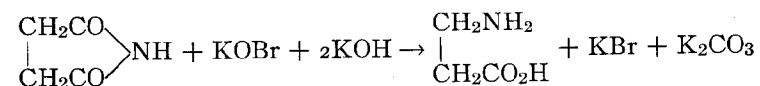


# ORGANIC SYNTHESSES

## I

### $\beta$ -ALANINE

( $\beta$ -Aminopropionic Acid)



Submitted by H. T. CLARKE and LETHA DAVIES BEHR.  
Checked by WALLACE H. CAROTHERS and W. L. McEWEN.

#### 1. Procedure

To a cold (0-5°) solution of 302 g. of potassium hydroxide (sticks) in 2720 cc. of distilled water is added slowly, with stirring, 96.6 g. (30.8 cc., 0.6 mole) of bromine. This solution is chilled to 0°, and 59.4 g. (0.6 mole) of succinimide (p. 75) is added with hand stirring. The mixture is warmed in a water bath to 55-60°, when it becomes colorless, and is held at that temperature for two hours (Note 1). After being allowed to stand overnight at room temperature, it is acidified to Congo red with concentrated hydrochloric acid (about 380 cc., sp. gr. 1.18) (Note 2) and evaporated to dryness on a steam bath under reduced pressure. The residue is treated with 1 l. of warm 95 per cent alcohol; the undissolved potassium bromide is filtered off and washed with 150-200 cc. of cold alcohol in small portions. The filtrate and washings are combined and evaporated to dryness under reduced pressure, and the residue is extracted with 100 cc. of 95 per cent alcohol. The resulting solution is again evaporated to dryness and the residue finally extracted with 140 cc. of hot absolute alcohol (Note 3). After distilling off the bulk of the alcohol, this

extract is diluted with about 200 cc. of distilled water and shaken out twice with 80-cc. portions of ether. The ether extracts are discarded (Note 4).

The aqueous solution is freed of ether and alcohol and then boiled under reflux for one to one and a half hours in order to hydrolyze any  $\beta$ -alanine ester. After evaporating under reduced pressure to remove as much as possible of the excess hydrochloric acid, the residue is dissolved in water and diluted to exactly 1000 cc. A 5-cc. portion of this solution is withdrawn for determination of total halides. A suspension of silver oxide prepared from 10 per cent more than the equivalent quantity of silver nitrate (Note 5) is added to the remaining portion of the solution, and the mixture is stirred well in order to bring about complete precipitation of the halides. After standing overnight the precipitate is filtered off and washed with water. The filtrate and washings are concentrated under reduced pressure to about 400 cc., saturated with hydrogen sulfide, and filtered through a thin layer of decolorizing carbon. The colorless filtrate is evaporated to a volume of about 100 cc., treated with decolorizing carbon if necessary, concentrated on the steam bath until crystallization begins, and chilled. The crystals are filtered with suction, washed with a little cold alcohol, and dried. A further crop is obtained by concentrating the mother liquor and again chilling (Note 6). The combined crops (28–30 g., m.p. 189–192°) are recrystallized from water, employing the same procedure, and yield 22–24 g. (41–45 per cent of the theoretical amount) of pure  $\beta$ -alanine, which melts at 197–198° (corr.) with decomposition. About 2 g. of less pure product can be secured from the final mother liquors.

## 2. Notes

1. The odor of ammonia is perceptible, indicating some hydrolysis.
2. On acidification a small amount of bromine may be liberated; this is removed rapidly during the subsequent evaporation.
3. In the last extraction the alcohol-insoluble material may be removed advantageously with a centrifuge.

4. This ether extraction removes small quantities of succinic acid and its esters.

5. The silver oxide is prepared by dissolving the silver nitrate in about five parts of cold water and adding a slight excess of pure sodium hydroxide in 10 per cent solution. The precipitate is well stirred, collected by filtration or centrifuging, and washed free of sodium salts. It should not be dried before use.

6. The final mother liquor consists of a rather viscous solution containing uncrystallizable by-products.

## 3. Methods of Preparation

The above directions are based upon the methods of Hoogewerff and Van Dorp,<sup>1</sup> as modified by Holm<sup>2</sup> and by Hale and Honan.<sup>3</sup>  $\beta$ -Alanine has also been prepared by the action of hypobromite upon succinimide and hydrolysis of the resulting  $\beta$ -ureidopropionic acid;<sup>4</sup> by the action of ammonia upon  $\beta$ -iodopropionic acid;<sup>5</sup> by the hydrolysis of methyl carbomethoxy- $\beta$ -aminopropionate, obtained by the action of sodium methoxide on succinbromimide;<sup>6</sup> by the reduction of  $\beta$ -nitrosopropionic acid;<sup>7</sup> by heating ethyl acrylate with alcoholic ammonia;<sup>8</sup> from succinylglycine ester by the azide synthesis;<sup>9</sup> and by the action of liquid ammonia upon methyl acrylate.<sup>10</sup>

<sup>1</sup> Hoogewerff and Van Dorp, *Rec. trav. chim.* **10**, 5 (1891).

<sup>2</sup> Holm, *Arch. Pharm.* **242**, 597 (1904).

<sup>3</sup> Hale and Honan, *J. Am. Chem. Soc.* **41**, 774 (1919).

<sup>4</sup> Weidel and Roithner, *Monatsh.* **17**, 172 (1896).

<sup>5</sup> Heintz, *Ann.* **156**, 25 (1870); Mulder, *Ber.* **9**, 1902 (1876); Abderhalden and Fodor, *Z. physiol. Chem.* **85**, 114 (1913).

<sup>6</sup> Lengfeld and Stieglitz, *Am. Chem. J.* **15**, 215, 504 (1893).

<sup>7</sup> v. Pechmann, *Ann.* **264**, 288 (1891).

<sup>8</sup> Wender, *Gazz. chim. ital.* **19**, 437 (1889).

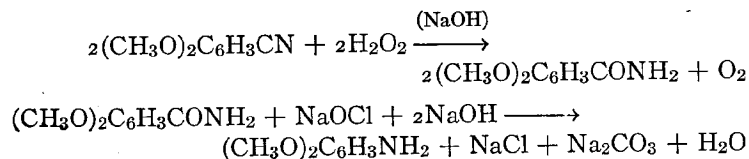
<sup>9</sup> Curtius and Hechtenberg, *J. prakt. Chem.* (2) **105**, 289 (1923).

<sup>10</sup> Morsch, *Monatsh.* **63**, 220 (1933).

## II

## 4-AMINOVERATROLE

## (3,4-Dimethoxyaniline)



Submitted by J. S. BUCK and W. S. IDE.

Checked by JOHN R. JOHNSON and H. B. STEVENSON.

## 1. Procedure

IN a 5-l. flask fitted with a mechanical stirrer are placed 1800 g. (1.6 moles) of fresh 3 per cent hydrogen peroxide solution, 100 g. of 25 per cent potassium hydroxide solution, and 57 g. (0.35 mole) of veratronic nitrile (p. 92). The mixture is warmed slowly to 45°, with stirring, and the source of heat is then withdrawn. The reaction proceeds with evolution of oxygen, and the temperature continues to rise (Note 1). The amide soon begins to separate; in about fifty minutes the reaction is complete and the temperature begins to fall. The mixture is cooled to 3–5° and allowed to remain in the cooling bath for one and one-half to two hours. The white crystalline product is filtered with suction and dried in the air. The veratric amide melts at 162.5–163.5° and weighs 55–58 g. (87–92 per cent of the theoretical amount).

An alkaline solution of sodium hypochlorite is prepared by passing chlorine (0.412 gram for each gram of the amide) (Note 2) into a mixture of 300 g. of cracked ice and a cold solution of 80 g. of sodium hydroxide in 500 cc. of water, contained in a 2-l. round-bottomed flask. The whole of the veratric amide (55–58 g.) is added in one portion, and the mixture is warmed slowly in

a water bath, with mechanical stirring. The material soon darkens in color, and at 50–55° (internal temperature) oily droplets begin to separate. The temperature is raised gradually to 70° and maintained at this point for one hour. A solution of 120 g. of sodium hydroxide in 120 cc. of water is added slowly, and the temperature is increased to 80° for an additional hour.

Upon cooling the mixture, the oily layer of amine solidifies to a red crystalline mass. The crude amine is filtered with suction, washed with two 60-cc. portions of ice-cold water, pressed thoroughly, and transferred to an ordinary 125-cc. Claisen flask. The filtrate is extracted with three 60-cc. portions of benzene, the extracts are transferred separately to the Claisen flask, and the benzene is distilled off at atmospheric pressure (Note 3). The residual amine is distilled under reduced pressure and is collected at 172–174°/24 mm. (Note 4). The distillate solidifies quickly to a mass of colorless crystals which melt sharply at 87.5–88° (Note 5). From 58 g. (0.32 mole) of veratric amide there is obtained 39–40 g. (80–82 per cent yield) of 4-aminoveratrole.

## 2. Notes

1. A large amount of frothing occurs, and the temperature rises to 52–55° during the reaction. The flask should be removed at intervals and shaken by hand to bring the material carried up by the froth into contact with the solution.

2. The quantity of chlorine indicated is 5 per cent more than the theoretical amount. The chlorine may be obtained from a cylinder, but for small amounts it is more accurate to generate chlorine by treating a weighed amount of potassium permanganate with an excess of concentrated hydrochloric acid (0.367 g.  $\text{KMnO}_4 \approx 0.412 \text{ g. Cl}_2$ ). For 55–58 g. of veratric amide the weight of permanganate to be used is 20.2–21.3 g.

For generating the chlorine, the requisite weight of potassium permanganate is placed in a 500-cc. distilling flask fitted with a separatory funnel and suspended so that the flask can be agitated. Concentrated hydrochloric acid (about 130 cc. is required) is allowed to drop slowly upon the permanganate crystals, and as

the reaction progresses the flask is heated. After all the acid has been added the mixture is boiled gently for a few minutes to expel the last portions of chlorine, and the delivery tube is removed rapidly from the alkaline hypochlorite solution to prevent the latter from being sucked back into the generator. It is recommended that a safety bottle be inserted between the side tube of the generator and the tube which delivers the chlorine into the alkali.

3. Distillation of the benzene extracts in this way serves to remove the water, and in the subsequent distillation of the amine no watery fore-run is obtained.

4. Since the aminoveratrole tends to solidify in the side tube of the distilling flask, it is advisable to distil the material rapidly and to employ a bath temperature about 60° higher than that of the distilling vapor. Care must be taken to avoid contaminating the distillate with a small amount of colored material which comes over if the distillation is carried too far.

5. The melting point of 4-aminoveratrole obtained by reduction of 4-nitroveratrole is reported as 85–86°.<sup>1</sup> The amine tends to discolor rapidly on exposure to air and light; it should be stored in a sealed, dark container.

### 3. Methods of Preparation

4-Aminoveratrole has been prepared by the reduction of 4-nitroveratrole with tin,<sup>1,2</sup> or stannous chloride,<sup>3</sup> and hydrochloric acid. The present procedure is based upon a method used for the preparation of aminopiperole (3,4-methylenedioxyaniline).<sup>4</sup>

<sup>1</sup> Moureu, Bull. soc. chim. [3] **15**, 647 (1896).

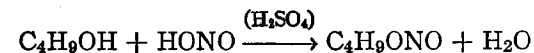
<sup>2</sup> Simonsen and Rau, J. Chem. Soc. **113**, 28 (1918); Pollecoff and Robinson, *ibid.* **113**, 645 (footnote) (1918).

<sup>3</sup> Heinisch, Monatsh. **15**, 232 (1894).

<sup>4</sup> Rupe and Majewski, Ber. **33**, 3401 (1900).

## III

### *n*-BUTYL NITRITE



Submitted by W. A. NOYES.

Checked by C. R. NOLLER and B. H. WILCOXON.

#### 1. Procedure

In a 3-l. three-necked, round-bottomed flask fitted with a mechanical stirrer (Note 1), a separatory funnel extending to the bottom of the flask, and a thermometer, are placed 380 g. (5.5 moles) of C.P. sodium nitrite and 1.5 l. of water. The flask is surrounded by an ice-salt mixture and the solution stirred until the temperature falls to 0°. A mixture of 100 cc. of water, 136 cc. (250 g., 2.5 moles) of concentrated sulfuric acid (sp. gr. 1.84) (Note 2), and 457 cc. (370 g., 5 moles) of commercial *n*-butyl alcohol is cooled to 0°, and by means of the separatory funnel is introduced slowly beneath the surface of the nitrite solution, with stirring. The alcohol solution is added slowly enough so that practically no gas is evolved, and the temperature is kept at ±1°. This usually requires from one and one-half to two hours.

The resulting mixture is allowed to stand in the ice-salt bath until it separates into layers, and the liquid layers are decanted from the sodium sulfate into a separatory funnel (Note 3). The lower aqueous layer is removed and the butyl nitrite layer washed twice with 50-cc. portions of a solution containing 2 g. of sodium bicarbonate and 25 g. of sodium chloride in 100 cc. of water. After drying over 20 g. of anhydrous sodium sulfate, the yield of practically pure butyl nitrite amounts to 420–440 g. (81–85 per cent of the theoretical amount) (Notes 4 and 5). If desired, the product may be distilled under reduced pressure when 98 per cent distils

at 24–27°/43 mm. (Note 6). Butyl nitrite boils at 75° under atmospheric pressure, with some decomposition.

## 2. Notes

1. A stirrer capable of keeping solid material in motion and driven by a strong motor should be used because of the precipitation of large amounts of sodium sulfate towards the end of the reaction.

2. The concentration of sulfuric acid which is used keeps the butyl alcohol in solution but does not dissolve butyl nitrite.

3. If more butyl nitrite separates from the sodium sulfate after the first decantation, a second decantation is made. Care must be exercised in handling butyl nitrite; inhalation of the vapor may cause severe headache and heart excitation.

4. The same procedure is quite satisfactory for runs of one-tenth this size. In small runs mechanical stirring is unnecessary since gentle rotation of the flask by hand gives good mixing.

5. *iso*-Amyl nitrite may be made in the same manner and with approximately the same yields.

6. Butyl nitrite decomposes slowly on standing and should be kept in a cool place and used within a few days or, at most, a few weeks after it is prepared. A sample which stood for five months during a warm summer seemed to contain only 20–25 per cent of the original nitrite. The products of decomposition consist of oxides of nitrogen, water, butyl alcohol, and polymerization products of butyraldehyde.

## 3. Methods of Preparation

Butyl nitrite has always been prepared by the action of nitrous acid on butyl alcohol.<sup>1</sup> The method here described is a modification of that of Wallach and Otto<sup>2</sup> for ethyl nitrite and has been published recently.<sup>3</sup>

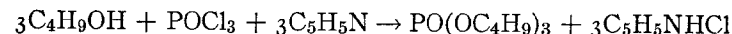
<sup>1</sup> Bertoni, Gazz. chim. ital. 18, 434 (1888); Adams and Kamm, J. Am. Chem. Soc. 40, 1285 (1918).

<sup>2</sup> Wallach and Otto, Ann. 253, 251 (1889).

<sup>3</sup> Noyes, J. Am. Chem. Soc. 55, 3888 (1933).

## IV

### *n*-BUTYL PHOSPHATE



Submitted by G. R. DUTTON and C. R. NOLLER.

Checked by JOHN R. JOHNSON and ANTHONY HUNT.

### 1. Procedure

In a 2-l. round-bottomed flask fitted with a reflux condenser, liquid-sealed mechanical stirrer, dropping funnel (Note 1), and thermometer are placed 222 g. (274 cc., 3 moles) of dry *n*-butyl alcohol, 260 g. (263 cc., 3.3 moles) of pyridine, and 275 cc. of dry benzene (Note 2). The solution is stirred and the flask is cooled in an ice-salt mixture until the temperature has fallen to –5°. With efficient stirring (Note 3), 153 g. (91 cc., 1 mole) of phosphorus oxychloride (b.p. 106–107°) is added dropwise at such a rate that the temperature does not exceed 10°. After the addition is completed the reaction mixture is heated slowly to the reflux point and held at that temperature for two hours. The mixture is cooled to room temperature, and 400–500 cc. of water is added to dissolve the pyridine hydrochloride (Note 4). The benzene layer is separated, washed with 100–150 cc. of water (Note 5), and dried over 20 g. of anhydrous sodium sulfate.

The benzene and other low-boiling materials are removed by distillation at 40–50 mm. pressure until the temperature of the distilling vapor reaches 90°. The *n*-butyl phosphate fraction is collected at 160–162°/15 mm., or 143–145°/8 mm., and weighs 190–200 g. (71–75 per cent of the theoretical amount) (Note 6).

### 2. Notes

1. The tip of the funnel should be placed sufficiently high above the surface of the reaction mixture to avoid encrustation

with pyridine hydrochloride. It is advantageous to use a thermometer such that the portion of the scale above  $-5^{\circ}$  is visible above the stopper; otherwise, the fog in the flask and the pyridine salt may obscure the scale.

2. The reactants and solvent were dried by distillation; fractions boiling over an interval of  $1^{\circ}$  were used.

3. The first 10-15 cc. of phosphorus oxychloride must be added very slowly to avoid vigorous reaction and overheating. Care must be exercised to avoid an initial temperature so low that unreacted phosphorus oxychloride accumulates and then suddenly reacts with violence. The mechanical stirrer should be of such dimensions and operated at such speeds that the heat of reaction is dissipated rapidly without throwing solid material (and occluded reactants) against the upper walls of the flask.

4. About 50 per cent of the pyridine may be recovered by concentrating this aqueous solution over a steam bath, treating with strong caustic soda solution, and distilling the pyridine layer.

5. The solution should be neutral before distillation. The presence of hydrogen chloride promotes decomposition of phosphoric esters into phosphoric acid and alkenes.<sup>1</sup> The benzene solution should not be washed with alkaline reagents, such as sodium carbonate solution, since alkaline reagents also cause decomposition during distillation.

