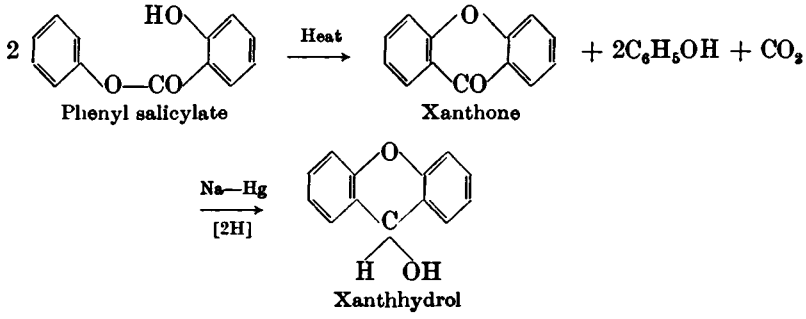
Mesityl oxide (Section III,79) (I) condenses with ethyl malonate in the presence of sodium ethoxide to give the sodium derivative of (II); this upon hydrolysis with aqueous potassium hydroxide, followed by acidification, gives the cyclic diketone 5 : 5-dimethyl-1 : 3-*cyclo*hexanedione (III), of which the enolic form is 5 : 5-dimethyldihydroresorcinol (IV):



Equip a dry 1 litre three-necked flask with a dropping funnel, a mercury-sealed stirrer, and an efficient double surface condenser. Place 11·5 g. of sodium in the flask, cool in an ice bath, and add 200 ml. of absolute ethyl alcohol in one portion. When the initial vigorous reaction has subsided, remove the ice bath and allow the reaction to proceed until all the sodium has reacted: warming on a water bath is sometimes necessary to dissolve the last traces of sodium. Place a calcium chloride (or cotton wool) guard tube at the top of the condenser. Introduce 85 g. of ethyl malonate (Section **III,153**) and then add through the dropping funnel 50 g. of freshly-distilled mesityl oxide (Section **III,79**) slowly. Reflux the mixture with stirring for 2 hours, then add a solution of 62·5 g. of potassium hydroxide in 300 ml. of water, and reflux again on a water bath with stirring for 6 hours. Acidify the reaction mixture (to litmus) while still hot with dilute hydrochloric acid (1 : 2 by volume): about 275 ml. are required. Fit the flask with a condenser for distillation, and distil off as much alcohol as possible by heating with stirring on a water bath. Allow the residue in the flask to cool somewhat, add 8 g. of decolourising carbon slowly, boil for 10 minutes and filter; repeat the treatment with decolourising carbon. Neutralise the residue to litmus by the addition of dilute hydrochloric acid (about 75 ml.) and boil again with 8 g. of decolourising charcoal. Filter and render the hot yellow filtrate distinctly acid to methyl orange with dilute hydrochloric acid (25–50 ml.), boil for a few minutes, and allow to cool whereupon the dimedone crystallises out. Filter at the pump, wash with ice-cold water, and dry in the air. The yield of dimethyldihydroresorcinol, m.p. 147–148°, is 60 g. Recrystallisation from acetone (about 8 ml. per gram) raises the m.p. to 148–149°, but this is generally unnecessary.

VII,16. XANTHHYDROL

Phenyl salicylate upon heating alone yields xanthone; the latter is reduced by sodium amalgam to xanthhydrol:



The substance is employed for the determination of urea and for the characterisation of amides (compare Section III,110).

Xanthone. Secure a 500 ml. Pyrex distilling flask with a side arm 20–25 cm. long and at least 10 mm. in diameter. Place 250 g. of phenyl salicylate in the flask and fit it with two thermometers, one extending just below the side arm and the other to the bottom of the flask. Use a conical flask as a receiver. Heat the flask on an asbestos-centred wire gauze. When the temperature of the liquid reaches 275–285°, phenol commences to distil. Regulate the heating so that the temperature on the upper thermometer never exceeds 175°, but preferably remains below 170°: phenol distils at the rate of 5–10 drops per minute. After 6–7 hours, the temperature of the liquid is 350–355° and phenol practically ceases to distil; the weight of distillate at this point is about 110 g. Change the receiver, raise the lower thermometer from the liquid and distil the contents of the flask as rapidly as possible with a free flame until the tarry residue begins to foam. Pour the distillate (*ca.* 85 g.) whilst still hot into a cold evaporating dish, allow to cool, grind it in a mortar with 50 ml. of 5 per cent. sodium hydroxide solution, then warm it on a water bath for 10–15 minutes with 200 ml. of this alkali solution. When cold, filter off the xanthone, wash it until free from alkali, and dry at 100°. Remove a small amount of low-melting impurity by boiling for 15 minutes with 125 ml. of methyl alcohol, filter when cold, and wash with a little methanol. The yield of xanthone, m.p. 171–172°, is 70 g.; this is sufficiently pure for the preparation of xanthhydrol. If it is required pure, recrystallise from rectified spirit (20 ml. per 1 g. of xanthone); the m.p. is thereby raised to 173–174°.

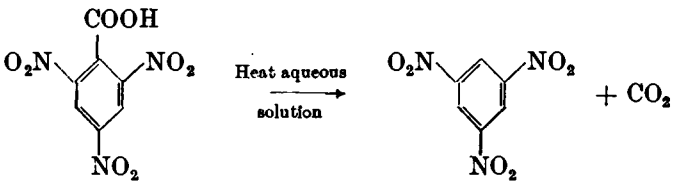
Xanthhydrol. Prepare an amalgam from 9·0 g. of clean sodium and 750 g. (55 ml.) of mercury (Section II,50,7, *Method 1*), and warm it to 50° in a 500 ml. Pyrex bottle. Add a cold suspension of 25 g. of xanthone in 175 ml. of rectified spirit, stopper the bottle and shake vigorously; raise the stopper from time to time to release the pressure. The temperature rises rapidly to 60–70°, the solid xanthone passes into solution, and a transient blue colour is developed. After about 5 minutes the alcoholic solution is clear and almost colourless. Shake for a further 10 minutes, separate the mercury, and wash it with 15 ml. of alcohol. Filter the

alcoholic solution whilst still warm, and pour it slowly and with stirring into 2 litres of cold distilled water. Filter the precipitated xanthhydrol with suction, wash it with water until free from alkali, and dry at 40–50° to constant weight. The yield of practically pure xanthhydrol, m.p. 122–123°, is 24 g. Recrystallisation from alcohol raises the m.p. by 1°.