6. This is a general method for preparing alkyl phosphates. Using a similar procedure, the *n*-propyl ester may be obtained in 60-65 per cent yields, the *sec.*-butyl ester in 40-45 per cent yields, and the *n*-amyl ester in 60-65 per cent yields, from the corresponding alcohols.<sup>2</sup>

### 3. Methods of Preparation

*n*-Butyl phosphate has been prepared by the action of phosphorus oxychloride upon *n*-butyl alcohol,<sup>3</sup> aluminum butoxide,<sup>4</sup> or sodium butoxide.<sup>5</sup> The above procedure<sup>2</sup> is similar to one that has been used for the preparation of alkyl phosphites.<sup>6</sup>

*n*-Butyl phosphate has also been prepared by the oxidation of *n*-butyl phosphite.<sup>7</sup>

<sup>1</sup> Balarev, Z. anorg. allgem. Chem. **101**, 227 (1917).

<sup>2</sup> Noller and Dutton, J. Am. Chem. Soc. **55**, 424 (1933).

<sup>3</sup> Nicolai, U. S. pat. 1,766,720 [C. A. **24**, 4053 (1930)].

<sup>4</sup> Bannister, U. S. pat. 1,799,349 [C. A. **25**, 3014 (1931)].

<sup>5</sup> Evans, Davies, and Jones, J. Chem. Soc. **1930**, 1310.

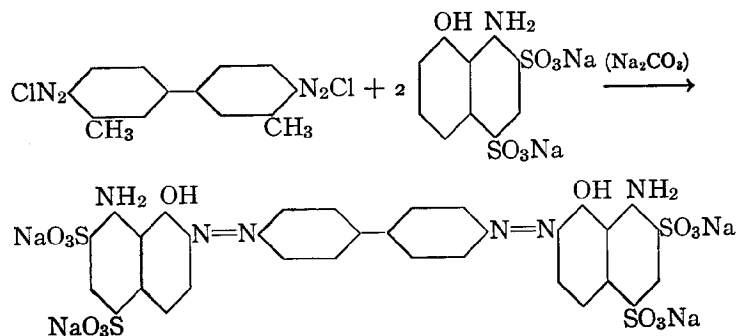
<sup>6</sup> Milobendski and Sachnowski, Chemik Polski **15**, 34 (1917) [C. A. **13**, 2865 (1919)].

<sup>7</sup> Brit. pat. 398,659 [C. A. **28**, 1362 (1934)].

V

COUPLING OF *o*-TOLIDINE AND CHICAGO ACID

(Preparation of a Salt-free Azo Dye)



Submitted by J. L. HARTWELL and L. F. FIESER.  
 Checked by W. W. HARTMAN and G. L. BOOMER.

## 1. Procedure

IN a 1-l. beaker 21.2 g. (0.1 mole) of *o*-tolidine is made into a thin paste with 300 cc. of water and dissolved by the addition of 20 cc. (23.6 g., 0.23 mole) of concentrated hydrochloric acid (sp. gr. 1.18), warming a little if necessary. The solution is cooled to 10° with ice, mechanical agitation is started, and 21 cc. (25 g., 0.24 mole) more of concentrated hydrochloric acid added (Note 1). This causes partial separation of *o*-tolidine dihydrochloride. Keeping the temperature at 10–15°, a solution of 14.5 g. (0.2 mole) of 95 per cent sodium nitrite in 40 cc. of water is run in rapidly, holding back the last 10 per cent which is added slowly and only as needed to give a distinct positive test for nitrous acid on starch-iodide paper. This excess is maintained for one-half hour. Throughout the diazotization an excess of hydrochloric acid should be present as shown by a strong test

on Congo red paper. When the diazotization is complete, the excess nitrous acid is eliminated by the careful addition of a small amount of *o*-tolidine hydrochloride solution, using starch-iodide paper to arrive at an exact balance (Note 2).

In a 3-l. beaker a paste is made from 82 g. (0.21 mole) of 88 per cent technical Chicago acid (1-amino-8-naphthol-2,4-disulfonic acid) (Note 3) and 500 cc. of water, and solution effected by the addition of 8 g. (0.2 mole) of sodium hydroxide in 30 cc. of water, testing with litmus toward the end and leaving the reaction still acid (Note 4). The solution is cooled to 18° by the addition of ice, and just before the coupling 35 g. (0.33 mole) of anhydrous sodium carbonate is added.

With vigorous mechanical agitation the diazonium salt solution is run into the Chicago acid solution rather rapidly. The blue dye which separates at first, gradually dissolves on further stirring. After one-half hour the solution is tested for alkalinity (Note 5) and for completeness of coupling (Notes 6 and 7).

After stirring for a total of two hours, the mixture is heated to 85°, 15 g. of decolorizing carbon is added, and the solution stirred for fifteen minutes and filtered. The filtrate is reheated to 85° with agitation and the volume estimated. For each 100 cc. of the solution 27 g. of hydrated sodium acetate (usually 450–500 g.) is added slowly, with vigorous stirring, in four or five portions (Note 8). The dye is thus caused to separate in an easily filterable form. On "spotting" a drop of the mixture on filter paper by means of a stirring rod, the dye should form a dark blue mass in the center of a red or violet rim (Note 9). The mixture, while still warm, is filtered with suction on a 20-cm. Buchner funnel, and as much as possible of the mother liquor is removed (Note 10). The filter cake is dissolved in 1200 cc. of water at 85° and resalted as above with about 300 g. of sodium acetate, in several portions, or until most of the dye is salted out. In a "spot" test on filter paper, little blue should be left in the rim. The product is collected, redissolved in 1200 cc. of water at 85°, and salted again. This time enough sodium acetate should be added to give a small rim which shows no red impurity (Note 11). The product is collected, dried in an oven at 110° for at

least twenty-four hours, ground, and passed through a 40-mesh sieve.

The sodium acetate is then extracted by digesting the sifted dye for ten to fifteen minutes with successive 500-cc. portions of boiling 95 per cent ethyl alcohol, filtering with suction after each extraction, and washing the product on the filter with a little alcohol (Note 12). After four alcohol extractions the filtrate should give a negative test for acetate. The product, which changes in appearance from bronze to green during the extraction, is dried in air at room temperature. The yield is 80-81 g. (83-84 per cent of the theoretical amount) of dyestuff free from inorganic salts and organic impurities (Note 13).

## 2. Notes

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

2. If a clear solution is not obtained at this point, any solid may be removed by filtration.

3. Owing to the fact that this intermediate is a technical product and has been isolated by salting out, a knowledge of its purity is necessary. The compound is actually present as the acid sodium salt (molecular weight 341). A rapid method of analysis, sufficiently accurate for this preparation, is to titrate a known weight in dilute, strongly acid solution with 0.5 *N* sodium nitrite solution standardized against sulfanilic acid, using starch-iodide paper in obtaining the end points.

4. Aminonaphthols rapidly turn dark in alkaline solution owing to oxidation. For this reason the solution is left faintly acid until just before coupling.

5. This test is made by removing a few drops of the coupling mixture by means of a stirring rod to one of the depressions in a white porcelain spot plate, salting out the dye by stirring with a little *c.p.* sodium chloride, and bringing a piece of litmus paper in contact with the mass.

6. The test for completeness of coupling involves testing for excess diazonium salt (*a*) and for excess Chicago acid (*b*):

(*a*) A drop or two of the coupling mixture is dissolved in about 20 cc. of water in a test tube and the solution divided equally in two test tubes. To one tube is added a few drops of a 10 per cent solution of Schaeffer's salt (2-naphthol-6-sulfonic acid) or R salt (2-naphthol-3,6-disulfonic acid) prepared from 0.5 g. of the salt, 5 cc. of water, and just enough sodium carbonate solution to dissolve the material. The other tube acts as a control. Both tubes are brought rapidly nearly to boiling and the colors compared. If too dark, both tubes are diluted equally with water until the solutions are light blue. The colors may be compared by pouring solution from each tube onto filter paper. If the color of the solution in the first tube is at all redder than that in the control tube, an excess of the diazonium compound is present in the coupling mixture.

(*b*) A few drops of the coupling mixture are salted out as in Note 5, the mass transferred to filter paper, and near the spot on the reverse side is placed a drop of solution of diazotized sulfanilic acid. A red or red-violet coloration at the meeting of the two spots shows the presence of excess Chicago acid.

7. Throughout the coupling an alkaline reaction should be maintained and sodium carbonate added if the alkalinity falls. If the mixture gives tests for both diazonium compound and Chicago acid, insufficient time has elapsed for complete coupling. A little more Chicago acid should be added (in alkaline solution) if a deficiency is shown.

8. The temperature of salting, speed of addition of salt, speed and duration of agitation, and alkalinity of the solution all affect the physical form of the dye and determine how well it will filter. The method described gives a product which filters rapidly.

9. The red impurity is another dye produced by coupling of the diazonium salt with an oxidation-product which is present in the technical Chicago acid. It is easier to free the blue dye of this red impurity by resalting than to purify the Chicago acid. However, in the case of Trypan blue (tolidine coupled with two moles of H acid) the red impurity cannot be removed by salting.



It may be removed completely by extraction with alcohol, in which it is more soluble than the blue component, preferably by precipitating a hot saturated aqueous solution of the dye with at least six times its volume of alcohol.

10. In this and subsequent filtrations it is advantageous to use a rubber dam held in place by rubber bands (Org. Syn. 14, 25, Note 3). The use of the rubber dam is especially advantageous for a slow filtration continuing overnight.

11. The most sensitive test for purity of the dye is the capillary test,<sup>1</sup> depending on the fact that the red impurity is more soluble in water than the blue compound and less readily adsorbed by filter paper. An amount of press cake corresponding roughly to 0.05 g. solid dye is dissolved in 200 cc. of water in a 400-cc. beaker, 0.5 g. of common salt is added, and the temperature raised to 95°. A 2 by 15 cm. strip of filter paper is immersed in the liquid and is supported on a stirring rod pushed through it and placed across the top of the beaker. The temperature is maintained at 95° for fifteen minutes and the filter paper removed. Any red impurity will show plainly above the blue. If purification is found to be incomplete, further resalting will produce a pure product.

12. The progress of the extraction may be followed by adding three drops of concentrated sulfuric acid to 10 cc. of the alcoholic filtrate in a test tube. If a white precipitate of sodium sulfate does not form at once, the solution is chilled in an ice bath. A precipitate will form with 0.002 g. of sodium acetate in 10 cc. of alcohol.

13. Using this procedure, other diamines such as benzidine and dianisidine may be diazotized and coupled with other aminonaphthols, such as S acid (1-amino-8-naphthol-4-sulfonic acid), J acid (2-amino-5-naphthol-7-sulfonic acid), Gamma acid (2-amino-8-naphthol-6-sulfonic acid), and H acid (1-amino-8-naphthol-3,6-disulfonic acid), or with simple naphthols such as NW acid (1-naphthol-4-sulfonic acid), Schaeffer's acid (2-naphthol-6-sulfonic acid), and R acid (2-naphthol-3,6-disulfonic acid). The procedure would be varied only in the manner of salting out the dyes, each of which would require a set of optimum conditions

peculiar to itself (see Note 8). In cases where the alkalinity of sodium acetate leads to a considerable increase in solubility of the dye, ammonium bromide may be used. The latter is extracted easily by hot ethyl alcohol, or better by hot methyl alcohol.

Naphthylamines cannot be used as second components by this procedure, as in these cases coupling takes place in acid solution.

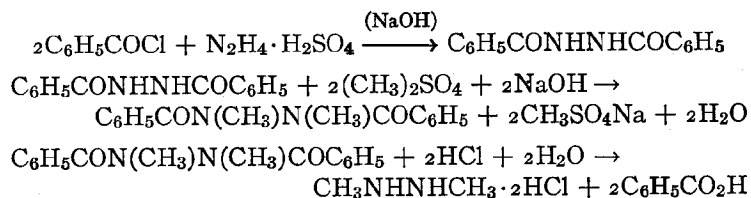
### 3. Methods of Preparation

Dyes of the types described in the procedure and those mentioned in Note 13 are described in the patent literature.<sup>2</sup> The ordinary methods of preparation give products that contain salt and other impurities.

<sup>1</sup> Mulliken, "Identification of the Commercial Dyestuffs," pp. 10-11. New York: John Wiley and Sons, (1910).

<sup>2</sup> Ger. pat. 35,341; 38,802 [Frld. 1, 469, 488 (1877-1887)]; Ger. pat. 3,949; 57,327; 75,469 [Frld. 3, 685, 687, 690 (1890-1894)].

## VI

**sym.-DIMETHYLHYDRAZINE DIHYDROCHLORIDE**

Submitted by H. H. HATT.

Checked by REYNOLD C. FUSON and ELLSWORTH ELLINGBOE.

**1. Procedure**

(A) *Dibenzoyldimethylhydrazine*.—In a 2-l. flask provided with a mechanical stirrer (Note 1) and cooled in a bath of cold water, are placed a solution of 48 g. (1.2 moles) of sodium hydroxide in 500 cc. of water and 65 g. (0.5 mole) of hydrazine sulfate (Org. Syn. Coll. Vol. 1, 302). With stirring, 145 g. (120 cc., 1.03 moles) of freshly distilled benzoyl chloride and 120 cc. of an aqueous solution containing 45 g. (1.1 moles) of sodium hydroxide are added slowly from separate dropping funnels. The benzoyl chloride is added over a period of one and one-half hours; the alkali is added slightly faster. After both additions are completed the mixture is stirred for two hours longer and then saturated with carbon dioxide (Note 2). The dibenzoyldimethylhydrazine is filtered with suction, pressed thoroughly, and ground to a paste with 50 per cent aqueous acetone. The material is filtered with suction, washed with water, and pressed as dry as possible. The crude product is dissolved in about 650 cc. of boiling glacial acetic acid, from which, on cooling, the dibenzoyldimethylhydrazine separates as a mass of fine white needles. These are filtered with suction, washed with cold water, and dried by heating under reduced

pressure on a water bath, in a slow current of air. This first fraction, m.p. 234–238°, amounts to 80–90 g. (66–75 per cent of the theoretical amount) and is practically pure. Small quantities of less pure material can be obtained by concentration of the mother liquor.

(B) *Dibenzoyldimethylhydrazine*.—The following operations should be performed under a hood. In a 2-l. three-necked flask provided with a mechanical stirrer, a thermometer, and two dropping funnels, are placed 80 g. (0.33 mole) of dibenzoyldimethylhydrazine, 10 g. (0.25 mole) of sodium hydroxide, and 600 cc. of water. The mixture is maintained at about 90° (Note 3) by heating on a water bath. With stirring, 320 g. (240 cc., 2.54 moles) of dimethyl sulfate (Note 4) and 250 cc. of an aqueous solution containing 125 g. (3.1 moles) of sodium hydroxide are added from separate dropping funnels. The dimethyl sulfate is added in 10-cc. portions at five-minute intervals, the sodium hydroxide solution at a rate that maintains the reaction mixture slightly alkaline. When markedly alkaline the mixture has a distinctly yellow color; it is best to maintain a degree of alkalinity slightly less than that required to produce this color.

During the additions, which require about two hours, the dibenzoyldimethylhydrazine separates as a supernatant liquid (Note 5); the semi-solid material thrown up on the sides of the flask must be washed down from time to time. After being heated for one-half hour longer the mixture is allowed to cool. The solid dibenzoyldimethylhydrazine is collected, crushed with water, filtered, and dissolved in 100 cc. of chloroform. The solution is filtered from insoluble impurities and dried over sodium sulfate; the chloroform is removed by heating on a water bath, finally under reduced pressure. The solid residue melts at 77–84° and is sufficiently pure for further use. The yield is 77–83 g. (86–93 per cent of the theoretical amount) (Note 6).

(C) *Dimethylhydrazine Dihydrochloride*.—In a 2-l. flask, a mixture of 67 g. (0.25 mole) of dibenzoyldimethylhydrazine and 250 cc. of 32 per cent hydrochloric acid (sp. gr. 1.16) is refluxed gently for two hours, under a hood. To remove the benzoic acid, the mixture is steam-distilled until 10 l. of distillate has collected

(Note 7); the residual liquor is evaporated to dryness under reduced pressure on a water bath. The crystalline dihydrochloride is treated with 25 cc. of absolute ethyl alcohol, and the mixture is evaporated to dryness under reduced pressure. This treatment is repeated, and the dihydrochloride is crushed with a mixture of 25 cc. of absolute alcohol and 2-3 cc. of concentrated hydrochloric acid, filtered and washed with 10-15 cc. of cold absolute alcohol. The first fraction of dimethylhydrazine dihydrochloride, after being dried in a vacuum desiccator, weighs 22-23 g. By evaporation of the mother liquors and further treatment with 5-6 cc. of absolute alcohol and a little hydrochloric acid, a second fraction of 3 g. of the hydrochloride is obtained. Repetition of this procedure yields a third fraction amounting to about 0.5 g. (Note 8). The total yield is 25-26 g. (75-78 per cent of the theoretical amount).

## 2. Notes

1. The reaction flask need neither be corked nor placed under a hood if a glass tube, connected to a filter pump, is passed a short way into the neck of the flask.

2. Most of the dibenzoylhydrazine separates during the reaction as a white precipitate; if the mixture is not saturated with carbon dioxide, about 3 g. of the product remains in solution.

3. The temperature may be determined by a thermometer sheathed in a glass tube, which passes through the stopper and dips into the liquid. A section of rubber tubing slipped over the upper end of the thermometer serves to hold it in place. This device also provides a convenient method of testing the alkalinity of the solution.

4. Since dimethyl sulfate is very toxic, care should be exercised to avoid spilling the liquid or inhaling the vapor of the reaction mixture. Ammonia is a specific antidote.

5. The stated quantities of dimethyl sulfate and sodium hydroxide are merely approximations of the amounts actually required. The dimethyl sulfate is added at the stated rate until all the solid dibenzoylhydrazine has disappeared, and then an

additional quantity of 25 cc. is added. Usually less than the stated amount of alkali is required.

6. The dibenzoyldimethylhydrazine can be obtained in a purer state by treating the cold, filtered chloroform solution with a 1 : 1 mixture of ether and petroleum ether (b.p. 40-60°) until crystallization begins and then adding slowly a moderate excess of petroleum ether. The hydrazine separates in small white needles, m.p. 84-87°.

7. It is found that this treatment removes the benzoic acid almost completely. Alternatively, the benzoic acid can be extracted with a 1 : 1 benzene-ether mixture.

8. The mono- and dihydrochlorides are very hygroscopic and should not be exposed to air for any length of time. Solutions of the dihydrochloride lose hydrochloric acid on evaporation, and the dihydrochloride obtained from solutions so treated tends to be oily. In recrystallization a little concentrated hydrochloric acid is added to the alcoholic solution.

The dihydrochloride may be crystallized by dissolving in boiling absolute ethyl alcohol (1 g. requires 20 cc. of alcohol), adding a little concentrated hydrochloric acid and, after cooling slightly, about one-fifth of the volume of ether. The dimethylhydrazine dihydrochloride separates as a white crystalline powder, melting at 165-167°.

## 3. Methods of Preparation

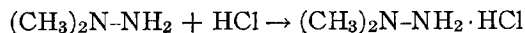
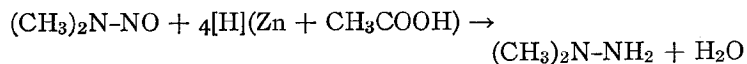
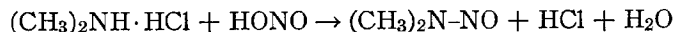
Symmetrical dimethylhydrazine has been obtained by heating the methiodide of 1-methylpyrazole.<sup>1</sup> It has usually been prepared by methylation of diformylhydrazine and subsequent hydrolysis with hydrochloric acid.<sup>2</sup> The present method is based on the observation of Folpmers that dibenzoylhydrazine may be similarly employed.<sup>3</sup>

<sup>1</sup> Knorr and Köhler, Ber. **39**, 3257 (1906).

<sup>2</sup> Harries and Klamt, *ibid.* **28**, 503 (1895); Harries and Haga, *ibid.* **31**, 56 (1898); Thiele, *ibid.* **42**, 2575 (1909).

<sup>3</sup> Folpmers, Rec. trav. chim. **34**, 34 (1915).

## VII

**unsym.-DIMETHYLHYDRAZINE HYDROCHLORIDE**

Submitted by H. H. HATT.

Checked by W. W. HARTMAN and W. D. PETERSON.

**1. Procedure**

(A) *Nitrosodimethylamine*.—In a 2-l. round-bottomed flask provided with a mechanical stirrer, are placed 245 g. (3 moles) of dimethylamine hydrochloride, 120 cc. of water, and 10 cc. of approximately 2 *N* hydrochloric acid. The resulting solution is stirred vigorously and maintained at 70–75° by heating on a water bath, while 235 g. (3.23 moles) of 95 per cent sodium nitrite suspended in 150 cc. of water is added from a dropping funnel over a period of an hour. The reaction mixture is tested frequently and maintained barely acid to litmus by further 1-cc. additions of 2 *N* hydrochloric acid when necessary (about 30–35 cc. of acid is required). Stirring and heating are continued for two hours after all the sodium nitrite has been added.

The flask is arranged for distillation, and the reaction mixture is distilled under slightly diminished pressure on a water bath until the residue is practically dry. To the residue 100 cc. of water is added, and the process of distillation to dryness is repeated. The distillates are combined and saturated with potassium carbonate (about 300 g. is required); the upper layer of dimethylnitrosoamine is removed, and the water layer is extracted with three 140-cc. portions of ether. The combined nitrosoamine and ethereal extracts are dried over anhydrous

potassium carbonate and distilled through a 30-cm. fractionating column. The yield of product boiling at 149–150°/755 mm. is 195–200 g. (88–90 per cent of the theoretical amount). Nitrosodimethylamine is a yellow oil which darkens in bright light.

(B) *unsym.-Dimethylhydrazine Hydrochloride*.—In a 5-l. round-bottomed flask provided with a mechanical stirrer, dropping funnel, and thermometer, are placed 200 g. (2.7 moles) of nitrosodimethylamine, 3 l. of water, and an amount of zinc dust corresponding to 650 g. (10 moles) of 100 per cent strength (Note 1). While the mixture is stirred and maintained at 25–30° by immersion in a water bath, 1 l. (14 moles) of 85 per cent acetic acid is added from the dropping funnel over a period of two hours. Subsequently the reaction mixture is heated for one hour at 60°, allowed to cool, and the excess zinc dust filtered and washed with a little water. The aqueous liquors are combined and transferred to a 12-l. flask arranged for steam distillation. The flask is fitted with a dropping funnel, and the steam inlet is provided with a trap. A large filtering or distilling flask serves as the receiver, and the side tube is connected with two absorption flasks, each containing 1 : 1 hydrochloric acid (Note 2). The aqueous liquors are made distinctly alkaline by adding a concentrated solution of 1000 g. of sodium hydroxide through the dropping funnel, and the mixture is then steam-distilled until a test portion of the distillate shows only a faint reduction with Fehling's solution. Usually about 5–6 l. of distillate suffices to remove the dimethylhydrazine. The distillation is more rapid if a free flame is placed under the distillation flask.

The aqueous distillate is treated with 650 cc. of concentrated hydrochloric acid and concentrated on a steam bath, under reduced pressure, until the residual liquor becomes a syrupy mass (Note 3). This is desiccated further by adding 150 cc. of absolute ethyl alcohol and evaporating under reduced pressure. Two or three such treatments with alcohol dry the crystalline material sufficiently so that it no longer sticks to the sides of the flask. The crude product is dried in a vacuum desiccator over calcium chloride. The pale yellow, dry, crystalline solid weighs 200–215 g. (77–83 per cent of the theoretical amount). The dried product

may be purified by dissolving it in an equal weight of boiling absolute ethyl alcohol and then chilling in an ice bath. The yield of pure white crystals melting at  $81-82^{\circ}$  is 180-190 g. (67-73 per cent of the theoretical amount) (Note 4).

## 2. Notes

1. The approximate strength of the zinc dust should be known in order to insure complete reduction.

2. If this step is carried out under a hood, the absorption flasks are unnecessary. During the first minutes of the subsequent steam distillation, volatile nitrogen bases, consisting chiefly of ammonia and methylamine, are driven over.

3. A concentrated aqueous solution of the free hydrazine may be obtained from the syrupy residue by allowing it to drop onto a large excess of solid sodium hydroxide, and distilling until the temperature reaches  $100^{\circ}$ . To obtain the anhydrous base, the concentrated aqueous solution is redistilled after standing over potassium hydroxide, the base is collected over barium oxide and after several days' standing is distilled again. The free hydrazine boils at  $62-65^{\circ}/765$  mm.; it is extremely hygroscopic and attacks cork and rubber.

4. The product is the monohydrochloride of the base.

## 3. Methods of Preparation

The preparation of unsymmetrical dimethylhydrazine by reduction of nitrosodimethylamine was described by Fischer<sup>1</sup> and by Renouf.<sup>2</sup> It has also been prepared by methylation of hydrazine,<sup>3</sup> by reduction of nitrodimehylamine,<sup>4</sup> and by the action of aminopersulfuric acid on dimethylamine.<sup>5</sup>

<sup>1</sup> Fischer, Ber. 8, 1587 (1875).

<sup>2</sup> Renouf, *ibid.* 13, 2170 (1880).

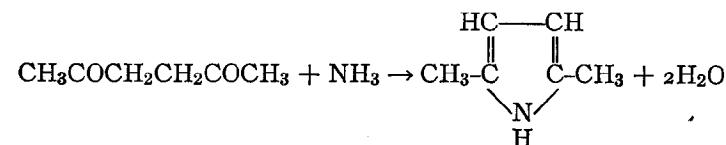
<sup>3</sup> Harries and Haga, *ibid.* 31, 56 (1898).

<sup>4</sup> Franchimont, Rec. trav. chim. 3, 427 (1884); Backer, *ibid.* 31, 150 (1912).

<sup>5</sup> Sommer and Templin, Ger. pat. 338,609 [Frld. 13, 203 (1916-1921)].

## VIII

### 2,5-DIMETHYLPYRROLE



Submitted by D. M. YOUNG and C. F. H. ALLEN.

Checked by JOHN R. JOHNSON and H. B. STEVENSON.

### 1. Procedure

In a 500-cc. Erlenmeyer flask, fitted with an air-cooled reflux condenser of large bore (Note 1), are placed 100 g. (0.88 mole) of acetylacetone (Note 2) and 200 g. (1.75 moles) of ammonium carbonate, in lumps. The mixture is heated in an oil bath at  $100^{\circ}$  until effervescence stops; this requires sixty to ninety minutes. The air-cooled condenser is replaced by a water-cooled condenser of large bore, and the mixture is refluxed gently at  $115^{\circ}$  (bath temperature) for thirty minutes longer (Notes 1 and 3). The mixture is cooled, and the upper, yellow layer of the pyrrole is separated (Note 4). The lower layer is extracted with 15 cc. of chloroform, which is added to the crude pyrrole. The whole is dried over anhydrous calcium chloride, in a tightly stoppered container which has been swept out with nitrogen beforehand.

The material is transferred (Note 4) to a modified Claisen flask having a fractionating side arm, and the chloroform is distilled off completely under reduced pressure (without being condensed). The dimethylpyrrole is collected at  $51-53^{\circ}/8$  mm. or  $78-80^{\circ}/25$  mm.; only a small residue (4-5 g., b.p.  $80-85^{\circ}/25$  mm.) remains. The product weighs 68-72 g. (81-86 per cent of

the theoretical amount) and is quite pure (Note 5); it should be stored in an inert atmosphere in a tightly sealed, dark glass container.

## 2. Notes

1. Care must be taken to prevent sublimed ammonium carbonate from blocking the condenser. From time to time the sublimate is pushed back into the reaction mixture by means of a stout glass rod.

2. Acetylacetone may be prepared conveniently by hydrolysis of 2,5-dimethylfuran. The following procedure is based upon directions supplied to the checkers by Mr. Gwyn Benson, of the Shawinigan Chemicals, Ltd. In a 500-cc. flask are placed 125 g. (1.2 moles) of 2,5-dimethylfuran (b.p. 93–96°), 60 g. of water, 50 g. of glacial acetic acid, and 3 cc. of 10 per cent sulfuric acid. The mixture is boiled gently for thirty-six hours, 1 g. of sodium acetate crystals is added to convert the sulfuric acid to sodium sulfate, and the material is distilled at atmospheric pressure through a fractionating column. The fraction boiling up to 155° is removed, and the residual liquid is distilled under reduced pressure. The acetylacetone is collected at 78–79°/15 mm., or 88–89°/25 mm., and weighs 128–133 g. (86–90 per cent of the theoretical amount).

3. At the end of the first and second periods of heating it is well to dissolve the sublimed ammonium carbonate, by pouring 5–10 cc. of hot water back and forth through the condenser, and return the solution to the reaction mixture.

4. In this and all the subsequent operations, the dimethylpyrrole should be manipulated with a minimum exposure to atmospheric oxygen. The distilling apparatus should be swept out with nitrogen at the start and nitrogen admitted, instead of air, whenever the vacuum is released.

5. Since 2,5-dimethylpyrrole does not form solid derivatives, the refractive index may be used as a criterion of purity. The value for a freshly distilled specimen is  $n_D^{22}$  1.500. On standing the material gradually turns red and the refractive index rises. This change is accelerated by air and light.

## 3. Methods of Preparation

2,5-Dimethylpyrrole has been prepared previously from acetylacetone by heating with alcoholic ammonia at 150° in a sealed tube.<sup>1</sup> It has also been prepared by hydrolysis and decarboxylation of 2,5-dimethyl-3,4-dicarbethoxypyrrole, obtained from ethyl diacetosuccinate and ammonia.<sup>2</sup>

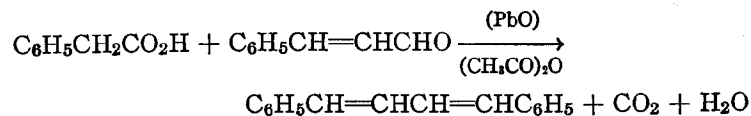
<sup>1</sup> Paal, Ber. 18, 2254 (1885).

<sup>2</sup> Knorr, *ibid.* 18, 299, 1565 (1885).

## IX

## 1,4-DIPHENYLBUTADIENE

(Bistyril)



Submitted by B. B. CORSON.

Checked by C. R. NOLLER and J. F. CARSON.

## 1. Procedure

IN a 1-l. round-bottomed flask equipped with a reflux condenser and protected by a calcium chloride tube are placed 150 g. (1.1 moles) of phenylacetic acid (Org. Syn. Coll. Vol. 1, 427), 147 g. (1.1 moles) of freshly distilled cinnamic aldehyde, 122 g. of litharge, and 155 cc. of acetic anhydride. The mixture is boiled for five hours (Note 1), poured while still hot into a beaker, and allowed to stand overnight. The semi-solid contents are stirred to a mush, filtered with suction in a large Buchner funnel, and pressed dry. The solid is washed on the funnel with two 35-cc. portions of ethyl alcohol, stirring the material thoroughly before applying suction. The cake is transferred to a beaker, stirred to a mush with 50 cc. of alcohol, and again filtered with suction. The material is washed with another 50-cc. portion of alcohol in the same manner (Note 2). The product, which is light yellow to tan in color, weighs 62-67 g. (27-29 per cent of the theoretical amount) (Note 3) and melts at 149.5-153.5°.

For purification the material is dissolved in 300 cc. of hot benzene, the solution boiled three minutes with 5 g. of decolorizing carbon, and filtered hot, with gentle suction, through a warm Buchner funnel. The benzene filtrate is treated with

500 cc. of hot ethyl alcohol, heated to boiling, and then cooled to 10° in an ice bath, with shaking. After filtering the crystals with suction and pressing thoroughly, 50 cc. of ethyl alcohol is allowed to soak into the cake and suction applied again. The recrystallized product weighs 52-57 g. (23-25 per cent of the theoretical amount) (Note 4) and melts at 152.5-153.5°. This product is the trans-trans form of the diene.

## 2. Notes

1. During the first half hour, the flask should be heated gently and shaken several times to facilitate solution of the lead oxide.
2. Thorough washing is essential.
3. About 8 g. of crude hydrocarbon can be recovered from the original mother liquor, but the recovery is tedious and is not recommended.
4. An additional quantity of about 5.5 g. can be obtained by evaporating the mother liquor to 25 cc. and allowing to crystallize.

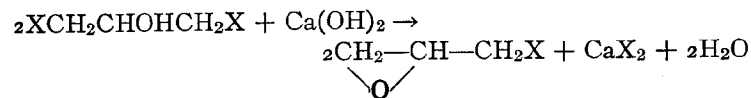
## 3. Methods of Preparation

The only method of preparative interest is the condensation of phenylacetic acid and cinnamic aldehyde.<sup>1</sup> The above procedure follows the method of Kuhn and Winterstein.<sup>2</sup> Bistyril has been obtained also from styrylmagnesium bromide and cupric chloride.<sup>3</sup>

<sup>1</sup> Thiele and Schlessner, *Ann.* **306**, 198 (1899).<sup>2</sup> Kuhn and Winterstein, *Helv. Chim. Acta* **11**, 103 (1928).<sup>3</sup> Sakellarios and Kyrimis, *Ber.* **57**, 325 (1924); see also, Gilman and Parker, *J. Am. Chem. Soc.* **46**, 2827 (1924), Gilman and Pickens, *ibid.* **47**, 2410 (1925).

## X

## EPICHLOROHYDRIN AND EPIBROMOHYDRIN



Submitted by GÉZA BRAUN.

Checked by W. W. HARTMAN and G. L. BOOMER.

## 1. Procedure

(A) *Epichlorohydrin*.—In a 5-l. round-bottomed flask, 1350 g. (988 cc., 10.5 moles) of glycerol  $\alpha,\gamma$ -dichlorohydrin (Org. Syn. Coll. Vol. 1, 286), 840 g. (10 moles) of technical, finely powdered calcium hydroxide (88 per cent), and 840 cc. of water (20°) are shaken vigorously for fifteen minutes (Note 1). The mixture forms a thick paste at the beginning, but the epichlorohydrin soon separates from the calcium salts as a mobile liquid. The flask is fitted with a rubber stopper carrying a wide delivery tube, and the mixture is distilled from a water bath, at first under 40–50 mm. pressure. The pressure is then lowered to 10 mm. and the temperature raised gradually to 95–100° (Note 2). The receiver must be cooled effectively in an ice-salt mixture to  $-5^\circ$  or below, to insure a maximum yield. The distillate is transferred to a separatory funnel, the aqueous (upper) layer returned to the reaction flask, and the distillation repeated. A third distillation in a similar manner gives a small additional amount of epichlorohydrin (Note 3). The lower layers from the successive distillations are combined and distilled through a fractionating column, under reduced pressure. The epichlorohydrin fraction is collected up to 75°/50 mm., and the residue (about 160–180 cc.), which contains a large percentage of dichlorohydrin, is returned to the original reaction flask, together with 150 cc. of water. This

material is distilled once under reduced pressure as described above, and the lower layer of the distillate is combined with the main fraction of epichlorohydrin. The crude product is distilled at ordinary pressure until the temperature of the vapor reaches 115°; at this point the distillation is stopped and the water layer removed from the distillate. The lower layer of the distillate is dried over anhydrous sodium sulfate and returned to the distilling flask. After a small fore-run, the epichlorohydrin distills at 115–117°. The yield is 650–700 g. (67–72 per cent of the theoretical amount).

(B) *Epibromohydrin*.—In a 5-l. round-bottomed flask, 2140 g. (1000 cc., 9.8 moles) of glycerol  $\alpha,\gamma$ -dibromohydrin (Org. Syn. 14, 42) is suspended in 1.5 l. of water, and 400 g. of technical, powdered calcium hydroxide (88 per cent) is added gradually, with shaking, in the course of about fifteen minutes. A further quantity of 400 g. of calcium hydroxide (total, 10 moles) is added at once, and the epibromohydrin is distilled at reduced pressure in the manner described for epichlorohydrin (Note 2). The combined lower layers from two such distillations (about 750 cc.) are dried over anhydrous sodium sulfate and fractionated at atmospheric or reduced pressure. The yield of epibromohydrin, b.p. 134–136° or 61–62°/50 mm., is 1130–1200 g. (84–89 per cent of the theoretical amount).

## 2. Notes

1. The prescribed amount of water should be used; more water causes frothing. The reaction is not exothermic.
2. Epichlorohydrin boils at 30–32°/10 mm., epibromohydrin at 61–62°/50 mm. Both these liquids are quite volatile with water vapor under reduced pressure.
3. The volume of the epichlorohydrin layer obtained in the successive distillations is roughly: (1) 500 cc., (2) 200 cc., (3) 20 cc.