The substance is comparatively unstable ; it should be prepared when required or else kept in an alcoholic solution.

VII,17. 1 : 3 : 5-TRINITROBENZENE

1 : 3 : 5-Trinitrobenzene may be prepared by heating the sodium salt of 2 : 4 : 6-trinitrobenzoic acid with water :

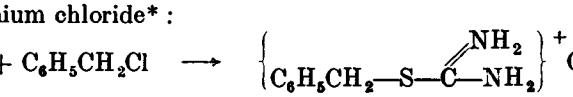


The compound is employed for the characterisation of aromatic hydrocarbons (compare Section IV,9), ethers and amines.

Dissolve 55 g. of crude 2 : 4 : 6-trinitrobenzoic acid (Section IV,142) in 400 ml. of water at 35° contained in a 1 litre bolt-head flask provided with a mechanical stirrer. Add 15 per cent. sodium hydroxide solution, with continuous stirring, until a *faint* red colour is *just* produced and take care that the temperature does not rise above 55° ; discharge the colour by means of one or two drops of acetic acid and filter, if necessary, from unchanged trinitrotoluene. Treat the solution (or filtrate) in a 1 litre bolt-head flask with 14 ml. of glacial acetic acid and warm the mixture gently with continuous stirring : reduce the flame when once the evolution of carbon dioxide sets in otherwise the mixture might foam over. The trinitrobenzene separates in a crystalline condition and floats on the surface of the liquid as a frothy layer. The evolution of gas ceases after about 90 minutes : heat and stir for a further 45 minutes, allow to cool, and filter the crystals. Test the filtrate for undecomposed trinitrobenzoic acid by adding sulphuric acid : if a precipitate is produced, continue the heating of the filtrate. Recrystallise the compound from glacial acetic acid. The yield of 1 : 3 : 5-trinitrobenzene, m.p. 121–122°, is 30 g.

VII,18. *S*-BENZYL-*ISO*-THIURONIUM CHLORIDE

Benzyl chloride reacts with thiourea in dilute alcoholic solution to give *S*-benzyl-*iso*-thiuronium chloride* :



The compound separates in either, sometimes as both, of two dimorphic forms, m.p. 150° and 175° respectively. The former may be converted into the higher m.p. form by dissolving it in alcohol and seeding with crystals of the form, m.p. 175° : the low m.p. form when warmed to 175° gives, after solidification, a m.p. of 175°. Both dimorphic forms give identical derivatives with carboxylic acids and sulphonic acids (see Sections III,85 and IV,33).

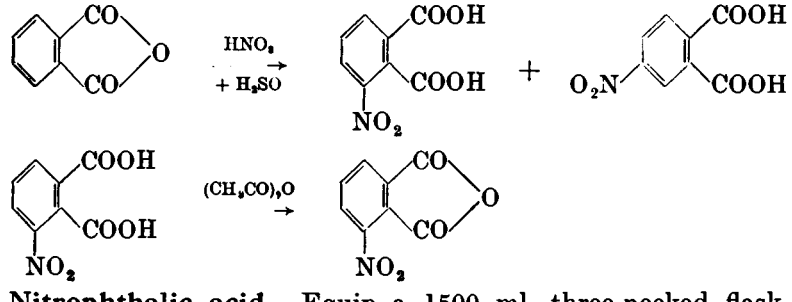
* Also known as *S*-benzyl-*ψ*-thiuronium chloride and as *S*-benzyl*iso*thiourea hydrochloride.

Method 1. Dissolve 76 g. of thiourea in 200 ml. of warm water in a 750 ml. or 1 litre round-bottomed flask. Dilute the solution with 135 ml. of rectified spirit and add 126·5 g. of benzyl chloride. Heat the mixture under reflux on a water bath until the benzyl chloride dissolves (about 15 minutes) and for a further 30 minutes taking care that the mixture is well shaken from time to time. Cool the mixture in ice : there is a tendency to supersaturation so that it is advisable to stir (or shake) the cold solution vigorously, when the substance crystallises suddenly. Filter off the solid at the pump. Evaporate the filtrate to about half bulk in order to recover a further small quantity of product. Dry the compound upon filter paper in the air. The yield of *S*-benzyl-*iso*-thiuronium chloride m.p. 174°, is 205 g. Recrystallise the salt from 400 ml. of 0·2*N* hydrochloric acid ; filter off the solid which separates on cooling. Concentrate the filtrate to recover a further small quantity. The yield of recrystallised salt, m.p. 175° is 185 g. ; some of the dimorphic form, m.p. 150°, may also separate.

Method 2. Place a mixture of 126·5 g. of benzyl chloride, 76 g. of thiourea and 150 ml. of rectified spirit in a 500 ml. round-bottomed flask fitted with a reflux condenser. Warm on a water bath. A sudden exothermic reaction soon occurs and all the thiourea passes into solution. Reflux the resulting yellow solution for 30 minutes and then cool in ice. Filter off the white crystals and dry in the air upon filter paper. Concentrate the filtrate to half its original volume and thus obtain a further small crop of crystals. The yield of crude *S*-benzyl-*iso*-thiuronium chloride, m.p. 145°, is 236 g. Recrystallise from 0·2*N* hydrochloric acid as in *Method 1* ; the m.p. is raised to 150°, although on some occasions the form, m.p. 175°, separates.

VII,19. 3-NITROPHTHALIC ANHYDRIDE

The nitration of phthalic anhydride with a mixture of concentrated sulphuric and nitric acids yields a mixture of 3-nitro- and 4-nitro-phthalic acids ; these are readily separated by taking advantage of the greater solubility of the 4-nitro acid in water. Treatment of 3-nitrophthalic acid with acetic anhydride gives 3-nitrophthalic anhydride.