## 3. Methods of Preparation

Epichlorohydrin<sup>1</sup> and epibromohydrin<sup>2</sup> have been prepared by treatment of glycerol dichloro- and dibromohydrins with



alkalies in various ways. The procedures described here represent a laboratory application of Griesheim's method.<sup>3</sup>

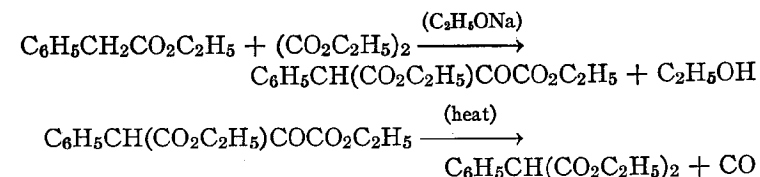
<sup>1</sup> Org. Syn. Coll. Vol. I, 229.

<sup>2</sup> Berthelot and Luca, Ann. chim. [3] 48, 306, 311 (1856); Reboul, *ibid.* [3] 60, 32 (1860).

<sup>3</sup> Griesheim, Ger. pat. 246,242 [Frdl. 10, 22 (1910-1912)]; Braun, J. Am. Chem. Soc. 54, 1248 (1932).

## XI

### ETHYL PHENYLMALONATE



Submitted by P. A. LEVENE and G. M. MEYER.

Checked by L. F. FIESER and C. H. FISHER.

#### 1. Procedure

In a 2-l. three-necked flask fitted with a mercury-sealed stirrer, reflux condenser, and dropping funnel is placed 500 cc. of absolute ethyl alcohol (Note 1), and 23 g. (1 gram atom) of cleanly cut sodium is added in portions. When the sodium has dissolved the solution is cooled to 60°, and 146 g. (1 mole) of ethyl oxalate (Org. Syn. Coll. Vol. 1, 256) (Note 2) is added in a rapid stream through the funnel with vigorous stirring. This is washed down with a small quantity of absolute alcohol, and is followed immediately by the addition of 175 g. (1.06 moles) of ethyl phenylacetate (Org. Syn. Coll. Vol. 1, 265) (Note 2). Stirring is discontinued at once, the reaction flask is lowered from the stirrer, and a 2-l. beaker is made ready. Within four to six minutes after the ethyl phenylacetate has been added crystallization sets in. The contents of the flask are transferred immediately to the beaker at the first sign of crystallization, which is nearly instantaneous.

The nearly solid paste of the sodium derivative is allowed to cool to room temperature and then stirred thoroughly with 800 cc. of dry ether. The solid is collected by suction and washed repeatedly with dry ether. The phenyloxaloacetic ester is liberated from the sodium salt with dilute sulfuric acid (29 cc.

of concentrated sulfuric acid in 500 cc. of water). The nearly colorless oil is separated, and the aqueous layer is extracted with three 100-cc. portions of ether, which are combined with the oil. The ethereal solution is dried over anhydrous sodium sulfate, and the ether is distilled off. The residual oil, contained in a modified Claisen flask having a fractionating side arm, is heated under a pressure of about 15 mm. in a bath of Wood's metal. The temperature of the bath is brought gradually to 175° and kept there until the evolution of carbon monoxide is complete. During this process the heating is momentarily discontinued in the event of a temporary increase in pressure. At the end of the reaction (five to six hours) the oil which has distilled is returned to the flask, and the ethyl phenylmalonate is distilled at reduced pressure. The fraction boiling at 158–162°/10 mm. weighs 189–201 g. (80–85 per cent of the theoretical amount).

## 2. Notes

1. A high grade of absolute alcohol is essential. Ordinary "absolute" alcohol may be treated with about 5 per cent of its weight of sodium and distilled directly into the reaction flask.

2. To insure absolutely dry and neutral reagents the ethyl oxalate and ethyl phenylacetate were shaken with anhydrous potassium carbonate and distilled carefully under reduced pressure, after a preliminary heating under atmospheric pressure until their boiling points were reached.

## 3. Methods of Preparation

The procedure is based upon the standard method of Wislicenus.<sup>1</sup> Ethyl phenylmalonate has also been obtained from benzyl cyanide and ethyl carbonate.<sup>2</sup> Phenylmalonic acid has been prepared by carbonation of the enolate of phenylacetic acid.<sup>3</sup>

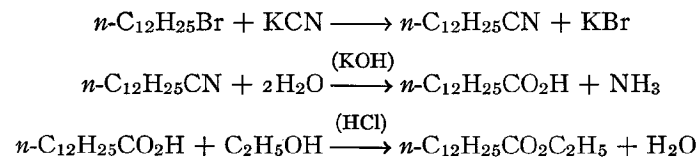
<sup>1</sup> Wislicenus, Ber. **27**, 1091 (1894); Ruhemann, J. Chem. Soc. **81**, 1214 (1902); Pickard and Yates, *ibid.* **95**, 1014 (1909); Forster and Müller, *ibid.* **97**, 135 (1910); Baker and Ingold, *ibid.* **1927**, 835; Blum-Bergmann, Ber. **65**, 109 (1932).

<sup>2</sup> Nelson and Cretcher, J. Am. Chem. Soc. **50**, 2760 (1928).

<sup>3</sup> Ivanoff and Spassoff, Bull. soc. chim. [4] **49**, 20 (1931).

## XII

### ETHYL *n*-TRIDECYLATE



Submitted by JOHN R. RUHOFF.

Checked by WALLACE H. CAROTHERS and W. L. MCEWEN.

## 1. Procedure

In a 12-l. flask fitted with a reflux condenser and an efficient, liquid-sealed mechanical stirrer (Note 1) are placed 2.5 l. of 95 per cent ethyl alcohol, 872 g. (3.5 moles) of pure *n*-dodecyl bromide (Org. Syn. **15**, 24) and 278 g. (3.85 moles) of powdered 90 per cent potassium cyanide (Note 2). The mixture is refluxed for fifteen hours, with stirring, in a water bath (Note 3). At the end of this time another 278-g. portion of potassium cyanide is added and the mixture refluxed, with stirring, for fifteen hours longer. The flask is allowed to cool, and a solution of 670 g. of 90 per cent potassium hydroxide in 1 l. of water is added (Note 4). The solution is refluxed and stirred for thirty hours. The flask is fitted with a head for steam distillation (Note 5), and steam is passed in until foaming prevents further distillation. When the flask has cooled somewhat, the steam inlet is replaced by a separatory funnel with a stem reaching to the bottom of the flask, and 1500 cc. of concentrated hydrochloric acid (sp. gr. 1.18) or the equivalent amount of more dilute acid is added. The flask is shaken occasionally to prevent stratification of the hydrochloric acid. The dropping funnel is then replaced by the steam

inlet, and steam is passed through for about one-half hour. At the end of this time the water layer is siphoned off and discarded (Note 6).

The crude acid while still warm and fluid is treated with 815 cc. (14 moles) of 95 per cent ethyl alcohol containing 20-30 g. (3-5 per cent by weight) of anhydrous hydrogen chloride (Org. Syn. Coll. Vol. 1, 287), and the solution is filtered from insoluble impurities. The filtrate is placed in a 3-l. flask fitted with a reflux condenser, 160 g. of anhydrous calcium chloride is added, and the mixture is refluxed for twenty-four hours (Note 7). The lower layer is siphoned off and diluted with twice its volume of water to recover any dissolved ester. The recovered ester is combined with the main portion, 408 cc. of alcohol containing 3-5 per cent of anhydrous hydrogen chloride and 80 g. of calcium chloride are added, and the mixture is refluxed for another twenty-four hours. The lower layer is siphoned off and the dissolved ester recovered as before. The upper layer is washed twice with an equal volume of warm water (30-40°) and transferred to a 2-l. separatory funnel; the volume of the oil is approximately 1000 cc. About 500 cc. of warm water and a few drops of phenolphthalein are also placed in the funnel, and very dilute aqueous ammonia (concentrated aqueous ammonia diluted with twenty volumes of water) is added, with shaking, until the resulting emulsion has a distinctly pink color (50-100 cc. is required). Alcohol is added in portions of about 100 cc. until the emulsion is broken and the layers begin to separate quite rapidly; usually two or three additions of alcohol suffice. The lower layer is drawn off and set aside (Note 8). The oil is washed three times with warm water; if necessary, alcohol is added to break the emulsion. The ester is dried with anhydrous calcium chloride, filtered, and distilled under reduced pressure. The yield of ethyl tridecylate, b.p. 163-165°/5 mm. (178-180°/20 mm.; 197-198°/60 mm.) is 615-660 g. (73-78 per cent of the theoretical amount). By refractionating the fore- and after-runs, an additional 50-70 g. of product is obtained; 15-30 g. of ester and acid are recovered from the ammoniacal washings and from the calcium chloride used to dry the main portion. The total yield

is 685-710 g. (81-84 per cent of the theoretical amount) (Notes 9 and 10).

## 2. Notes

1. A mercury-sealed stirrer may be used, but a "vaseline seal" is very satisfactory.

2. Potassium cyanide gives better results than sodium cyanide. It is essential that the material be finely powdered.

3. The entire operation should be carried out in a hood. A small wash tub placed on the bench and heated from the side with a Bunsen burner is a convenient water bath.

4. This corresponds to 3.85 moles of potassium hydroxide plus a quantity sufficient so that, after the hydrolysis is completed, the solution will contain 10 per cent of alkali. When less than that amount is used the quantity of unhydrolyzed nitrile is greater.

5. The condenser should lead to a 2-l. suction flask the side arm of which is connected directly to the vent of the hood. The alcohol has the odor of hydrocyanic acid and should be discarded.

6. The crude acid may be used for some purposes, but it contains a small quantity of unhydrolyzed nitrile, some material of very disagreeable odor (possibly isocyanide), and usually a small amount of a blue precipitate (an iron-cyanide complex salt). In the preparation of the ester, the precipitate is removed by filtering the alcohol solution of the acid as its presence will interfere with the removal of the free tridecylic acid after esterification.

7. A few pieces of porous plate should be added to prevent bumping.

8. By addition of acid to the washings a small amount (15-30 g.) of ester and acid may be recovered.

9. For larger runs, the procedure is the same and the yields are somewhat higher. Thus, in runs by the author using twice the above quantities, yields of 88-89 per cent were obtained.

10. Pentadecylic acid and ethyl pentadecylate have been prepared by the same procedure from *n*-tetradecyl bromide (Org. Syn. 15, 26) with approximately the same yield.

## 3. Methods of Preparation

Tridecylic acid has been prepared by the malonic ester synthesis from undecyl iodide,<sup>1</sup> by the oxidation of  $\alpha$ -hydroxymyristic acid in acetone with potassium permanganate,<sup>2</sup> by the action of dodecyl bromide on potassium cyanide and subsequent hydrolysis,<sup>3</sup> and from undecyl iodide and ethyl cyanoacetate.<sup>4</sup> The present method is an adaptation of that of Ruzicka, Stoll, and Schinz.<sup>3</sup>

<sup>1</sup> Levene, West, Allen, and van der Scheer, *J. Biol. Chem.* **23**, 73 (1915).

<sup>2</sup> Levene and West, *ibid.* **18**, 465 (1914).

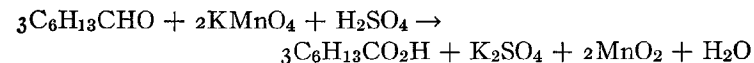
<sup>3</sup> Ruzicka, Stoll, and Schinz, *Helv. Chim. Acta* **11**, 685 (1928).

<sup>4</sup> Robinson, *J. Chem. Soc.* **125**, 230 (1924).

## XIII

*n*-HEPTOIC ACID

## (Enanthic Acid)



Submitted by JOHN R. RUHOFF.

Checked by C. R. NOLLER and M. PATT.

## 1. Procedure

IN a 5-l. flask fitted with a mechanical stirrer and cooled in an ice bath are placed 2.7 l. of water and 350 cc. (644 g.) of concentrated sulfuric acid (sp. gr. 1.84). When the temperature has fallen to 15°, 342 g. (403 cc., 3 moles) of heptaldehyde (Note 1) is added, followed by 340 g. (2.15 moles) of potassium permanganate in 15-g. portions. The permanganate is added at such a rate that the temperature does not rise above 20° (Note 2). When the addition of the permanganate is complete, sulfur dioxide is passed through the solution until it becomes clear (Note 3). The oily layer is separated, washed once with water, and distilled from a modified Claisen flask having a 30-cm. fractionating side arm. The fore-runs are separated from any water and distilled again; this is followed by a redistillation of the high-boiling fractions. The yield of material boiling at 159–161°/100 mm. is 296–305 g. (76–78 per cent of the theoretical amount) (Note 4). This product is sufficiently pure for many purposes; titration indicates a purity of 95–97 per cent.

For further purification the product is dissolved in a solution of 140 g. (3.5 moles) of sodium hydroxide in 700 cc. of water and steam-distilled from a 2-l. flask until a test portion of the distillate is free of oil. The solution remaining in the flask is cooled to room temperature and acidified with 375 cc. (4.5 moles) of concen-

trated hydrochloric acid. The heptonic acid is separated and distilled from a Claisen flask with fractionating side arm. The recovery of acid boiling at 155–157°/80 mm. is 85–90 per cent of the weight of impure material used. Titration indicates it to be 100 per cent pure.

## 2. Notes

1. Freshly distilled heptaldehyde boiling at 85.5–87.5°/90 mm. was used.
2. The stirring must be vigorous. The time required for the addition of the permanganate is about two hours.
3. Sulfur dioxide, in the presence of sulfuric acid, reduces the precipitated manganese dioxide to the soluble sulfate; the removal of this large quantity of flocculent material greatly facilitates separation of the heptonic acid. The addition of sulfur dioxide requires about two hours, and an excess is to be avoided. Sodium bisulfite may be used if gaseous sulfur dioxide is not available.
4. Occasionally the heptonic acid has a yellow color which cannot be removed by fractionation.

## 3. Methods of Preparation

Heptonic acid has been prepared by the oxidation of heptaldehyde with nitric acid,<sup>1</sup> with potassium permanganate in alkaline aqueous solution<sup>2</sup> or in acetone solution,<sup>3</sup> and with potassium dichromate and sulfuric acid.<sup>4</sup>

<sup>1</sup> Tilley, Ann. **67**, 107 (1848); Mehlis, *ibid.* **185**, 360 (1877); Krafft, Ber. **15**, 1717 (1882).

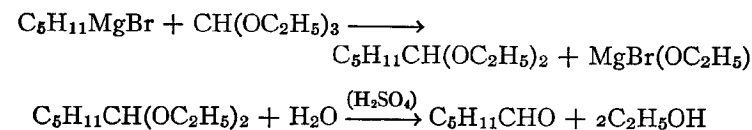
<sup>2</sup> Fournier, Bull. soc. chim. [4] **5**, 921 (1909).

<sup>3</sup> Rogers, J. Am. Pharm. Assoc. **12**, 503 (1923) [C. A. **18**, 152 (1924)].

<sup>4</sup> Grimshaw and Schorlemmer, Ann. **170**, 141 (1873).

## XIV

### *n*-HEXALDEHYDE



Submitted by G. BRYANT BACHMAN.

Checked by C. R. NOLLER and W. S. WOON.

## 1. Procedure

IN a 2-l. three-necked round-bottomed flask fitted with a liquid-sealed mechanical stirrer, a 250-cc. dropping funnel, and a reflux condenser to which is attached a calcium chloride tube, are placed 30 g. (1.25 gram atoms) of magnesium turnings, 50 cc. of dry ether, and a small crystal of iodine. Stirring is started, and 5 cc. (6 g.) of *n*-amyl bromide is added (Note 1). As soon as the reaction has started, 300 cc. of dry ether is added and then, more slowly, a solution of 183 g. (total, 189 g.; 1.25 moles) of *n*-amyl bromide in 150 cc. of dry ether. If external cooling is provided, all the alkyl halide may be added within half an hour; the solution is refluxed gently for another half-hour to complete the reaction. The heat is removed, the flask cooled to 50°, and 148 g. (1 mole) of ethyl orthoformate (Org. Syn. Coll. Vol. **1**, 253) is added during the course of fifteen to twenty minutes. The mixture is refluxed for six hours (Note 2); at the end of this time the condenser is arranged for distillation and the ether is removed completely with the aid of a steam bath.

The reaction mixture is cooled and treated carefully with 750 cc. of chilled 6 per cent hydrochloric acid. The contents of the flask are kept cool by the occasional addition of ice while

the acid is being introduced. As soon as all the solid has dissolved (Note 3), the upper oily layer of hexaldehyde acetal is separated. The acetal is hydrolyzed by distilling it with a solution of 100 g. (55 cc.) of concentrated sulfuric acid in 700 cc. of water. The free aldehyde distils rapidly, and the distillation is complete when a sample of fresh distillate contains 5 per cent or less of immiscible oil. The distillate is collected in a solution of 100 g. (1 mole) of sodium bisulfite in 300 cc. of water. The mixture is shaken vigorously for several minutes; the oily layer remaining undissolved in the bisulfite solution is principally *n*-amyl alcohol and is discarded. To remove the remainder of the amyl alcohol and other impurities the bisulfite solution is steam-distilled until 200 cc. of distillate has been collected.

The residual aldehyde-bisulfite solution is cooled to 40–50°, a suspension of 80 g. of sodium bicarbonate in 200 cc. of water is added carefully, and the free aldehyde is removed by steam distillation. The upper layer of the distillate is separated, washed with three 50-cc. portions of water (Note 4), dried with 20 g. of anhydrous sodium sulfate, and distilled through a 20-cm. column. The yield of *n*-hexaldehyde, b.p. 126–129°, is 45–50 g. (45–50 per cent of the theoretical amount).

## 2. Notes

1. The *n*-amyl bromide was prepared in the usual manner (Org. Syn. Coll. Vol. 1, 23) and distilled at 127–129°.

2. Sometimes a white precipitate begins to form immediately, but more often it does not appear until after twenty to thirty minutes of refluxing. If this period of heating is materially decreased, a sudden exothermic reaction occurs when the ether is removed and the yield may be seriously reduced. Longer periods of heating do not increase the yield of hexaldehyde.

3. Solution takes place slowly and is hastened considerably by the use of a mechanical stirrer.

4. The aldehyde dissolved by the wash water may be recovered by steam distillation, but this is scarcely worth while since hexaldehyde is not very soluble in water.

## 3. Methods of Preparation

Hexaldehyde has been prepared from caproic acid by passing it over zinc dust at 300°,<sup>1</sup> by reaction with amylene at 300° in the presence of thorium oxide,<sup>2</sup> by passing it over manganous oxide at 300–360° with two volumes of formic acid,<sup>3</sup> and by distillation of the calcium salt with calcium formate.<sup>4</sup> It has also been prepared by heating  $\alpha$ -hydroxyheptoic acid or better  $\alpha$ -acetoxyheptoic acid,<sup>5</sup> and by the reaction of ethyl orthoformate with *n*-amylmagnesium bromide.<sup>6</sup>

<sup>1</sup> Maihle, Chem. Ztg. **33**, 243 (1909).

<sup>2</sup> Maihle, *ibid.* **34**, 1174 (1910).

<sup>3</sup> Sabatier and Maihle, Compt. rend. **158**, 986 (1914).

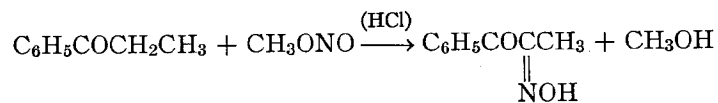
<sup>4</sup> Lieben and Janecek, Ann. **187**, 130 (1877).

<sup>5</sup> Bagard, Bull. soc. chim. [4] **1**, 309 (1907).

<sup>6</sup> Bachman, J. Am. Chem. Soc. **55**, 4281 (1933).

## XV

## ISONITROSOPROPIOPHENONE



Submitted by WALTER H. HARTUNG and FRANK CROSSLEY.  
Checked by REYNOLD C. FUSON and R. F. PETERSON.

## 1. Procedure

A 3-l. three-necked, round-bottomed flask (A, Fig. 1) is provided with a reflux condenser, liquid-sealed mechanical stirrer,

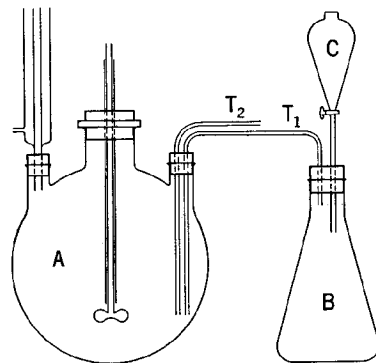


FIG. 1.

and two gas delivery tubes ( $T_1$  and  $T_2$ ) which extend as far as possible into the flask. Methyl nitrite is generated in a 2-l. Erlenmeyer flask B which is fitted with a 500-cc. dropping funnel C and connected to A by the tube  $T_1$ . Dry hydrogen chloride (Org. Syn. Coll. Vol. 1, 287) is introduced through  $T_2$ . The apparatus is assembled preferably in a hood with effective draft.

In A is placed a solution of 469 g. (3.5 moles) of propiophenone

(Note 1) in 2300 cc. of ordinary ethyl ether and in B a mixture of 290 g. (4.0 moles) of 95 per cent sodium nitrite, 180 cc. (142 g., 4.5 moles) of methyl alcohol, and 170 cc. of water. In the dropping funnel C is placed 455 cc. of cold dilute sulfuric acid (prepared by adding one volume of concentrated acid to two volumes of water).

The stirrer is started, and hydrogen chloride is introduced through  $T_2$  at the rate of 6–10 bubbles a second. The acid in C is allowed to drop slowly into B, and the gaseous methyl nitrite (Note 2) is introduced through  $T_1$  into the reaction mixture. The solution in A develops a brown-red color, and after about ten minutes the ether begins to reflux gently (Note 3). The rate of evolution of methyl nitrite is then adjusted so that the ether continues to reflux gently. The time required for addition of the methyl nitrite is about four hours. Stirring and addition of hydrogen chloride are continued for thirty minutes longer; at the end of this time the solution has ceased boiling and has assumed a clear yellow color.

The reaction mixture is allowed to stand for several hours (preferably overnight) and is then extracted repeatedly with 500-cc. portions of 10 per cent sodium hydroxide solution, until the alkaline extracting medium remains practically colorless when shaken with the ethereal solution (Note 4). Usually five 500-cc. portions of the sodium hydroxide solution are required. The combined alkaline extracts are poured slowly, with stirring, into a mixture of 700–750 cc. of concentrated hydrochloric acid and about 1 kg. of ice. The crystals of isonitrosopropiophenone are filtered with suction and dried. The product weighs 370–390 g. (63–66 per cent of the theoretical amount) and melts at 111–113°. This material can be crystallized from toluene (about 550 cc.) and yields 315–335 g. of snow-white crystals, m.p. 112–113° (Note 5).

## 2. Notes

1. Propiophenone may be prepared in 70–80 per cent yields from benzene and propionyl chloride or propionic anhydride, in the presence of aluminum chloride.

2. For the preparation of small amounts of the isonitroso-ketone it is more convenient to employ a higher-boiling alkyl nitrite, such as butyl nitrite (p. 7), which can be added directly to the reaction mixture by substituting a dropping funnel for the tube T<sub>1</sub>. Butyl nitrite must be freshly prepared or redistilled shortly before use.

3. The rate of stirring must be kept fairly constant since an abrupt increase in speed may cause the ether to reflux at a dangerous rate.

4. The ethereal solution remaining from the alkaline extractions contains unreacted propiophenone which may be recovered by distilling off the ether and fractionating the residue. The amount of recovered propiophenone, collected at 210–216°, varies from 80 to 110 g.

5. About 25–30 g. of material may be recovered from the toluene mother liquor by extraction with alkali and reprecipitation with acid.

### 3. Methods of Preparation

Isonitrosopropiophenone has been prepared from esters of  $\alpha$ -benzoylpropionic acid by a process involving saponification, nitrosation, and decarboxylation;<sup>1</sup> from phenylmethylglyoxal by the action of hydroxylamine;<sup>2</sup> from propiophenone by treatment with amyl nitrite,<sup>3</sup> methyl nitrite,<sup>4</sup> or butyl nitrite.<sup>5</sup>

<sup>1</sup> v. Pechmann and Müller, Ber. **21**, 2119 (1888).

<sup>2</sup> Kolbe, Ann. **291**, 292 (1896).

<sup>3</sup> Claisen and Manasse, Ber. **22**, 529 (1889).

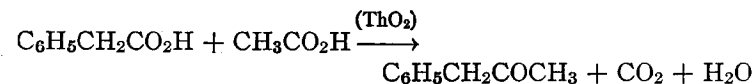
<sup>4</sup> Slater, J. Chem. Soc. **117**, 590 (1920).

<sup>5</sup> Hartung and Munch, J. Am. Chem. Soc. **51**, 2263 (1929).

## XVI

### METHYL BENZYL KETONE

(Phenylacetone)



Submitted by R. M. HERBST and R. H. MANSKE.  
Checked by C. R. NOLLER and C. F. LOVE.

#### 1. Procedure

THE reaction is carried out in the apparatus shown in Fig. 2. A–A is a Pyrex combustion tube, 90 cm. long and 2 cm. in diameter, fitted with a receiving chamber B, having a sealed-in side

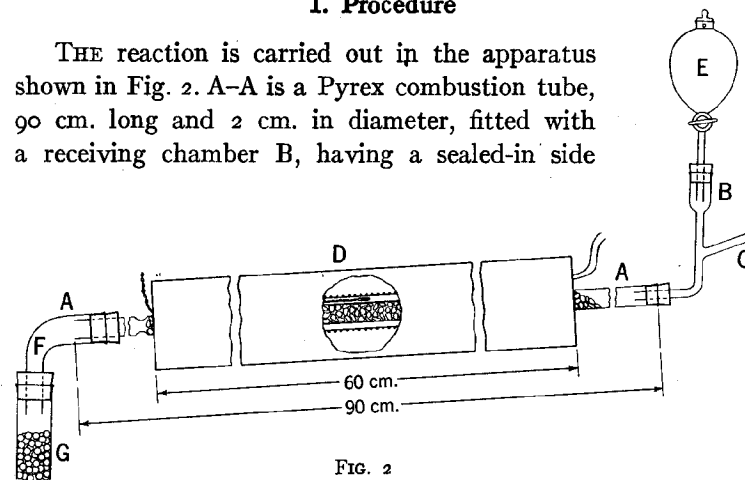


FIG. 2

arm C and bearing a separatory funnel E. The center 60 cm. of the tube is filled with thorium oxide catalyst (Note 1) held in place at the lower end by indentations in the combustion tube. The hot junction D of a pyrometer is placed in contact with the glass tube at its center, and the catalyst-filled section of the tube is wrapped with a thin layer of asbestos paper. The tube is supported in an electrically heated cylindrical furnace, 60 cm. in



length, which is inclined slightly from the horizontal. The annular space between the tube and the furnace is plugged at the ends with asbestos in order to produce a uniform temperature throughout the tube and to hold the glass tube in place. The lower end of the reaction tube is connected through the adapter F to a vertical glass tube G, 40 cm. long and 2 cm. in diameter, which is filled with glass beads and serves as the condenser. An Erlenmeyer flask or other suitable receiver is placed at the lower end of G.

The furnace is heated to 430–450°, and simultaneously the tube is swept out thoroughly with a stream of carbon dioxide, introduced through the side arm C. The carbon dioxide is passed through a wash bottle of concentrated sulfuric acid to dry it and to estimate the rate of flow. A solution of 136 g. (1 mole) of phenylacetic acid, m.p. 77–79° (Org. Syn. Coll. Vol. 1, 427), in 120 cc. (120 g., 2 moles) of glacial acetic acid is placed in the separatory funnel E and is introduced into the receiving chamber B at the rate of twelve to fifteen drops per minute. The entire solution should run through in twelve to fifteen hours. Meanwhile a very slow stream of carbon dioxide (one bubble per second) is passed through the tube C, to keep the gases in motion. After all the solution has been added, the funnel is rinsed with 10 cc. of glacial acetic acid, and this is passed through the reaction tube to facilitate removal of the product. The distillate consists of a slightly fluorescent light brown oil and an aqueous layer. The whole is treated with 300 g. of a mixture of ice and water, and rendered alkaline to litmus with a slight excess of 50 per cent sodium hydroxide solution (Note 2).

The oil is separated (Note 3), and the aqueous layer is extracted with two 50-cc. portions of benzene. The extracts are combined with the oil, and the solvent is distilled off. Fractionation of the residue under reduced pressure gives 80–95 g. of a methyl benzyl ketone fraction, boiling at 110–120°/21–22 mm., and a residue of dibenzyl ketone (Note 4). The main fraction on redistillation yields 74–87 g. (55–65 per cent of the theoretical amount) of methyl benzyl ketone boiling at 110–115°/21–22 mm. (Notes 5, 6, and 7).

## 2. Notes

1. The catalyst is prepared as follows: An amount of screened pumice (about the size of a pea) sufficient to fill the tube is soaked in hot concentrated nitric acid and then washed thoroughly with hot distilled water. In a porcelain dish the pumice is mixed with a solution of 40 g. of thorium nitrate crystals  $[\text{Th}(\text{NO}_3)_4 + 12\text{H}_2\text{O}]$  in 100 cc. of water and is evaporated to dryness, with frequent stirring to insure uniform deposition of the salt. The impregnated pumice is ignited over a Bunsen burner until decomposition of the nitrate is complete. The pumice carries about 15 g. of thorium oxide.

2. From the alkaline solution about 10–15 per cent of the phenylacetic acid may be recovered by acidification with sulfuric acid. The acid separates as an oil which crystallizes slowly on cooling.

3. Salt may be added to facilitate the separation.

4. When several runs are made, the residues may be combined and distilled under reduced pressure. The fraction boiling at 190–210°/20 mm. amounts to about 19 g. per run and is chiefly dibenzyl ketone.

5. Further purification of the product may be effected by converting the ketone into the bisulfite compound, washing this with ether, decomposing with sodium bicarbonate, and steam-distilling.

6. When several runs are to be made, the catalyst should be regenerated after each run by passing air through the reaction tube for about three hours while the temperature is raised gradually to 550°. The yield in the first run may be low, especially if all the oxides of nitrogen have not been removed from the reaction tube.

7. Using the same procedure the following ketones may be obtained in similar yields: ethyl benzyl ketone from phenylacetic acid and propionic acid, methyl  $\beta$ -phenylethyl ketone from hydrocinnamic acid and acetic acid, and ethyl  $\beta$ -phenylethyl ketone from hydrocinnamic acid and propionic acid.

## 3. Methods of Preparation

Methyl benzyl ketone has been prepared by distilling a mixture of the barium<sup>1</sup> or calcium<sup>2</sup> salts of phenylacetic and acetic acids, and by passing the vapors of these acids over a heated thorium oxide catalyst.<sup>3,4</sup> It has been prepared by the reaction of phenylacetyl chloride with zinc methyl,<sup>5</sup> by rearrangement of  $\alpha$ -phenyl  $\beta$ -methyl ethylene oxide,<sup>6</sup> by heating  $\alpha$ -phenyl  $\beta$ -methyl ethylene glycol with dilute sulfuric acid,<sup>7</sup> by heating the addition product of chloroacetone and phenylmagnesium bromide,<sup>7</sup> and by the hydrolysis of  $\alpha$ -phenylacetoacetic ester<sup>8</sup> or of phenacylmalonic ester.<sup>9</sup> The procedure given here is based upon that of Senderens<sup>3</sup> and of Pickard and Kenyon.<sup>4</sup> It has been reported recently that "thoria aëroge" is superior to other forms of thoria catalysts for the preparation of ketones from aliphatic acids or esters.<sup>10</sup>

<sup>1</sup> Radziszewski, Ber. **3**, 198 (1870).

<sup>2</sup> Young, J. Chem. Soc. **59**, 621 (1891).

<sup>3</sup> Senderens, Ann. chim. [8] **28**, 318 (1913).

<sup>4</sup> Pickard and Kenyon, J. Chem. Soc. **105**, 1124 (1914).

<sup>5</sup> Popow, Ber. **5**, 500 (1872).

<sup>6</sup> Fourneau and Tiffeneau, Compt. rend. **141**, 663 (1905).

<sup>7</sup> Tiffeneau, Ann. chim. [8] **10**, 345, 368 (1907).

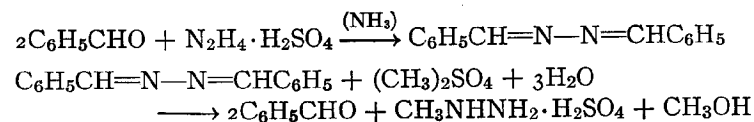
<sup>8</sup> Beckh, Ber. **31**, 3163 (1898).

<sup>9</sup> Metzner, Ann. **298**, 378 (1897).

<sup>10</sup> Swann, Appel, and Kistler, Ind. Eng. Chem. **26**, 388, 1014 (1934).

## XVII

## METHYLHYDRAZINE SULFATE



Submitted by H. H. HART.

Checked by W. W. HARTMAN and W. D. PETERSON.

## 1. Procedure

(A) *Benzalazine*.—In a 5-l. round-bottomed flask, provided with a stout glass mechanical stirrer, are placed 240 g. (1.85 moles) of powdered hydrazine sulfate (Org. Syn. Coll. Vol. **1**, 302), 1800 cc. of water, and 230 cc. (207 g., 3.4 moles) of 28 per cent aqueous ammonia (sp. gr. 0.90). The mixture is stirred, and, when the hydrazine sulfate has dissolved, 440 cc. (460 g., 4.35 moles) of benzaldehyde (Note 1) is added from a separatory funnel during the course of four to five hours (Note 2). After the mixture has been stirred for a further two hours, the precipitated benzalazine is filtered with suction, washed with water, and pressed thoroughly on a Buchner funnel. The product is dissolved in 800 cc. of boiling 95 per cent ethyl alcohol, and on cooling the azine separates in yellow needles melting at 92–93°. The yield is 350–360 g. (91–94 per cent of the theoretical amount); an additional 10–15 g. of less pure material can be isolated from the mother liquors. The azine is freed of ethyl alcohol by drying in a vacuum desiccator over calcium chloride.

(B) *Methylhydrazine Sulfate*.—Two hundred grams (0.96 mole) of benzalazine, 350 cc. of dry, thiophene-free benzene, and 100 cc. (133 g., 1.05 moles) of dimethyl sulfate (Note 3) are mixed in a 3-l. round-bottomed flask, provided with a reflux condenser

bearing a calcium chloride tube. The mixture is heated continuously, with occasional shaking, on a water bath to gentle refluxing for five hours. The mixture is cooled, and the solid addition product is decomposed by adding 600 cc. of water and shaking until all the solid material has disappeared. The benzene and benzaldehyde are removed by steam distillation; the residual liquor, after cooling, is treated with 15-20 cc. of benzaldehyde and left overnight. The resin and benzalazine are filtered off (Note 4).

The filtrate is evaporated under reduced pressure on a water bath until a semi-crystalline mass remains, which is further desiccated by evaporating twice under reduced pressure with 50-cc. portions of absolute ethyl alcohol. The resulting crystalline cake is crushed with 50 cc. of absolute ethyl alcohol, filtered, and the process repeated. The white, crystalline product is almost pure methylhydrazine sulfate and contains very little hydrazine sulfate. After drying in a vacuum desiccator over calcium chloride, the yield is 105-110 g. (76-80 per cent of the theoretical amount). For purification, the sulfate is dissolved in about 250 cc. of boiling 80 per cent ethyl alcohol, and any undissolved material (chiefly hydrazine sulfate) is filtered off. On cooling, the methylhydrazine sulfate separates in white plates, which are filtered with suction and washed with a little absolute alcohol. After drying over calcium chloride, the first fraction, m.p. 141-142°, weighs 70-75 g. (51-54 per cent of the theoretical amount) (Note 5).

## 2. Notes

1. The benzaldehyde should be freed of benzoic acid by shaking with aqueous sodium carbonate solution.
2. The mixture is stirred vigorously during the reaction, and one or two stout glass rods are clamped in the flask to act as baffles and to break up the lumps of benzalazine.
3. Since dimethyl sulfate is very toxic, care should be exercised to avoid spilling the liquid or inhaling the vapor of the reaction mixture. Ammonia is a specific antidote.

4. Unreacted hydrazine sulfate is removed by conversion to benzalazine. The filtrate should not give an appreciable precipitate when mixed with 5 cc. of benzaldehyde and left for four hours.