3-Nitrophthalic acid. Equip a 1500 ml. three-necked flask, supported on a water or steam bath, with a dropping funnel, a mechanical stirrer and a thermometer : the neck through which the stirrer passes should be open and the stirrer should be connected by means of a belt to the motor (nitrous fumes are evolved in the subsequent reaction and these would damage the motor if supported directly over the reaction

mixture). Place 250 g. of technical phthalic anhydride and 325 ml. of concentrated sulphuric acid in the flask and heat it until the temperature of the mixture rises to 80°. Shut off the steam or cool the water bath, and add 105 ml. of fuming nitric acid (sp. gr. 1·5) slowly from the dropping funnel at such a rate so as to maintain the temperature of the stirred mixture at 100–110° (about 1 hour). Then add 450 ml. of concentrated nitric acid (sp. gr. 1·42) as rapidly as possible without causing the temperature to rise above 110°. Heat the mixture on the water or steam bath, with stirring, for 2 hours. Allow the reaction mixture to stand overnight and then pour it into 750 ml. of cold water contained in a 2 litre beaker. Cool and filter the mixture of 3- and 4-nitrophthalic acids through a sintered glass funnel. Return the wet cake of acids to the rinsed-out beaker and stir it thoroughly with 100 ml. of water, which dissolves a large amount of the 4-nitrophthalic acid (1). Filter again at the pump and dissolve the solid in 100–150 ml. of boiling water : filter the hot solution and stir mechanically until crystallisation commences and then leave overnight until crystallisation is complete. Filter again with suction and dry upon filter paper. The yield of crude 3-nitrophthalic acid, m.p. 208–210° (sealed tube), is 110 g. Recrystallisation from about 250 ml. of boiling water (2) gives about 90 g. of the pure acid, m.p. 216–118° (sealed capillary tube).

Notes.

(1) The mother liquors from the washings and recrystallisations are saved for the recovery of the 4-nitrophthalic acid. The combined mother liquors are concentrated to a small bulk and the acid is extracted with ether. Upon esterification by the Fischer-Speier method, the 3-nitro acid forms only the acid ester and may be removed by shaking the product with sodium carbonate solution, whilst the neutral ester of 4-nitrophthalic acid remains unaffected. Hydrolysis of the neutral ester gives the pure 4-nitrophthalic acid, m.p. 165°.

(2) The acid may also be crystallised from glacial acetic acid.

3-Nitrophthalic anhydride. In a 250 ml. round-bottomed flask, fitted with a reflux condenser, place 75 g. of 3-nitrophthalic acid and 70 g. (65 ml.) of redistilled acetic anhydride. Heat the mixture to gentle boiling until a clear solution is obtained, and then for about 10 minutes longer. Pour the hot mixture (*FUME CUPBOARD*) into a large porcelain dish and allow to cool. Grind the crystalline mass thoroughly in a mortar and filter at the pump through a sintered glass funnel. Return the crystals to the mortar, grind them with 50 ml. of sodium-dried ether and filter. Again return the crystals to the mortar and wash once more with 50 ml. of dry, alcohol-free ether. Dry in the air for a short time, and then to constant weight at 100°. The yield of 3-nitrophthalic anhydride, m.p. 163–164°, is 60 g. If the m.p. is unsatisfactory, recrystallise the anhydride from benzene or from benzene - light petroleum.

VII,20. DIAZOMETHANE

Liquid diazomethane CH_2N_2, b.p. −24°, is an explosive compound and explosions may also occur in the gaseous state if the substance is dry and undiluted. The gas may be handled with safety by diluting it with nitrogen. For synthetical work, a dry ethereal solution of the gas is employed and this can be handled with safety ; due regard must, however, be paid to the poisonous

and highly toxic character of the gas by carrying out all operations in an efficient fume cupboard (hood).

An ethereal solution of diazomethane is usually prepared immediately before it is required for reaction. Two intermediates may be used for this purpose, *viz.*, nitrosomethylurea and *p*-tolylsulphonylmethylnitrosamide: a number of methods are available for obtaining the former; the latter is prepared from methylamine and *p*-toluenesulphonyl chloride. Nitrosomethylurea is not very stable at room temperatures and must be kept at 0°; on the other hand *p*-tolylsulphonylmethylnitrosamide is a stable solid, which can be kept for long periods at room temperature in a dark bottle.

Nitrosomethylurea is conveniently prepared by treating acetamide (2·0 mols) with bromine (1·1 mols), followed by 10–25 per cent aqueous caustic alkali (2·0 mols) when acetylmethylurea is produced:

$$CH_3CONH_2 + Br_2 + 2NaOH \longrightarrow CH_3N{=}C{=}O + 2NaBr + 2H_2O$$
$$CH_3N{=}C{=}O + CH_3CONH_2 \longrightarrow CH_3NHCONHCOCH_3$$

Excess of alkali must be avoided, otherwise the *iso*cyanate (formed intermediately) is converted into an amine:

$$CH_3N{=}C{=}O + 2NaOH \longrightarrow CH_3NH_2 + Na_2CO_3$$

The acetylmethylurea is converted by concentrated hydrochloric acid into methylurea; the latter yields nitrosomethylurea with nitrous acid:

$$CH_3NHCONHCOCH_3 + H_2O \longrightarrow CH_3NHCONH_2 + CH_3COOH$$
$$CH_3NHCONH_2 + HONO \longrightarrow CH_3N(NO)CONH_2 + H_2O$$

An alternative method of preparation involves the interaction of methylamine hydrochloride with urea to give methylurea, followed by interaction with nitrous acid as above:

$$CH_3NH_3Cl + H_2NCONH_2 \longrightarrow CH_3NHCONH_2 + NH_4Cl$$

Upon shaking nitrosomethylurea in the cold with a mixture of aqueous potassium hydroxide solution and pure ether, diazomethane is formed: the latter may be distilled off at 50° and collected in ether:

$$CH_3N(NO)CONH_2 + KOH \longrightarrow CH_2N_2 + KCNO + 2H_2O$$

***p*-Tolylsulphonylmethylnitrosamide** is obtained as follows. Interaction of *p*-toluenesulphonyl chloride and methylamine yields *p*-toluenesulphonylmethyl amide:

$$p\text{-}CH_3.C_6H_4.SO_2Cl + 2CH_3NH_2 \longrightarrow p\text{-}CH_3.C_6H_4.SO_2.NHCH_3 + CH_3NH_2,HCl$$

In order to secure the maximum conversion of the methylamine into the sulphonylmethylamide, the *p*-toluenesulphonyl chloride is introduced in several portions, and sodium hydroxide solution is added after each portion to liberate the methylamine from the hydrochloride formed in the reaction:

$$CH_3NH_2,HCl + NaOH \longrightarrow CH_3NH_2 + NaCl + H_2O$$

Treatment of the sulphonylmethylamide with nitrous acid gives *p*-tolylsulphonylmethylnitrosamide:

$$p\text{-}CH_3.C_6H_4.SO_2.NHCH_3 + HNO_2 \longrightarrow p\text{-}CH_3.C_6H_4.SO_2N(NO)CH_3 + H_2O$$