5. From the mother liquors about 12 g. of less pure material, m.p. 133-136°, can be recovered.

## 3. Methods of Preparation

The procedure given above is essentially the method of Thiele.<sup>1</sup> Methylhydrazine has also been prepared by reduction and subsequent hydrolysis of nitrosomethylurea,<sup>2</sup> nitromethylurethane,<sup>3</sup> and nitrosomethylamine sulfonic acid,<sup>4</sup> and by methylation of hydrazine hydrate with methyl iodide<sup>5</sup> or diazomethane.<sup>6</sup>

<sup>1</sup> Thiele, *Ann.* **376**, 244 (1910).

<sup>2</sup> Brüning, *ibid.* **253**, 7 (1889).

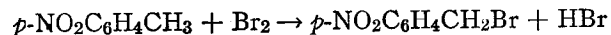
<sup>3</sup> Backer, *Rec. trav. chim.* **31**, 193 (1912).

<sup>4</sup> Traube and Brehmer, *Ber.* **52**, 1286 (1919).

<sup>5</sup> Harries and Haga, *ibid.* **31**, 56 (1898).

<sup>6</sup> Staudinger and Kupfer, *ibid.* **45**, 501 (1912).

## XVIII

*p*-NITROBENZYL BROMIDE

Submitted by G. H. COLEMAN and G. E. HONEYWELL.

Checked by WALLACE H. CAROTHERS and W. L. MCEWEN.

## 1. Procedure

IN a 1-l. three-necked flask is placed 300 g. (2.19 moles) of technical *p*-nitrotoluene (m.p. 51–52°). The flask is fitted with a liquid-sealed stirrer, reflux condenser, and a separatory funnel arranged so that the stem reaches nearly to the bottom of the flask. The condenser is provided with a tube for disposing of the hydrogen bromide evolved (Org. Syn. 14, 2). The flask is heated in an oil bath at 145–150° (Note 1), and 368 g. (118 cc., 2.3 moles) of bromine is added dropwise over a period of two hours (Note 2).

After all the bromine has been added, the heating and stirring are continued for ten minutes. While still liquid, the contents of the flask (Note 3) are poured into a 5-l. round-bottomed flask containing 4 l. of hot ligroin (b.p. 90–100°), and 15 g. of decolorizing carbon (Norite) is added. The material is brought into solution by heating on an electric hot plate, and after boiling for ten minutes the solution is filtered rapidly with suction (Note 4). After cooling to 20°, the crystals are filtered with suction, pressed thoroughly, and washed with two 50-cc. portions of cold ligroin. The crude product, m.p. 94–97°, weighs 280–315 g. (59–66 per cent of the theoretical amount) and is sufficiently pure for some purposes. For purification, this material is dissolved in 3–3.5 l. of hot ligroin, boiled with 10–15 g. of decolorizing carbon, and filtered with suction (Note 4). After cooling in an ice bath the crystals are collected on a Buchner funnel, pressed, and

## 2. Notes

1. The temperature should be kept within the limits mentioned to obtain the best results.
2. The bromine should be added within two hours even though a small amount may be lost through the condenser.
3. *p*-Nitrobenzyl bromide and its solution should be handled with caution. If the substance comes in contact with the skin, bathing the affected parts in alcohol will give relief.
4. The inverted filtration method of Bost and Constable (p. 81) is particularly advantageous for filtering hot solutions of nitrobenzyl bromide, since it reduces the fire hazard and the manipulation of the lachrymatory solutions. To avoid clogging, a tube of 8–10 mm. bore must be used for connecting the filtering flasks. About 3.5 l. of ligroin may be recovered from the mother liquors.
5. *p*-Nitrobenzyl bromide has been used as a reagent for the identification of many acids<sup>1</sup> and phenols<sup>2</sup> by conversion into their *p*-nitrobenzyl esters and ethers.

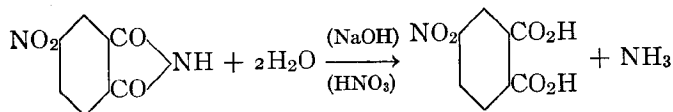
## 3. Methods of Preparation

*p*-Nitrobenzyl bromide has usually been prepared by brominating *p*-nitrotoluene.<sup>1,3</sup> It has also been prepared by treating *p*-nitrobenzyl alcohol with hydrobromic acid,<sup>4</sup> and by nitrating benzyl bromide.<sup>5</sup>

<sup>1</sup> Reid, J. Am. Chem. Soc. 39, 126 (1917); Lyons and Reid, *ibid.* 39, 1728 (1917).<sup>2</sup> Reid, *ibid.* 39, 304 (1917); Lyman and Reid, *ibid.* 42, 615 (1920).<sup>3</sup> Brewster, *ibid.* 40, 406 (1918).<sup>4</sup> Norris, Watt and Thomas, *ibid.* 38, 1077 (1916).<sup>5</sup> Moureu and Brown, Bull. soc. chim. [4] 29, 1008 (1921).

## XIX

## 4-NITROPHTHALIC ACID



Submitted by E. H. HUNTRESS, E. I. SHLOSS, JR., and P. EHRLICH.  
Checked by W. W. HARTMAN and G. W. SAWDEY.

## 1. Procedure

To a solution of 26.6 g. (0.66 mole) of sodium hydroxide in 240 cc. of water is added 80 g. (0.416 mole) of 4-nitrophthalimide (p. 58) (Note 1). The mixture is heated rapidly to boiling and boiled gently for ten minutes. The solution is made barely acid to litmus with concentrated nitric acid (sp. gr. 1.42); after the neutral point is reached, an additional 70 cc. (100 g., 1.1 moles) of nitric acid is added (Note 2). The solution is again boiled for three minutes, then cooled below room temperature, transferred to a 1-l. separatory funnel, and extracted with two 300-cc. portions of alcohol-free ether (Note 3). Care is taken to insure thorough mixing before separation of the layers. After drying the extract over anhydrous sodium sulfate, the ether is distilled off until solid begins to separate. The concentrated ether solution is poured into a porcelain dish and the residual solvent allowed to evaporate in a hood (Note 4). The practically white crystals of 4-nitrophthalic acid which separate melt at 163–164° (uncorr.) and have a neutralization equivalent of 105.5 (theoretical, 105.5). The yield is 85–87 g. (95–99 per cent of the theoretical quantity).

## 2. Notes

1. If a large amount of 4-nitrophthalimide is to be hydrolyzed, it will generally be found convenient to carry out a series of small runs of the size given here.

2. The quantity of alkali used at the start is sufficient to neutralize the nitro-imide and leave the resulting alkaline solution approximately 1 *N*. When the solution is neutralized the red color changes to a dirty brown, which turns to a pale yellow on acidification. The 70-cc. portion of concentrated nitric acid suffices to set free all the 4-nitrophthalic acid but avoids the presence of a large excess during the ether extraction.

The use of nitric acid appears to be preferable to that of hydrochloric or sulfuric acid. The yields are similar, but the product obtained using nitric acid is pure white and in better physical condition.

3. The simultaneous presence of nitric acid and alcohol in the ether extract must be avoided as explosive oxidation might occur during evaporation of the ether. Furthermore, the presence of alcohol may lead to contamination of the product with traces of the acid ester.

4. Evaporation of the last portion of ether proceeds slowly; the rather soft, fluffy crystals of acid which separate at first gradually become hard and dense. No trouble was experienced from nitric acid remaining with the ether extract, if the ether was free from alcohol and the specified amount of nitric acid was used.

## 3. Methods of Preparation

4-Nitrophthalic acid has usually been prepared by nitration of phthalic acid<sup>1</sup> or phthalic anhydride,<sup>2,3</sup> followed by separation from the accompanying 3-nitrophthalic acid.<sup>4,5,6</sup> It has also been prepared from 6-nitro-2-naphthol-4-sulfonic acid (obtained from the technical diazo-anhydride of 6-nitro-1-amino-2-naphthol-4-sulfonic acid).<sup>7</sup> The present procedure is more convenient than any of the earlier methods.

<sup>1</sup> Miller, Ann. **208**, 223 (1881); Huisinga, Rec. trav. chim. **27**, 261 (1908).

<sup>2</sup> Levy and Stephen, J. Chem. Soc. **1931**, 79.

<sup>3</sup> Culhane and Woodward, Org. Syn. Coll. Vol. **1**, 399.

<sup>4</sup> Bogert and Boroschek, J. Am. Chem. Soc. **23**, 752 (1901).

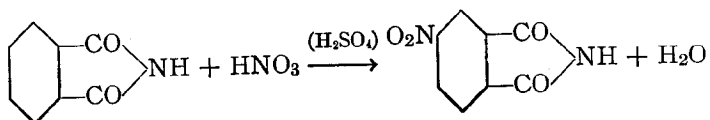
<sup>5</sup> Cohen, Woodroffe and Anderson, J. Chem. Soc. **109**, 232 (1916).

<sup>6</sup> Lawrence, J. Am. Chem. Soc. **42**, 1872 (1920).

<sup>7</sup> Ruggli, Knapp, Merz, and Zimmerman, Helv. Chim. Acta **12**, 1043 (1929).

XX

## 4-NITROPHthalIMIDE



Submitted by E. H. HUNTRESS, E. L. SLOSS, JR., and P. EHRLICH.  
Checked by W. W. HARTMAN and G. W. SAWDEY.

## 1. Procedure

To 1400 cc. of concentrated c.p. sulfuric acid (sp. gr. 1.84) in a 3-l. beaker is added 240 cc. (5.7 moles) of c.p. fuming nitric acid (sp. gr. 1.50), and the mixture is cooled to 10°. The beaker is placed in an ice-water bath, and 200 g. (1.36 moles) of commercial phthalimide is stirred in rapidly (Note 1). The solution is allowed to stand at a temperature not above 20° for five hours (Note 2).

The clear, pale yellow solution is poured slowly with vigorous stirring onto 4500 g. of cracked ice (Note 3) and the crude nitration product filtered through cloth on a 20-cm. Buchner funnel with suction. The paste is pressed as dry as possible and washed several times with cold water (Note 4). Without being dried the moist cake is transferred to a 5-l. flask and recrystallized from 3 l. of boiling 95 per cent alcohol (Notes 5 and 6). The pale yellow 4-nitrophthalimide is filtered with suction, washed with cold alcohol, and dried in the air. The product melts at 197–198° and weighs 157–173 g. (60–67 per cent of the theoretical quantity).

## 2. Notes

1. Care must be taken that the nitrating mixture is brought to 10–15° prior to the addition of the phthalimide. If a higher temperature is used, the reaction mixture tends to heat up spon-

taneously, temperature control becomes difficult, and the yield is diminished.

2. Since the phthalimide dissolves readily, motor stirring is unnecessary. Five hours' standing for the solution is sufficient, but if convenient it may be left overnight and diluted the next day with considerable saving of time. The solution may stand as long as twenty-eight hours without deleterious effect, but leaving it for several days decreases the yield.

3. This dilution may be done conveniently in a 3-gal. crock or by dividing the material between two 4-l. beakers. Care must be exercised to avoid local heating with resultant hydrolysis of the imide.

4. It is important to wash all nitric acid from the crude material.

5. If the crude material is dried at this point, the yield is 60–70 per cent of the theoretical and the product melts at 180–185°. Such drying is not recommended since the physical state of the product changes to a hard form not readily soluble in the recrystallizing medium.

6. If the 4-nitrophthalimide is to be used for the preparation of 4-nitrophthalic acid, an entirely satisfactory product is obtained by digesting with 1500 cc. of boiling alcohol, cooling, and filtering the solid with suction. This process extracts the impurities and leaves a yellowish white product which melts at the same point as the recrystallized material (197–198°). In this way the use of the larger volume of alcohol may be avoided.

## 3. Methods of Preparation

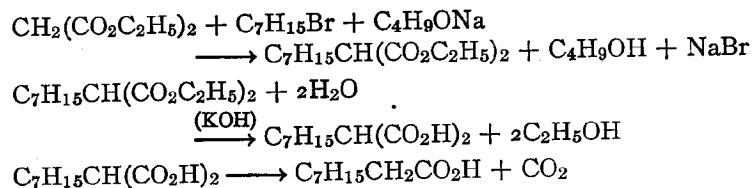
4-Nitrophthalimide has been prepared from 4-nitrophthalic acid,<sup>1</sup> and by nitrating phthalimide.<sup>2</sup> The present procedure is a modification of the method of Levy and Stephen.<sup>2</sup>

<sup>1</sup> Seidel, Ber. **34**, 4351 (1901); Seidel and Bittner, Monatsh. **23**, 420 (1902); Bogert and Renshaw, J. Am. Chem. Soc. **30**, 1137 (1908).

<sup>2</sup> Levy and Stephen, J. Chem. Soc. **1931**, 79.

## XXI

## PELARGONIC ACID

*(n*-Nonoic Acid)

Submitted by E. EMMET REID and JOHN R. RUHOFF.

Checked by W. W. HARTMAN and G. W. SAWDEY.

## 1. Procedure

A 5-l. three-necked flask is fitted with a liquid-sealed mechanical stirrer, reflux condenser, dropping funnel, and thermometer. In the flask is placed 2.5 l. of anhydrous butyl alcohol (Note 1), and 115 g. (5 gram atoms) of clean, bright sodium cut in small pieces is added at one time. Solution of the sodium may be facilitated by stirring, but heating is unnecessary. After the sodium has dissolved completely, the solution is allowed to cool to 70–80°, and then 800 g. (760 cc., 5 moles) of redistilled ethyl malonate (b.p. 135–136°/100 mm.) is added rapidly with stirring. After heating the reaction solution to 80–90°, 913 g. (687 cc., 5.1 moles) of pure heptyl bromide (b.p. 179–180°) is added. The bromide should be added rather slowly at first, until precipitation of sodium bromide begins; it may then be added at such a rate that the butyl alcohol refluxes gently. Usually about one hour is required for the introduction of the heptyl bromide. The mixture is refluxed gently until it is neutral to litmus (about one hour).

The entire mixture, including the precipitated sodium bromide, is transferred to a 12-l. flask together with a small

amount of water used to rinse the reaction flask. A solution of 775 g. (12.5 moles) of 90 per cent potassium hydroxide in an equal weight of water is added slowly with shaking. The mixture is heated cautiously, with occasional shaking, until refluxing starts (Note 2), and refluxing is continued until saponification is complete (about four or five hours). The flask is fitted at once for steam distillation (Org. Syn. Coll. Vol. 1, 467) and the mixture distilled until no more butyl alcohol passes over (Note 3). To the residue 1350 cc. (15.5 moles) of concentrated hydrochloric acid (sp. gr. 1.18) is added carefully, with shaking, and the mixture is refluxed for about one hour (Note 4). After cooling, the water layer is siphoned off and discarded (Note 5).

The oil obtained in the preceding step is transferred to a 3-l. round-bottomed flask and heated under an air-cooled reflux condenser in an oil bath at about 180°. When the evolution of carbon dioxide has ceased (about two hours), the oil is decanted from a small amount of solid material. The solid residue on treatment with 200–300 cc. of concentrated hydrochloric acid gives an additional small quantity of oil which is added to the main portion.

The crude pelargonic acid is distilled in a modified Claisen flask having a fractionating side arm, and the material boiling at 140–142°/12 mm. (188–190°/100 mm.) is collected. The yield is 525–590 g. (66–75 per cent of the theoretical quantity). The melting point of the pure acid is 12–12.5°.

## 2. Notes

1. Commercial butyl alcohol was dried over solid potassium carbonate and distilled through a 90-cm. indented column. The portion boiling at 117–118° was used.

2. Two layers are formed at first, but the solution becomes homogeneous as saponification occurs. Boiling chips should be placed in the flask, and heating should be done carefully at first, with occasional shaking, or the reaction may get beyond control.

3. The flask should not be allowed to cool between saponification and distillation. It is advisable to heat the flask to prevent

the volume of distillate from becoming too large. Usually about 7 l. of distillate is collected, from which the butyl alcohol can be recovered.

4. When the oily layer ceases to increase, decomposition of the potassium heptylmalonate is complete. A layer of salt sometimes accumulates at the bottom of the flask. Care must be taken in heating to prevent cracking the flask.

5. It is unnecessary to extract the aqueous layer with an organic solvent.

6. *n*-Caproic acid may be prepared by this method from *n*-butyl bromide in similar yields (see also *Org. Syn.* **11**, 78). In this case a partial decomposition of the substituted malonic acid is brought about by refluxing the aqueous solution in the 12-l. flask after the addition of the hydrochloric acid. Butylmalonic acid is appreciably soluble in water, and separation of the oily layer does not occur until it has been largely decomposed to caproic acid. The time required is about eight to ten hours. It is advisable to heat the acid layer under air reflux as in the case of pelargonic acid.

### 3. Methods of Preparation

Pelargonic acid has been prepared by the oxidation of oleic acid<sup>1</sup> and by hydrolysis of octyl cyanide<sup>2</sup> or heptylacetoacetic ester.<sup>3</sup>

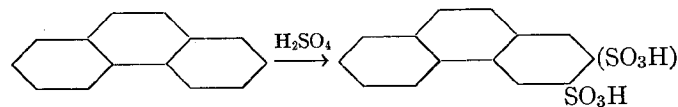
<sup>1</sup> Redtenbacher, *Ann.* **59**, 52 (1846); Harries and Thieme, *ibid.* **343**, 355 (1905); Harries and Turk, *Ber.* **39**, 3737 (1906); Molinari and Soncini, *ibid.* **39**, 2739 (1906); Molinari and Barozzi, *ibid.* **41**, 2795 (1908); Jegorow, *J. prakt. Chem.* [2] **86**, 531 (1912).

<sup>2</sup> Zincke and Franchimont, *Ann.* **164**, 333 (1872).

<sup>3</sup> Jourdan, *ibid.* **200**, 107 (1880).

## XXII

### PHENANTHRENE-2- AND 3-SULFONATES



Submitted by L. F. FIESER.

Checked by W. W. HARTMAN and G. L. BOOMER.

#### 1. Procedure

THE sulfonation is carried out in a 2-l. round-bottomed, three-necked flask fitted with a thermometer, a dropping funnel, and a stirrer (Note 1). Five hundred grams (2.8 moles) of pure phenanthrene (Note 2) is melted in the flask, which is clamped in an oil bath heated to 110°. Mechanical stirring is started, and 327 cc. (600 g., 5.8 moles) of concentrated sulfuric acid is run in at such a rate that the internal temperature does not rise above 120° (ten to fifteen minutes). The reaction mixture is stirred and maintained at a temperature of 120–125° for three and one-half hours, when a test portion should give a nearly clear solution in water. The reaction is exothermic, and the bath must be kept at a temperature 5–10° below that of the mixture. Some sulfur dioxide is given off, and the mixture becomes green.