If alcoholic potassium hydroxide is added to an ethereal solution of the methylnitrosamide and the mixture distilled, an ethereal solution of diazomethane is obtained in high yield:

$$p\text{-}CH_3\cdot C_6H_4\cdot SO_2\cdot N(NO)CH_3 + KOH \longrightarrow p\text{-}CH_3.C_6H_4.SO_2.OK + CH_2N_2 + H_2O$$

The structure of diazomethane is probably best represented as resonance hybrid :

$$H_2C{=}N{\rightleftarrows}N \longleftrightarrow H_2C{\leftarrow}N{\equiv}N$$

or as

$$H_2C{=}\overset{+}{N}{=}\overset{-}{\underset{\cdot\cdot}{N}}: \longleftrightarrow H_2\overset{-}{\underset{\cdot\cdot}{C}}{-}\overset{+}{N}{\equiv}N:$$

Nitrosomethylurea. *Acetamide method.* To a solution of 59 g. of acetamide in 88 g. (28 ml.) of bromine (1) in a 4-litre beaker add dropwise, with hand stirring, a solution of 40 g. of sodium hydroxide in 160 ml. of water. Heat the resulting yellow reaction mixture on a steam bath until effervescence sets in (2), after which continue the heating for 2–3 minutes. Crystallisation of the product from the yellow or red coloured solution usually commences immediately. Cool in an ice bath for 1–2 hours, collect the product by suction filtration, wash with a little ice-cold water, and dry in the air. The yield of colourless **acetylmethylurea**, m.p. 178–180°, is 50 g.

Heat a mixture of 49 g. of acetylmethylurea (3) and 50 ml. of concentrated hydrochloric acid, with hand stirring, on a steam bath until it is apparent that no more solid is dissolving (4) and continue the heating for 3–4 minutes longer : the total time of heating on the steam bath should be 8–12 minutes. Dilute the solution with 50 ml. of water and cool below 10° in an ice bath. Run in slowly and with stirring a cold saturated solution of 38 g. of A.R. sodium nitrite in 55 ml. of water below the level of the liquid. Keep the mixture in the ice bath for 5–10 minutes, filter the solid at the pump and wash it with 8–10 ml. of ice-cold water. Dry the nitrosomethylurea (pale yellow crystals) in the air or in a vacuum desiccator (5) ; the yield is 34 g., m.p. 123–124°.

Methylamine hydrochloride method. Place 100 g. of 24 per cent. methylamine solution (6) in a tared 500 ml. flask and add concentrated hydrochloric acid (about 78 ml.) until the solution is acid to methyl red. Add water to bring the total weight to 250 g., then introduce 150 g. of urea, and boil the solution gently under reflux for two and three-quarter hours, and then vigorously for 15 minutes. Cool the solution to room temperature, dissolve 55 g. of 95 per cent. sodium nitrite in it, and cool to 0°. Prepare a mixture of 300 g. of crushed ice and 50 g. of concentrated sulphuric acid in a 1500 ml. beaker surrounded by a bath of ice and salt, and add the cold methylurea - nitrite solution slowly and with mechanical stirring and at such a rate (about 1 hour) that the temperature does not rise above 0°. It is recommended that the stem of the funnel containing the methylurea - nitrite solution dip below the surface of the acid solution. The nitrosomethylurea rises to the surface as a crystalline foamy precipitate. Filter at once at the pump, and drain well. Stir the crystals into a paste with about 50 ml. of cold water, suck as dry as possible, and dry in a vacuum desiccator to constant weight. The yield is 55 g. (5).

Diazomethane. *CAUTION. Diazomethane is highly toxic : its preparation should be carried out only in a fume cupboard (hood) provided with a powerful exhaust system. The use of a screen of safety glass is recommended.*

Place 60 ml. of 50 per cent. aqueous potassium hydroxide solution and 200 ml. of pure ether in a 500 ml. round-bottomed flask. Cool the

mixture to 5°, and add 20·6 g. of nitrosomethylurea with shaking. Equip the flask with a condenser set for distillation, attach to the lower end of the condenser an adapter passing through a two-holed rubber stopper and dipping below the surface of 40 ml. of pure ether contained in a 300 ml. conical flask and immersed in an ice-salt mixture ; pass the exit gases through a second 40 ml. portion of ether in a 300 ml. wash bottle cooled below 0°. Place the reaction flask on a water bath at 50° and bring it to the boiling point of the ether (7) ; shake occasionally. Distil the ether until it passes over colourless ; this is usually the case when about two-thirds of the ether has been distilled. *Under no circumstances should all the ether be distilled as an explosion may result.* The combined ether solutions in the receivers contain 5·4–5·9 g. of diazomethane (8) : this is sufficiently dry for most purposes. If a really dry solution is required, the ether solution may be allowed to stand for 2–3 hours over pellets of A.R. potassium hydroxide. The anhydrous ethereal solution may be kept for a day or two, but it undergoes gradual decomposition with the liberation of gas. The containing vessel should therefore be protected by a calcium chloride (or cotton wool) guard tube and kept in a refrigerator.

p*-Tolylsulphonylmethylnitrosamide. Divide 320 g. of *p*-toluenesulphonyl chloride, m.p. 68–69° (9) into three portions of 190, 90 and 40 g. Prepare a solution of 70 g. of sodium hydroxide in 70 ml. of water and cool to room temperature. Place 210 ml. of 33 per cent. aqueous methylamine solution (or 174 ml. of the 40 per cent. aqueous solution) in a 1-litre round-bottomed flask and add the 190 g. of *p*-toluenesulphonyl chloride in portions with swirling during about 5 minutes. The mixture becomes warm. Allow the temperature to rise to 80–90° in order to maintain the sulphonylmethylamide (m.p. 78°) in a molten condition, otherwise the latter may form a hard cake and reaction may be incomplete ; also do not permit the temperature to rise above 90° as appreciable loss of methylamine may result. The mixture should be acid to litmus within 5 minutes after the completion of the first addition of the sulphonyl chloride (10). Then add 50 ml. of the 50 per cent. sodium hydroxide solution carefully with swirling, followed immediately by 90 g. of the sulphonyl chloride in portions as before. When the mixture has again become acidic (10), introduce 25 ml. of the sodium hydroxide solution, followed by 40 g. of the *p*-toluenesulphonyl chloride with vigorous swirling. After the mixture has again become acidic, add the remainder of the sodium hydroxide solution. The liquid phase of the final mixture should be alkaline ; if it is acidic, indicating excessive loss of methylamine, add sufficient methylamine solution to render the mixture basic.

Rinse the walls of the flask with a little water and complete the reaction by heating the mixture (which consists of two layers and a precipitate of sodium chloride) on a boiling water bath for 15 minutes with vigorous mechanical stirring. Pour the *hot* reaction mixture into 1500 ml. of glacial acetic acid contained in a 4-litre round-bottomed flask ; rinse the flask with 250 ml. of acetic acid. Cool the solution in an ice bath to 5° (11), stir mechanically, and add a solution of 125 g. of sodium nitrite in 250 ml.

* These experimental details are reproduced by kind permission of Professor H. J. Backer.

of water from a dropping funnel during about 45 minutes : maintain the temperature below 10° and continue the stirring for 15 minutes after the addition is complete. The nitroso derivative separates as a yellow crystalline solid during the reaction. Add 1 litre of water to the reaction mixture and collect the precipitate by suction filtration; press it on the funnel and wash with about 500 ml. of water. Transfer the product to a beaker, stir it well with about 400 ml. of water, then filter and wash again on the funnel until the odour of acetic acid is no longer apparent. Dry to constant weight in a vacuum desiccator over concentrated sulphuric acid. The yield of *p*-tolylsulphonylmethylnitrosamide, m.p. 58–60°, is 325 g. This is sufficiently pure for the preparation of diazomethane. It should be kept in a dark bottle. It may be recrystallised by dissolution in boiling ether (1 ml./g.), addition of an equal volume of light petroleum, b.p. 40–50°, and cooling in a refrigerator.

Diazomethane. *CAUTION. Diazomethane is very toxic ; its preparation should be carried out only in a fume cupboard (hood) provided with a powerful exhaust system. The use of a screen of safety glass is recommended.*

The following procedures may be used for the preparation of ethereal solutions of diazomethane containing ethyl alcohol ; they differ slightly according to as to whether large or small quantities are required. The presence of alcohol is not harmful for many applications of diazomethane. (It may be pointed out that ethereal diazomethane solution prepared from nitrosomethylurea is free from alcohol.)

(*a*) Add 50 ml. of 96 per cent. ethanol to a solution of 10 g. of potassium hydroxide in 15 ml. of water. Place this solution in a 200 ml. distillation flask equipped with a dropping funnel and an efficient double surface condenser. Connect the condenser to two conical flasks (of 500 ml. and 100 ml. capacity respectively) to act as receivers ; charge the smaller flask with 40 ml. of ether and arrange that the inlet tube of the smaller receiver dips below the surface of the ether. Cool both receivers in an ice - salt mixture. Heat the distilling flask in a water bath at 60–65° (7); place a solution of 43 g. of *p*-tolylsulphonylmethylnitrosamide in about 250 ml. of ether in the dropping funnel and introduce it into the flask over a period of 45 minutes. Adjust the rate of addition so that it is about equal to the rate of distillation. When the dropping funnel is empty, add more ether (*ca.* 30 ml.) gradually until the ether distilling over is colourless. The combined ethereal solutions in the receivers contain 5·9–6·1 g. of diazomethane (8).

(*b*) For smaller quantities of diazomethane, the use of a dropping funnel is unnecessary. Dissolve 2·14 g. of *p*-tolylsulphonylmethylnitrosamide in 30 ml. of ether, cool in ice, and add a solution of 0·4 g. of potassium hydroxide in 10 ml. of 96 per cent. ethanol. If a precipitate forms, add more ethanol until it just dissolves. After 5 minutes, distil the ethereal diazomethane solution from a water bath (7). The ethereal solution contains 0·32–0·35 g. of diazomethane (8).

An ethereal solution of diazomethane free from alcohol may be prepared as follows : such a solution is required, for example, in the Arndt-Eistert reaction with acid chlorides (compare Section VI,17). In a 100 ml. long-necked distilling flask provided with a dropping funnel and an efficient downward condenser, place a solution of 6 g. of potassium hydroxide in

10 ml. of water, 35 ml. of carbitol (diethyleneglycol monethyl ether) and 10 ml of ether : connect the condenser to two conical flasks in series containing 10 and 35 ml. of ether respectively and cooled in an ice-salt bath. Heat the mixture on a water bath at 70–75° (7) and as soon as the ether commences to distil, add a solution of 21·5 g. of *p*-tolylsulphonylmethylnitrosamide in 125 ml. of ether through the dropping funnel during a period of about 15 minutes. Shake the flask vigorously during the distillation; alternatively, pass a slow stream of nitrogen through the distilling flask during the distillation. After the addition of the nitrosamide, add 30–40 ml. of ether through the dropping funnel and distil until the distillate is colourless. The ethereal solution in the conical flasks contains about 3·4 g. of diazomethane (8).

Notes.

(1) It may be necessary to heat gently on a steam bath to dissolve the acetamide, and care should be taken that only the minimum amount of bromine is lost during the heating.

(2) The effervescence may become quite brisk: this is the reason for using a large container.

(3) The total yield of crude acetylmethylurea may be used without drying.

(4) If much sodium bromide is present in the crude acetylmethylurea, this will not dissolve in the concentrated hydrochloric acid ; it dissolves, however, when the solution is diluted and has no effect upon the subsequent treatment with sodium nitrite.

(5) The preparation can be kept for long periods in a refrigerator, preferably in smooth, brown, alkali-free bottles ; it should not be kept above 20° for more than a few hours : at 30°, it may undergo sudden decomposition and a serious explosion may result.

(6) Determine the methylamine content of the commercial solution by titration with standard acid using methyl orange as indicator. Adjust the quantity of methylamine solution in accordance with the methylamine content ; for some commercial samples, the figure may be 33–40 per cent.

(7) Diazomethane is easily decomposed by rough surfaces : for this reason glass apparatus with scratches and also "porous pot" ("boiling stones") should not be used.

(8) To determine the exact diazomethane content, allow an aliquot portion of the ethereal diazomethane solution to react with an accurately weighed amount (say, about 1 g.) of A. R. benzoic acid in 50 ml. of anhydrous ether. The solution should be completely decolourised, thus showing that the benzoic acid is present in excess. Dilute the solution with water and titrate the excess of benzoic acid with standard 0·1*N* alkali using phenolphthalein as indicator.

(9) It may be recrystallised from benzene - light petroleum, b.p. 60–80° (1 : 20).

(10) Occasionally the liquid may not become acidic after the first or second addition, even through the sulphonyl chloride has reacted completely. (This is due to a smaller loss of methylamine than is expected.) If such is the case, no more than 5 minutes should be allowed between successive additions of sulphonyl chloride and alkali. The whole procedure occupies about 30 minutes.