The viscous solution, while still hot, is dissolved in 4 l. of water, and a solution of 400 g. of sodium hydroxide in 600–800 cc. of water is added. After thorough cooling in an ice bath, the precipitated sodium salt is collected on a large funnel, pressed well, and washed thoroughly with 1 l. of half-saturated sodium chloride solution (about 180 g. per liter). The precipitate contains chiefly the sodium 2- and 3-sulfonates. The filtrate contains a mixture of disulfonates and is discarded (Note 3). In order to effect a preliminary concentration of the less soluble



2-isomer, the sodium salt mixture is dissolved in 7-8 l. of boiling water containing 100 cc. of concentrated hydrochloric acid (Note 4), and the filtered solution is then neutralized with sodium hydroxide and allowed to crystallize. After separating the mother liquor (A), which is saved, the crystals (consisting largely of the sodium 2-sulfonate) are dissolved in about 8 l. of boiling water (Note 5), and 100 g. of solid barium chloride dihydrate is added to the hot solution. The fine white precipitate of barium phenanthrene-2-sulfonate which forms is digested at the boiling point for a short time and then brought onto a 20-cm. Buchner funnel, preheated on the steam bath. The mother liquor (B) is saved.

The precipitated barium 2-sulfonate always retains a certain quantity of the 3-sulfonate, which must be extracted with hot water. The precipitate is digested at the boiling point with 6-l. portions of boiling water until the residual salt is found to be free from isomers. The purity is determined from the melting point of the *p*-toluidine salt, in the manner described below. Usually two or three such washings are required. The mother liquor (B) from the barium 2-sulfonate is combined with the various washings, and the whole is boiled down to a volume of about 6 l. Sulfuric acid (25-30 cc. of concentrated acid, diluted with water) is then added to precipitate the barium; the filtered solution (Note 6) is concentrated to about 2 l. and neutralized with potassium hydroxide to bring down a mixture of potassium sulfonates (C). The filtrate from the potassium salts may be boiled down further and treated with potassium chloride to insure complete recovery of the potassium sulfonates, and then discarded. The potassium salt mixture collected in these operations is set aside (C).

The mother liquor (A) from the sodium salt crystallization is boiled down to a volume of about 2-3 l., and 200 g. of potassium chloride is added to the hot solution. The potassium salt mixture which separates on cooling is collected and combined with the potassium salts (C) described in the preceding paragraph; the filtrate is discarded. The combined material is dissolved in the minimum amount of hot water, and the filtered solution is

heated to boiling and allowed to cool without disturbance. It deposits a large crop of the potassium 3-sulfonate in a very pure condition (180-210 g.). The mother liquor, containing more of the 3-sulfonate together with some of the 2-sulfonate, is concentrated to a small volume; the product is salted out with potassium chloride and washed free of sulfate ion with potassium chloride solution. A hot aqueous solution of this material is then treated with 10 g. of barium chloride dihydrate, and the precipitated barium 2-sulfonate (5-10 g.) is washed free of isomers. The original filtrate is reserved, but the washings are discarded. From the original filtrate by evaporation, precipitation of the barium with sulfuric acid, neutralization with potassium hydroxide, and crystallization of the product, there is obtained an additional quantity of the pure potassium 3-sulfonate (50-70 g.).

The yields are: barium phenanthrene-2-sulfonate, 150-200 g. (17-21 per cent); potassium phenanthrene-3-sulfonate, 200-220 g. (24-26 per cent) (Notes 7, 8).

*Identification and Test of Purity.*—The method<sup>1</sup> consists in the preparation and examination of a test sample of the *p*-toluidine salt of the sulfonic acid (Note 9). An aqueous solution of the free sulfonic acid (or of the sodium or potassium salt) is treated with an excess of *p*-toluidine and hydrochloric acid, enough water is added to bring all the material into solution at the boiling point, and crystallization is allowed to take place. The crystals should be washed well with water. A barium salt should be boiled with dilute sulfuric acid, a little decolorizing carbon added, and the filtered solution treated with *p*-toluidine. If the amine salt separates in an oily condition, the walls of the vessel should be scratched, for the *p*-toluidine salt, particularly that of the 3-acid, may remain as an oil for a short time, even when nearly pure. On the other hand, a rather impure acid gives a *p*-toluidine salt which remains as an oil almost indefinitely. This property characterizes a mixture of isomers nearly as definitely as the depression in the melting point, though this is large. In determining the melting point of an amine salt, the sample may be dried by pressing the material on a filter paper, but the capillary should be placed in the bath when the temperature is below 130°. The

preliminary heating gives ample provision for thorough drying, without which the material may melt 20–30° below the true melting point.

The *p*-toluidine salt of phenanthrene-2-sulfonic acid forms flat needles or plates melting at 282° (291° corr.); that of the 3-acid forms thick needles melting at 217° (222° corr.).

## 2. Notes

1. A convenient form of stirrer is made by bending a glass rod to an angle of 45° about 4 cm. from the end. This type of stirrer can be used to dislodge material adhering to the walls of the flask.

2. A pure grade of phenanthrene should be used. Technical 70 per cent phenanthrene may be purified by the method of Cohen and Cormier.<sup>2</sup> It is important to note that the presence of more than about 2 per cent of anthracene in phenanthrene raises the melting point.

3. It is estimated that no less than twelve isomeric disulfonates are present. No useful products have been obtained from the mixture.

4. The solubility of the sulfonates is increased appreciably by the presence of a mineral acid.

5. A 10-l. enameled pail heated with a ring burner serves as a convenient, if not very durable, vessel for boiling and evaporating the large volumes of solution involved. The contents may be ladled out with a casserole.

6. The addition of a little decolorizing carbon greatly facilitates the coagulation of barium sulfate and aids in retaining it on the filter.

7. The low yield of the monosulfonates is due in large part to the fact that disulfonic acids are invariably formed along with the mono acids.

8. For some reactions, such as alkali fusion, the barium salt is a suitable form in which to use the phenanthrene-2-sulfonic acid. For conversion into the potassium salt, it is highly advisable to use the barium salt in the moist and finely divided condi-

tion in which it is first obtained. Since the reaction is slow at best, several fresh portions of sulfuric acid should be employed for precipitating the barium.

9. This is recommended as a general method of identifying sulfonates. In economy of time and material it is superior to the preparation of the free acid, the acid chloride, the ester, the amide, or the phenol. By this method one can identify quickly a few milligrams of an acid or of any of its metal salts, whether it is in the solid state or in solution.

## 3. Methods of Preparation

The sulfonation of phenanthrene has been studied by Werner and his students,<sup>3</sup> by Sandqvist,<sup>4</sup> by Fieser,<sup>1</sup> and by Ioffe.<sup>5</sup>

<sup>1</sup> Fieser, *J. Am. Chem. Soc.* **51**, 2460, 2471 (1929).

<sup>2</sup> Cohen and Cormier, *ibid.* **52**, 4363 (1930).

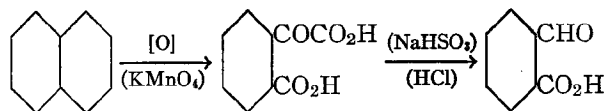
<sup>3</sup> Werner *et al.*, *Ann.* **321**, 248 (1902).

<sup>4</sup> Sandqvist, *ibid.* **392**, 76 (1912).

<sup>5</sup> Ioffe, *J. Gen. Chem. (U.S.S.R.)* **3**, 448 (1933) [*C. A.* **28**, 1694 (1934)].

## XXIII

## PHTHALALDEHYDE ACID



Submitted by J. H. GARDNER and C. A. NAYLOR, JR.  
Checked by C. R. NOLLER and CARL LINN.

## 1. Procedure

In a 3-l. three-necked flask provided with a liquid-sealed mechanical stirrer, a reflux condenser, and a dropping funnel, are placed 500 cc. of 0.5 *N* sodium hydroxide solution and 32 g. (0.25 mole) of pure naphthalene. The mixture is heated to boiling, and a boiling solution of 212 g. (1.34 moles) of potassium permanganate in 1500 cc. of water is added in small portions during one and one-half hours with vigorous stirring (Note 1). After the last addition, the mixture is boiled for thirty to forty-five minutes to complete the oxidation. Any unchanged permanganate is reduced by the addition of 20 cc. of alcohol, the flask is cooled to solidify the residual naphthalene, and the mixture is filtered.

The filtrate is acidified with 150 cc. (1.8 moles) of concentrated hydrochloric acid (sp. gr. 1.18), evaporated to 500 cc., cooled, and filtered. The filtrate is neutralized with 30 per cent sodium hydroxide solution (150–160 cc.), 50 g. (0.48 mole) of sodium bisulfite is added, and the mixture is evaporated to dryness on a steam bath. The residue is stirred with 100 cc. of concentrated hydrochloric acid and evaporated to dryness on a steam bath. The hydrochloric acid treatment and evaporation are repeated (Note 2).

The residue is extracted thoroughly with benzene in a large Soxhlet extractor (Note 3), and the benzene extract is evaporated to dryness. The crude product is dissolved in 50 cc. of hot water, the solution filtered, and the filtrate cooled in an ice bath with stirring (Note 4). The crystals are filtered with suction and dried in the air. The yield of slightly colored product melting at 94–95° is 15–15.5 g. (40–41 per cent of the theoretical amount).

When this material is recrystallized from 40 cc. of water with 1 g. of decolorizing carbon, and the filtrate cooled to 0°, there is obtained 14–14.5 g. of white crystals melting at 96–96.5°.

## 2. Notes

1. During the addition of the hot permanganate solution no external heat is applied. From time to time steam is passed through the condenser jacket to return the sublimed naphthalene to the reaction flask.

2. The treatment with hydrochloric acid and the evaporation are repeated in order to decompose completely the phthalaldehyde acid bisulfite compound. Wegscheider and Bondi<sup>1</sup> state that it is necessary to heat the bisulfite compound on the water bath several days with a large excess of hydrochloric acid, but the treatment described above has been found adequate.

3. The material requires two extraction thimbles of the 45 by 125 mm. size or four of the 30 by 75 mm. size. It is advantageous to use a modified Soxhlet extractor of the Clausnitzer type,<sup>2</sup> which allows the vapor of the boiling solvent to surround the extractor tube.

4. It is essential to control carefully the volume of water used in recrystallization. The crude acid contains considerable amounts of phthalic acid, and too small a volume of water results in a contaminated product; too large an amount causes a decided decrease in yield.

## 3. Methods of Preparation

Phthalaldehyde acid has been prepared by the hydrolysis of 2-bromophthalide,<sup>3</sup> of *o*-trichloromethylbenzal chloride,<sup>4</sup> of

*o*-cyanobenzal chloride,<sup>5</sup> and of *o*-dichloromethylbenzoyl chloride;<sup>6</sup> by the ozonation of naphthalene;<sup>7</sup> and by the alkaline oxidation of naphthalene,<sup>8</sup> or  $\alpha$ -nitronaphthalene<sup>9</sup> followed by the preparation and decomposition of the aniline condensation product<sup>10</sup> or the bisulfite compound<sup>11</sup> of phthalonic acid.

<sup>1</sup> Wegscheider and Bondi, *Monatsh.* **26**, 1055 (1905).

<sup>2</sup> Houben-Weyl, "Die Methoden der organischen Chemie," 3rd. Ed., Vol. I, p. 565, Verlag Georg Thieme, Leipzig (1925).

<sup>3</sup> Racine, *Ann.* **239**, 78 (1887).

<sup>4</sup> Coulson and Gautier, *Bull. soc. chim. [2]* **45**, 507 (1886).

<sup>5</sup> Gabriel and Weise, *Ber.* **20**, 3197 (1887); Drory, *ibid.* **24**, 2571 (1891).

<sup>6</sup> Davies, Perkin, and Clayton, *J. Chem. Soc.* **121**, 2202 (1922).

<sup>7</sup> Seekles, *Rec. trav. chim.* **42**, 706 (1923).

<sup>8</sup> Tcherniac, *Ger. pat.* 79,693 [Frdl. **4**, 162 (1894-97)]; *Ger. pat.* 86,914 [Frdl. **4**, 163 (1894-97)].

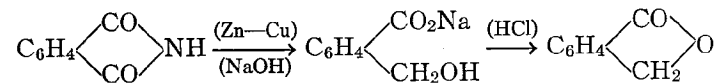
<sup>9</sup> Gardner, *J. Am. Chem. Soc.* **49**, 1831 (1927).

<sup>10</sup> *Ger. pat.* 97,241 [Frdl. **5**, 139 (1897-1900)]; Fuson, *J. Am. Chem. Soc.* **48**, 1093 (1926).

<sup>11</sup> Graebe and Trümpy, *Ber.* **31**, 369 (1898); Sidgwick and Clayton, *J. Chem. Soc.* **121**, 2263 (1922).

## XXIV

## PHTHALIDE



Submitted by J. H. GARDNER and C. A. NAYLOR, JR.  
Checked by H. T. CLARKE and D. BLUMENTHAL.

## 1. Procedure

In a 2-l. round-bottomed flask 180 g. (2.75 gram atoms) of zinc dust is stirred to a thick paste with a solution of 1 g. of copper sulfate in about 35 cc. of water (Note 1) and 400 g. (327 cc.) of 20 per cent aqueous sodium hydroxide added. The flask is equipped with a mechanical stirrer, the contents cooled to 5° by means of an ice bath, and 147 g. (1.0 mole) of phthalimide (*Org. Syn. Coll. Vol. 1*, 446) added in small portions at such a rate that the temperature does not rise above 8° (about thirty minutes is required). After all the phthalimide has been added, stirring is continued for one-half hour. The mixture is diluted with 400 cc. of water, warmed on a steam bath until evolution of ammonia has ceased (about three hours), and concentrated to a volume of about 400 cc. by distillation under reduced pressure. The material is filtered and the filtrate made acid to Congo red with concentrated hydrochloric acid (about 150 cc. is required). The mixture, in which the phthalide has separated as an oil, is boiled for one hour in order to complete the lactonization of the hydroxymethylbenzoic acid, and transferred while hot to a beaker. On cooling, the oily product solidifies to a hard red-brown cake. After chilling overnight in a refrigerator, when a further quantity of crystalline solid separates from the aqueous layer, the cold mixture is filtered with suction (Note 2). The crude phthalide, which contains a considerable quantity of

sodium chloride, is recrystallized in 20-g. portions from 1500 cc. of water; the mother liquor from the first crop is employed or recrystallization of the subsequent portions. Each portion is filtered hot and cooled to below 5° before collecting the crystals, which are finally washed with small quantities of ice-cold water (Note 3). The phthalide crystallizes in transparent plates which melt at 72–73°. The yield is 90–95 g. (67–71 per cent of the theoretical amount) (Note 4).

## 2. Notes

1. In checking these directions complete failure was repeatedly encountered with good commercial grades of zinc dust, and only when the metal was activated with copper sulfate did reduction proceed at all.

2. The mother liquor, on concentrating to less than half its volume, yields no further crystals on chilling.

3. On cooling, a minute amount of a yellow impurity separates with the phthalide at the beginning of crystallization. This impurity apparently cannot be eliminated by boiling with charcoal but is present in too small amount to affect the melting point of the product.

4. Concentration of the final mother liquor to a volume of 500 cc. yields a further small quantity of phthalide but this operation is scarcely worthwhile.

## 3. Methods of Preparation

The present procedure is based upon the method of Reissert.<sup>1</sup> Phthalide has also been prepared by reduction of phthalic anhydride,<sup>2</sup> and by bromination of *o*-toluic acid followed by hydrolysis.<sup>3</sup>

<sup>1</sup> Reissert, Ber. 46, 1489 (1913); Ger. pat. 267,596 [Fr. 11, 196 (1912–1914)].

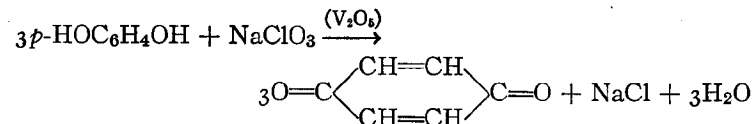
<sup>2</sup> Wislicenus, Ber. 17, 2181 (1884); Godchot, Bull. soc. chim. [4] 1, 830 (1907); Sabatier and Kubota, Compt. rend. 172, 736 (1921).

<sup>3</sup> Hjelt, Ber. 19, 412 (1886); Salkind and Ssemenow, J. Russ. Phys. Chem. Soc. 46, 512 (1914) (Chem. Zentr. 1914, II, 1271); Davies and Perkin, J. Chem. Soc. 121, 2207 (1922).

## XXV

### QUINONE

(Benzoquinone)



Submitted by H. W. UNDERWOOD, JR., and W. L. WALSH.  
Checked by L. F. FIESER and D. J. POTTER.

## 1. Procedure

In a 2-l. round-bottomed flask equipped with a mechanical stirrer are placed 1 l. of 2 per cent sulfuric acid, 0.5 g. of vanadium pentoxide (Note 1), 110 g. (1 mole) of hydroquinone, and 60 g. (0.56 mole) of sodium chlorate. The mixture is vigorously stirred for about three hours, when the green quinhydrone first formed is converted to yellow quinone. The temperature of the reaction mixture rises to about 40° (Note 2). The reaction is usually complete in three and one-half to four hours. The flask is then disconnected and cooled under the tap, the mixture is filtered with suction, and the quinone is washed once with about 100 cc. of cold water. After drying in a desiccator over calcium chloride, the product weighs 86–90 g. and melts at 110–112°. This material is pure enough for most purposes. Extraction of the filtrate and washings with four 100-cc. portions of benzene yields a further 12–14 g. of quinone, and brings the total amount to 99–104 g. (92–96 per cent of the theoretical yield) (Note 3).

Very pure quinone can be obtained either by vacuum sublimation or recrystallization from boiling ligroin (b.p. 90–120°). One hundred grams of the crude quinone requires about 1200 cc. of

ligroin for recrystallization and yields 92-97 g. of bright yellow quinone, m.p. 111-113°.