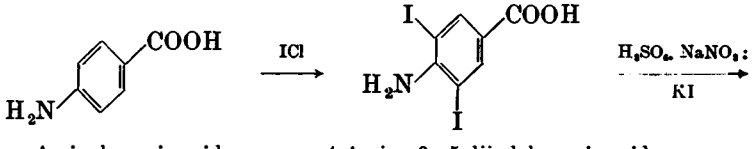
(11) A reaction temperature below 0° should be avoided because the total volume of acetic acid is just sufficient to keep the sulphonylmethylamide in solution above 0°.

The diazomethane-ether solution should be dry. If in doubt, it may be dried with A.R. potassium hydroxide pellets. The anhydrous ethereal solution may be stored in a smooth glass flask or bottle in a refrigerator for a week or so ; since slow decomposition occurs with liberation of gas, the containing vessel should be protected by a calcium chloride (or cotton wool) guard tube.

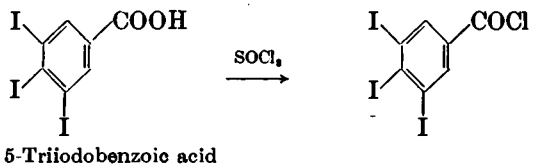
Methylation with diazomethane may be carried out as follows (*FUME CUPBOARD!*): Dissolve 2–3 g. of the compound (say, a phenol or a carboxylic acid) in a little anhydrous ether or absolute methanol, cool in ice, and add the ethereal solution of diazomethane in small portions until gas evolution ceases and the solution acquires a pale yellow colour. Test the coloured solution for the presence of excess of diazomethane by removing a few drops into a test-tube and introducing a glass rod moistened with glacial acetic acid : immediate evolution of gas should occur. Evaporate the solvent, and purify the product by distillation or crystallisation.

VII,21. 3 : 4 : 5-TRIIODOBENZOYL CHLORIDE

3 : 4 : 5-Triiodobenzoyl chloride may be prepared by the following series of reactions :



p-Aminobenzoic acid 4-Amino-3 : 5-diiodobenzoic acid



3 : 4 : 5-Triiodobenzoic acid

It is an excellent reagent for the characterisation of alcohol-ethers (see Section III,27).

4-Amino-3 : 5-diiodobenzoic acid. In a 2 litre beaker, provided with a mechanical stirrer, dissolve 10 g. of pure *p*-aminobenzoic acid, m.p. 192° (Section IX,5) in 450 ml. of warm (75°) 12·5 per cent. hydrochloric acid. Add a solution of 48 g. of iodine monochloride (1) in 40 ml. of 25 per cent. hydrochloric acid and stir the mixture for one minute : during this time a yellow precipitate commences to appear. Dilute the reaction mixture with 1 litre of water whereupon a copious precipitate is deposited. Raise the temperature of the well-stirred mixture gradually and maintain it at 90° for 15 minutes. Allow to cool to room temperature, filter, wash thoroughly with water and dry in the air ; the yield of crude acid is 24 g. Purify the product by dissolving it in dilute sodium hydroxide solution and precipitate with dilute hydrochloric acid : the yield of air-dried 4-amino-3 : 5-diiodobenzoic acid, m.p. >350°, is 23 g.

3 : 4 : 5-Triiodobenzoic acid. Dissolve 6·8 g. of 3 : 5-diiodo-4-aminobenzoic acid in 30 ml. of cold concentrated sulphuric acid, add a large excess (3·0 g.) of powdered sodium nitrite, and allow the mixture to stand at 0° for 2 hours. Treat the cold diazonium solution with a solution of 17·0 g. of potassium iodide in 40 ml. of water ; a dark red precipitate separates. Warm the mixture on a water bath until the evolution of nitrogen ceases, and remove any residual iodine with a little

sodium bisulphite. Filter the light yellow precipitate of crude 3 : 4 : 5-triiodobenzoic acid, and recrystallise from dilute alcohol. The yield of the pure acid, m.p. 289–290°, is 6·8 g.

3 : 4 : 5-Triiodobenzoyl chloride. Reflux 5 g. of 3 : 4 : 5-triiodobenzoic acid, m.p. 289–290°, gently with 10 ml. of redistilled thionyl chloride for 2 hours. Distil off the excess of thionyl chloride on a water bath, and recrystallise the residue from carbon tetrachloride - light petroleum with the use of a little decolourising charcoal. The yield of the acid chloride (bright yellow needles, m.p. 138°) is 3·8 g.; it keeps well in a stoppered bottle.

Note.

(1) Iodine monochloride may be prepared as follows. Pass dry chlorine into 127 g. of iodine contained in a 125 ml. distilling flask until the weight has increased by 34·5 g. The chlorine should be led in at or below the surface of the iodine whilst the flask is gently shaken; it is essential to have an excess of iodine. Distil the iodine chloride in an ordinary distillation apparatus: use a filter flask, protected from atmospheric moisture by a calcium chloride (or cotton wool) guard tube, as a receiver. Collect the fraction b.p. 97–105°; the yield is 140 g. Preserve the iodine monochloride in a dry, glass-stoppered bottle.

Since iodine monochloride attacks cork and rubber, the use of an all-glass apparatus is recommended. If it should come into contact with the skin, an effective antidote is dilute hydrochloric acid (1 : 1).

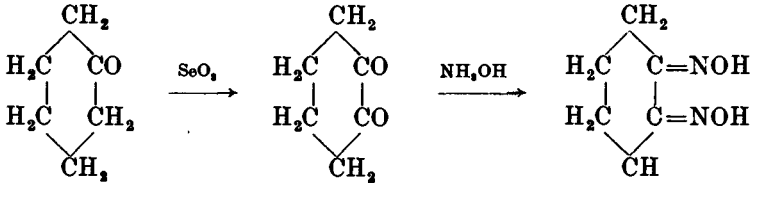
VII,22. 3 : 5-DINITROBENZOYL CHLORIDE

Place a mixture of 30 g. of 3 : 5-dinitrobenzoic acid (Section IV,168 and 33 g. of phosphorus pentachloride in a Claisen flask: fit a reflux condenser into the short neck and cork the other neck and side arm (compare Fig. *III*, *31*, 1). Heat the mixture in an oil bath at 120–130° for 75 minutes. Allow to cool. Remove the phosphorus oxychloride by distillation under reduced pressure (25°/20 mm.); raise the temperature of the bath to 110°. The residual 3 : 5-dinitrobenzoyl chloride solidifies on cooling to a brown mass; the yield is quantitative. Recrystallise from carbon tetrachloride: the yield is 25 g., m.p. 67–68° and this is satisfactory for most purposes. Further recrystallisation from a large volume of light petroleum b.p. 40–60°, gives a perfectly pure product, m.p. 69·5°.

3 : 5-Dinitrobenzoyl chloride reacts readily with water and it should be kept in sealed tubes or under light petroleum. When required for qualitative organic analysis it is usually best prepared from 3 : 5-dinitrobenzoic acid immediately before use (see Section III,27,*I*).

VII,23. 1 : 2-*CYCLO*HEXANEDIONE-DIOXIME (NIOXIME)

*cyclo*Hexanone is oxidised by selenium dioxide to 1 : 2-*cyclo*hexanedione, and the latter is converted into the dioxime by treatment with aqueous hydroxylamine hydrochloride and aqueous potassium hydroxide.



This reagent, to which the name nioxime has been given, is employed for the determination of palladium and may also be used for nickel: it is soluble in water, and possesses advantages over dimethylglyoxime. The latter is used as a solution in alcohol and may therefore contaminate the palladium or nickel precipitate when added to an aqueous solution.

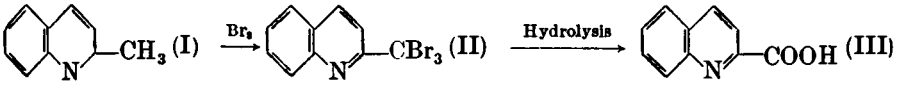
1 : 2-*cyclo*Hexanedione. Equip a 1-litre, three-necked flask with a reflux condenser, thermometer and dropping funnel. Place 250 g. of pure *cyclo*hexanone (preferably ex bisulphite compound) in the flask, heat to 70–80°, and add a solution of 280 g. of pure selenium dioxide in 1500 ml. of rectified spirit (95 per cent. ethyl alcohol) from the dropping funnel over a period of 2 hours, maintaining the temperature at 70–80°. Reflux the reaction mixture for a further 2 hours. Distil off as much of the alcohol as possible and decant the liquid residue from the elementary selenium. Wash the latter several times with ether, and combine the ether extracts with the decanted liquid. Remove the ether by distillation and distil the residue under reduced pressure (*ca.* 25 mm.): about 200 g. of an oil, consisting of 1 : 2-*cyclo*hexanedione, *cyclo*hexanone and water, is obtained. Dissolve the oil in 1 litre of ether, and extract thrice with ice-cold 10 per cent. potassium hydroxide solution; the total amount of potassium hydroxide solution should be equivalent to 1·5 times that necessary to react with the oil assumed to be the pure dione in the monoenol form. Shake the alkaline extract once with ether to remove *cyclo*hexanone, acidify with ice-cold hydrochloric acid, and then saturate with salt. Extract the hydrochloric acid solution with ether, dry the ethereal extract with anhydrous magnesium sulphate, remove the ether by distillation at normal pressure, and distil the residue under reduced pressure. Collect the 1 : 2-*cyclo*hexanedione (a pale green liquid) at 96–97°/25 mm.; the compound decomposes slightly on keeping. The yield is 55–56 g.

It is important that the synthesis should be carried out as quickly as possible, particularly the washing with alkali at 0°, since the latter tends to convert the product into *cyclo*pentane-α-hydroxycarboxylic acid.

1 : 2-*cyclo*Hexanedione-dioxime. Dissolve 55 g. of the freshly distilled dione in 500 ml. of water, cool the solution to 0°, and dissolve 170 g. of pure hydroxylamine hydrochloride in it. Add a solution of 225 g. of potassium hydroxide in 1 litre of water at 0° dropwise over a period of 15 minutes with constant mechanical stirring. Heat the mixture on a steam bath for 2 hours, cool to 0°, neutralise with "dry ice," saturate with salt, filter off the precipitated dioxime, and wash with a little ice-cold water. Recrystallise the crude dioxime from water. The yield of pure *cyclo*hexanedione-dioxime (white needles), m.p. 187–188° (decomp.), is 39 g.

VII,24. QUINALDINIC ACID

Bromination of quinaldine (I) (Section V,2) with bromine in glacial acetic acid in the presence of anhydrous sodium acetate affords ω-tribromoquinaldine or 2-(tribromomethyl)-quinaldine (II); hydrolysis of the latter by boiling with dilute sulphuric acid gives quinaldinic acid (III).



Fit a 500 ml. bolt-head flask with a reflux condenser and dropping funnel. Place a mixture of 50 g. of anhydrous, powdered sodium acetate, 100 g. of glacial acetic acid and 14 g. of pure quinaldine in the flask, and a solution of 48 g. (15·5 ml.) of bromine in 100 g. of glacial acetic acid in the dropping funnel. Heat the flask to 70° in a water bath, and add the bromine solution during 10–15 minutes whilst keeping the mixture thoroughly shaken. Boil the solution for a few minutes (until the separation of sodium bromide causes violent bumping), then heat for 30 minutes on a water bath, and allow to cool. Pour the reaction mixture into 300 ml. of ice-water, collect the precipitate by suction filtration, and wash thoroughly with water. The yield of crude product, after drying at 100°, is 36 g. Recrystallise if from alcohol or glacial acetic acid: the pure ω-tribromoquinaldine has m.p. 128°.

Hydrolyse the ω-tribromoquinaldine by boiling it under reflux with excess of dilute (1 : 10) sulphuric acid until a test portion, on neutralisation, yields no unchanged halogen compound. The quinaldinic acid is best isolated, via the copper salt, in the following manner. Cool, nearly neutralise the solution and add excess of copper sulphate solution. Collect the pale green copper quinaldinate by suction filtration and wash it well with cold water. Suspend the copper salt in hot water and subject it to prolonged treatment with hydrogen sulphide gas. Filter off the copper sulphide and evaporate the clear filtrate to dryness on a water bath. Recrystallise the residual quinaldinic acid from glacial acetic acid; it then melts at 157°. The yield is almost quantitative.

VII,25. GIRARD'S REAGENTS 'T' and 'P'

Girard's reagent 'T' is carbohydrazidomethyltrimethylammonium chloride (I) and is prepared by the reaction of the quaternary ammonium salt formed from ethyl chloroacetate and trimethylamine with hydrazine hydrate in alcoholic solution:

$$(CH_3)_3N + ClCH_2COOC_2H_5 \longrightarrow Cl\{(CH_3)_3NCH_2COOC_2H_5\}$$

$$Cl\{(CH_3)_3NCH_2COOC_2H_5\} + H_2NNH_2 \longrightarrow Cl\{(CH_3)_3NCH_2CONHNH_2\}(I) + C_2H_5OH$$

Girard's reagent 'P' is the corresponding pyridinium compound, prepared by replacing the trimethylamine by pyridine. The reagent 'T', unlike the reagent 'P', is very deliquescent, but is nevertheless widely used for laboratory work because of its greater solubility. The quaternary ammonium grouping imparts water solubility.

The main use of the Girard reagents 'T' and 'P' is for the isolation of small amounts of ketones from admixture with other organic matter contained in various natural products; the carbonyl derivatives are water soluble. The ketonic material, dissolved in alcohol containing 10 per cent. acetic acid, is heated for 30–60 minutes with the reagent in slight excess, the volume being adjusted to give 5 or 10 per cent. solution of the reagent. The cooled solution is diluted with water containing enough alkali to neutralise 90 per cent. of the acid and to give an alcohol content of 10–20 per cent. It is then exhaustively extracted with ether to remove non-ketonic compounds; the water-soluble hydrazone derivatives are decomposed by the addition of mineral acid up

to a concentration of 0·5*N* and, after about 1 hour at room temperature, the liberated ketonic compound is isolated by extraction with ether.

$$\text{Girard's reagent 'T'} + RR'C{=}O \underset{HCl}{\overset{C_2H_5OH,\ HOAc}{\rightleftharpoons}} \{(CH_3)_3NCH_2CONHN{=}CRR'\}Cl + H_2O$$

Girard's Reagent 'T'. Place a solution of 98·5 g. (84·5 ml.) of ethyl chloroacetate and 200 ml. of absolute ethanol in a 1-litre three-necked flask, fitted with a thermometer, stirrer and a Dewar type of condenser (Fig. *II*, *1*, 4,*h*) filled with ice (1). Cool the solution to 0° by stirring in an ice-salt bath, stop the stirrer and add 49 g. (74 ml., measured after precooling to −5°) of trimethylamine all at once. Control the exothermic reaction sufficiently by external cooling so that the temperature of the mixture rises to 60° during about 1 hour. When there is no further evolution of heat, allow the reaction mixture to stand at room temperature for 20–24 hours. Remove the condenser, replace the thermometer by a dropping funnel, and add 40 g. of 100 per cent. hydrazine hydrate (2) with stirring during 10–15 minutes. Stir for a further 45 minutes, cool the solution slightly and, unless crystallisation commences spontaneously, scratch the walls of the vessel with a glass rod to induce crystallisation. The product separates in fine, colourless needles. Cool in an ice bath, collect the highly hygroscopic salt rapidly on a Buchner funnel, wash with 150 ml. of cold absolute ethanol and press dry under a rubber dam. Dry the product in a vacuum desiccator over concentrated sulphuric acid; the yield is 105 g., m.p. 175–180° (decomp.). (This material (3) contains a small amount of the symmetrical dihydrazide, but is quite satisfactory as a reagent for the separation of ketones.) A further crop of 12 g. may be obtained after distilling off 200–300 ml. of solvent from the mother liquor and washings at the pressure of the water pump.

(1) Alternatively, a glass spiral, fitted by means of a cork at the lower end into a glass or metal vessel filled with ice, may be used.

(2) Hydrazine hydrate of 95–100 per cent. concentration is a commercial product. The 40–60 per cent. solution may be concentrated to 80–85 per cent. strength by distillation with xylene in an all-glass apparatus.

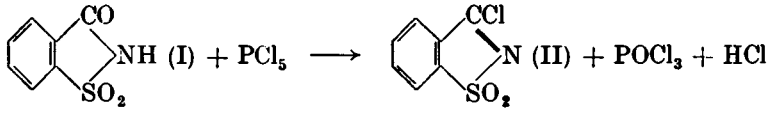
(3) The deliquescent solid must be stored in a dry, tightly-stoppered container. If exposed to the air it deteriorates rapidly, developing an unpleasant odour. Samples that have been kept for some time are best recrystallised from absolute ethanol before use.

Girard's reagent 'P', $\{C_5H_5NCH_2CONHNH_2\}Cl$. In a 1-litre three-necked flask, equipped as in the previous preparation, place 200 ml. of absolute ethyl alcohol, 63 g. (64·5 ml.) of pure anhydrous pyridine and 98·5 g. (84·5 ml.) of ethyl chloroacetate. Heat the mixture under reflux for 2–3 hours until the formation of the quaternary salt is complete; acidify a small test-portion with dilute sulphuric acid; it should dissolve completely and no odour of ethyl chloroacetate should be apparent. Cool the mixture in ice and salt. Replace the thermometer by a dropping funnel, and add a solution of 40 g. of 100 per cent. hydrazine hydrate in 50 ml. of absolute ethanol all at once. A vigorous exothermic reaction soon develops and is accompanied by vigorous effervescence. The product separates almost immediately. When cold, filter with suction, wash

with ice-cold ethanol, and dry in the air. The yield of Girard's reagent 'P' is 135 g.; this is satisfactory for the isolation of ketones. A pure product may be obtained by recrystallisation from methanol.

VII,26. PSEUDO-SACCHARIN CHLORIDE

Pseudo-saccharin chloride (II) is prepared by the action of phosphorus pentachloride upon saccharin (I):



Mix intimately in a glass mortar 35 g. of saccharin (Section IV,209) and 70 g. of phosphorus pentachloride, transfer to a 250 ml. round-bottomed flask connected by a ground glass joint to a reflux condenser; attach the latter through a calcium chloride guard tube to a gas absorption trap (Fig. *II*, *8*, 1). Heat the mixture in an oil bath at 175–180° for 90 minutes; at the end of this period the vigorous evolution of hydrogen chloride will have subsided. Replace the reflux condenser by a fractionating column, distil off the phosphorus oxychloride, and pour the warm residue upon finely crushed ice. Extract the crude solid pseudo-saccharin chloride with chloroform, dry the chloroform solution with anhydrous magnesium sulphate, and distil off the solvent. Recrystallise the residue from chloroform or from dry benzene. The yield of pure pseudo-saccharin chloride, m.p. 143–145° (decomp.), is 26 g. It is best kept in a sealed glass tube or in a glass-stoppered bottle.