## 2. Notes

1. Vanadium pentoxide may be obtained from the Vanadium Corporation of America or prepared from ammonium metavanadate by the method of Milas<sup>1</sup> (Org. Syn. 11, 47).

2. If quantities larger than one mole of hydroquinone are used the temperature should not be allowed to rise above 40°.

3. By the use of a suitable organic solvent the same oxidizing agent (Note 4) can be employed for the preparation of anthraquinone. A mixture of 90 g. (0.51 mole) of finely powdered pure anthracene, 0.5 g. of vanadium pentoxide, 76 g. of sodium chlorate, 1 l. of glacial acetic acid, and 200 cc. of 2 per cent sulfuric acid is warmed under reflux until a vigorous reaction commences. The source of heat is removed, and the reaction allowed to proceed for about twenty minutes. The mixture is refluxed for one hour longer and then cooled in ice. The light yellow solid is filtered with suction, washed well with water, and dried at 110°. The yield is 92-96 g. (88-91 per cent of the theoretical amount) of a product melting at 273-275° (uncorr.).

4. The oxidizing agent employed is not very powerful, and, although it attacks easily the particularly reactive anthracene, it is not suitable for the conversion of hydrocarbons of the naphthalene and phenanthrene series into the corresponding quinones or for the oxidation of acenaphthene or fluorene (observation of the checkers).

## 3. Methods of Preparation

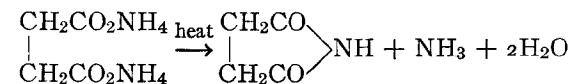
The oxidation of hydroquinone by means of sodium dichromate in sulfuric acid solution, and references to other methods of preparation, are given in earlier volumes of this series.<sup>2</sup>

<sup>1</sup> Milas, J. Am. Chem. Soc. 49, 2005 (1927).

<sup>2</sup> Vliet, Org. Syn. 2, 85; Coll. Vol. 1, 471.

## XXVI

### SUCCINIMIDE



Submitted by H. T. CLARKE and LETHA DAVIES BEHR.

Checked by WALLACE H. CAROTHERS and W. L. McEWEN.

### 1. Procedure

In a 1-l. distilling flask fitted with a side arm 40 cm. in length and not less than 10 mm. in internal diameter (Note 1) is placed 236 g. (2 moles) of succinic acid. To this is added slowly, with cooling and shaking, 270 cc. (243 g., 4 moles) of 28 per cent aqueous ammonia (sp. gr. 0.90). Most of the acid dissolves, forming a clear solution. The flask is set for downward distillation, and a water-cooled 500-cc. distilling flask is attached to the side arm. Provision may be made for removal of ammonia from the side tube of the receiver. The mixture is heated gently over a free flame; solution takes place rapidly, and a small amount of uncombined ammonia passes over with the first portions of the distillate. The temperature of the vapor rises to 100° and remains at this point until about 200 cc. of water has distilled. The flame is then increased, and the ammonium succinate begins to decompose, with evolution of ammonia; the temperature of the vapor falls to 97° during the distillation of the next 30 cc. When the vapor temperature has risen to 102°, the receiver is changed and an intermediate fraction collected from this point to 275°. The succinimide then distils and is collected over the range 275-289°, largely at 285-289°. Decomposition takes place to a small extent with formation of a black tar; the distillation is stopped when the tarry residue begins to decompose with evolution of yellow fumes.

The crude succinimide, which solidifies completely, amounts to about 168 g. The intermediate fraction is redistilled from a smaller flask, when a further quantity of about 10 g. is collected over the range 275–289°. The crude succinimide is recrystallized from 95 per cent ethyl alcohol, employing 1 cc. of solvent for every gram of product. If the mixture is chilled to 0° for some hours before filtration and about 25 cc. of cold alcohol employed for washing the crystals, the first crop amounts to 163–164 g. (82–83 per cent of the theoretical amount). On concentrating the mother liquor to one-third of its volume, a second crop amounting to 4–5 g. can be secured (Note 2). The product melts at 123–125° and contains no water of crystallization.

## 2. Notes

1. It is essential to employ a side arm of at least this diameter in order to avoid clogging by crystals of succinimide when this first passes over.

2. A further small quantity of a less pure product can be obtained by evaporating the dark mother liquor to dryness and recrystallizing the residue from fresh 95 per cent alcohol.

## 3. Methods of Preparation

Succinimide has usually been prepared by heating succinic acid in a current of ammonia<sup>1,2</sup> or by distilling ammonium succinate.<sup>1,3</sup>

<sup>1</sup> Fehling, *Ann.* **49**, 198 (1844).

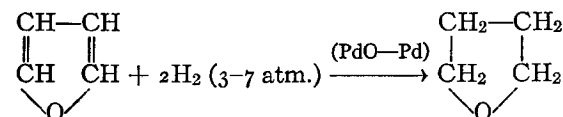
<sup>2</sup> Franchimont and Friedman, *Rec. trav. chim.* **25**, 79 (1906).

<sup>3</sup> Bunge, *Ann. Suppl.* **7**, 118 (1870); Menschutkin, *Ann.* **162**, 166 (1872).

## XXVII

### TETRAHYDROFURAN

(Tetramethylene Oxide; 1,4-Epoxybutane)



Submitted by DONALD STARR and R. M. HIXON.

Checked by JOHN R. JOHNSON and H. B. STEVENSON.

## 1. Procedure

(A) *Preparation of Palladous Oxide.*—In a 350-cc. casserole, 2.2 g. (0.02 gram atom) of palladium metal is dissolved in a small amount of aqua regia, and the solution (Note 1) is treated with 55 g. of C.P. sodium nitrate and enough distilled water to make a thick paste. The substances are thoroughly mixed and then heated gently to drive off the water. The heating is increased until the mixture melts (about 270–280°) and continued cautiously. Just above the melting point the mixture must be stirred and heated carefully as oxides of nitrogen are evolved and foaming occurs. After the evolution of gases is nearly complete (about five minutes) the full flame of a Bunsen burner is applied for about ten minutes. The entire time of heating should be about one-half hour. As the mass cools, the casserole is rotated to allow the melt to solidify on the sides of the dish. After digesting with distilled water (about 200 cc.) until the sodium salts are completely dissolved, the dark brown precipitate of palladous oxide is filtered and washed thoroughly with 1 per cent sodium nitrate solution (Note 2). The oxide must not be washed with pure water since it shows a marked tendency to become colloidal. After drying in a vacuum desiccator the palladous

oxide weighs 2.3–2.4 g. (91–95 per cent of the theoretical amount) (Note 3).

(B) *Tetrahydrofuran*.—In the pressure bottle of an apparatus for catalytic reduction (Note 4) are placed 10 g. of pure furan (Note 5) and 0.2 g. of palladous oxide. The bottle is swept out with hydrogen (Note 6), and an initial hydrogen pressure of about 7 atm. (100 lb.) is applied (Note 7). After a lag of about ten minutes the reduction proceeds smoothly, and in an hour the theoretical amount of hydrogen is absorbed; the reaction is noticeably exothermic. After the reaction has ceased 20 g. of furan and 0.2 g. of palladous oxide are added (Note 6), the bottle swept out with hydrogen, and the hydrogen pressure raised to 7 atm. After this addition the lag is short and the reaction proceeds somewhat more rapidly than before; the temperature rises to 40–50°. When the reaction nears completion, 30 g. of furan and 0.2 g. of palladous oxide are added, and the reduction is continued. Successive portions of 30 g. of furan and 0.2 g. of palladous oxide are added in the same manner, until the bottle is about two-thirds filled. To insure complete reduction, another portion of palladous oxide is added and the mixture shaken until no more hydrogen is taken up. The catalyst is allowed to settle (Note 8), and the tetrahydrofuran is decanted through a filter into a flask for distillation. The reduction product distils completely at 64–66°.

The reduction of 120 g. (128 cc., 1.76 moles) of furan requires about fifteen to twenty hours, depending upon the purity of the furan and the activity of the catalyst (Note 9). The yield of redistilled tetrahydrofuran is 114–118 g. (93–96 per cent of the theoretical amount). Since reduction is practically quantitative, the yield is determined largely by the care exercised in handling the volatile furan and tetrahydrofuran.

## 2. Notes

1. An aqueous solution of the equivalent quantity of Eimer and Amend's C.P. or Merck's REAGENT palladium chloride may be used.

2. The filtrates should be clear and colorless; if they show a yellow-orange opalescence, some of the oxide has become colloidal. The palladium may be recovered<sup>1</sup> as the oxide by evaporating the filtrates to dryness and re-fusing, or as palladium black by rendering slightly alkaline with sodium carbonate and heating with formaldehyde.

3. A small amount of palladous oxide adheres to the casserole and cannot be removed by the ordinary means. The oxide is not dissolved readily by aqua regia but is easily removed by boiling with 48 per cent hydrobromic acid.

4. If initial pressures of 6–7 atm. are to be applied, the ordinary apparatus for catalytic reduction (Org. Syn. Coll. Vol. 1, 53) must be modified by using a flexible coil of copper tubing instead of rubber tubing for the connection between the hydrogen tank and the reduction bottle. To avoid dangerous accidents and loss of materials, it is advisable to cover the reduction bottle at all times with a screen of wire mesh and to test the bottle at the higher pressures before use. Brass fittings are used to hold the mouth of the bottle against a rubber gasket; before use the gasket is treated with alkali, washed thoroughly, and dried.

5. As in all catalytic reductions, the purity of the starting material is of great importance. Redistilled furan, b.p. 31–32°, prepared by the method of Wilson (Org. Syn. Coll. Vol. 1, 269) is quite satisfactory. It has been reported that furan prepared by the method of Gilman and Louisinian<sup>2</sup> should be dried over calcium chloride and fractionated carefully.<sup>3</sup> It is advisable to redistil the furan shortly before use and to avoid contact with rubber stoppers.

6. Owing to the high volatility of furan and tetrahydrofuran the bottle is not evacuated, as is customary, before the hydrogen pressure is applied; instead, the air is displaced by hydrogen. For the same reason, appreciable losses will occur if the reduction bottle is not cooled before the hydrogen pressure is released for the introduction of fresh portions of furan and catalyst. Effective and rapid cooling may be obtained by directing a jet of ether, from a wash bottle, over the surface of the reduction bottle while the shaking motor is in operation.



7. The hydrogenation of furan may be carried out with initial pressures of only 3 atm. (4.5 lb.), but the reduction is slower.

8. The catalyst may be removed, dried in a vacuum desiccator over sulfuric acid, and used again. The second reduction usually proceeds much more slowly, and it is advantageous to use one or two portions of fresh oxide along with the recovered material. Spent catalyst may be regenerated by conversion to the oxide as described in part A.

9. In the high-pressure apparatus of Adkins, 120 g. of furan can be hydrogenated with 10 g. of Raney nickel catalyst<sup>4</sup> in a single run. Using pressures of 100–150 atm. and a temperature range of 100–150° the reduction is extremely rapid and is strongly exothermic. Platinum oxide-platinum black is not a satisfactory catalyst for the reduction of furan.<sup>3</sup>

### 3. Methods of Preparation

The preparation of palladous oxide-palladium black and its use as a catalyst in the reduction of organic compounds have been studied by Shriner and Adams.<sup>1</sup> Palladium black and colloidal palladium have been widely used as hydrogenation catalysts.<sup>5</sup>

Tetrahydrofuran has been prepared by the reduction of furan in the vapor phase with a nickel catalyst at 170°,<sup>6</sup> in butyl alcohol at 50° with Raney nickel catalyst,<sup>7</sup> and with palladous oxide-palladium black in the absence of a solvent.<sup>3</sup>

<sup>1</sup> Shriner and Adams, *J. Am. Chem. Soc.* **46**, 1684 (1924); Kern, Shriner and Adams, *ibid.* **47**, 1147 (1925).

<sup>2</sup> Gilman and Louisinian, *Rec. trav. chim.* **52**, 156 (1933).

<sup>3</sup> Starr and Hixon, *J. Am. Chem. Soc.* **56**, 1595 (1934).

<sup>4</sup> Covert and Adkins, *ibid.* **54**, 4116 (1932).

<sup>5</sup> Sabatier, "Catalysis in Organic Chemistry," transl. by E. Emmet Reid. New York: D. Van Nostrand Co., 1922.

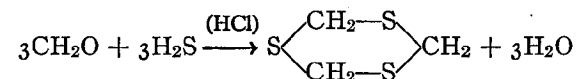
<sup>6</sup> Bourguignon, *Bull. soc. chim. Belg.* **22**, 88 (1908).

<sup>7</sup> Cloke and Ayers, *J. Am. Chem. Soc.* **56**, 2144 (1934).

## XXVIII

### *sym.*-TRITHIANE

(Trithioformaldehyde)



Submitted by R. W. BOST and E. W. CONSTABLE.

Checked by REYNOLD C. FUSON and C. F. WOODWARD.

### 1. Procedure

A MIXTURE of 326 g. (3.9 moles) of a 36 per cent formaldehyde solution (Note 1) and 700 cc. of concentrated hydrochloric acid (sp. gr. 1.18) is placed in a tall glass cylinder (Note 2), and hydrogen sulfide is passed through the solution until no more precipitate is formed. In order to facilitate the process, the accumulated mass of crystals is removed from time to time by filtration. The time required for completion of the reaction varies from twelve to twenty-four hours. A crude yield of 176 g. (98 per cent of the theoretical amount) of fine, nearly colorless needles melting at 210–213° is obtained.

The product is purified by the inverted filtration method. The apparatus used is shown in Fig. 3. A 2-l. round-bottomed flask is equipped with a reflux condenser and a bent glass tube, 8–10 mm. in diameter (Note 3). To the lower end of this tube is attached, by means of a cork, a 25-mm. tip prepared from a paper Soxhlet thimble and packed with glass wool. A 2-l. conical flask serves as a receiver for the hot filtrate.

The crude product is placed in the round-bottomed flask, 1 l. of benzene is added, and heat is applied until the solvent boils vigorously. After a few minutes the source of heat is withdrawn and the mixture is allowed to become quiet. The filterin

thimble, which up to this point is kept at the top of the flask (see Fig. 3), is now lowered to its normal position and the conical flask is attached. Gentle suction is applied, and the liquid is drawn over into the conical flask. The hot solution is removed, allowed to cool, and filtered. In the meantime, the extraction process is repeated with a second 1-l. portion of benzene. The two portions of benzene are used alternately over and over in the manner described until all the crude product has been recrystallized.

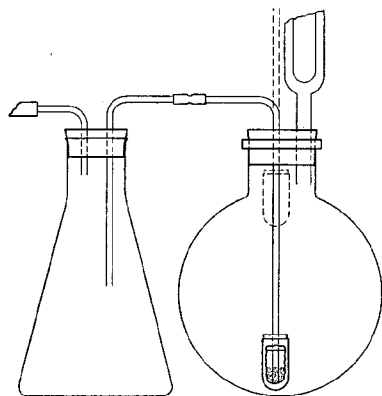


Fig. 3

This requires about ten separate extractions, using each 1-l. portion of benzene five times.

The yield of pure product, melting at 214–215°, is 165–169 g. (93–94 per cent of the theoretical amount).

## 2. Notes

1. Since commercial solutions of formaldehyde contain methyl alcohol, it is grossly inaccurate to estimate the amount of formaldehyde present by reference to specific gravity tables (*cf.* *Org. Syn.* 14, 92). The formaldehyde content of the solution is determined by analysis, for which the iodimetric method of Borgstrom and Horsch<sup>5</sup> is recommended. The yield is calculated upon the basis of the amount of formaldehyde actually present, as shown by analysis.

2. A tall cylindrical vessel insures good contact between the solution and the gas bubbling through it. Hydrogen sulfide from a commercial cylinder was used.

3. Successful use of the inverted filtration method requires attention to these details: (a) use of a sufficiently wide transference tube; (b) minimum exposure of tubing between the flasks; (c) rapid transfer of the hot solution; (d) avoidance of too strong an application of suction.

The inverted filtration device is convenient for simple recrystallizations as well as repeated extractions. It is of particular advantage for the manipulation of volatile, inflammable solvents and of lachrymatory solutions.

## 3. Methods of Preparation

sym.-Trithiane has been prepared by treating carbon bisulfide,<sup>1</sup> ethyl isothiocyanate,<sup>2</sup> or potassium thiocyanate<sup>2</sup> with zinc and hydrochloric acid; by heating methylene iodide with alcoholic sodium hydrosulfide,<sup>3</sup> and by treating aqueous formaldehyde with hydrogen sulfide and concentrated hydrochloric acid.<sup>4</sup>

<sup>1</sup> Girard, *Compt. rend.* 43, 96 (1856)[*Ann.* 100, 306 (1856)].

<sup>2</sup> Hofmann, *Ber.* 1, 176, 179 (1868).

<sup>3</sup> Husemann, *Ann.* 126, 293 (1863).

<sup>4</sup> Hofmann, *ibid.*, 145, 360 (1868); Baumann, *Ber.* 23, 67 (1890).

<sup>5</sup> Borgstrom and Horsch, *J. Am. Chem. Soc.* 45, 1493 (1923).

## APPENDIX

### LATER REFERENCES TO PREPARATIONS IN THE PRECEDING VOLUMES

(The following references are to methods of possible preparative value that have been described recently. The numbers in parentheses following the name of the compound refer to the volume and page of Organic Syntheses.)

**Allyl Alcohol** (Coll. Vol. 1, 34): By passing propylene oxide over activated alumina at 200°-400°. Can. pat. 328,050 [C. A. 27, 1012 (1933)].

**Allyl Cyanide** (Coll. Vol. 1, 38): From allyl chloride and cuprous cyanide. FALAISE and FROGNIER, Bull. soc. chim. Belg. 42, 427 (1933) [Chem. Zentr. 105, I, 529 (1934)].

**Arsanilic Acid** (Coll. Vol. 1, 63): Reduction of the salts of nitroarylarsonic acids in the presence of a nickel catalyst. INOUE and KIMURA, J. Pharm. Soc. Japan 53, 1105 (1933) [C. A. 28, 3391 (1934)]; STEVINSON and HAMILTON, J. Am. Chem. Soc. 57, 1298 (1935).

**Benzanthrone** (15, 4): In 90 per cent yield by reducing anthraquinone with a mixture of nine parts copper turnings and one part zinc dust, and carrying out the condensation with glycerol and sulfuric acid at 105-108°. LUKIN, Anilino-krasoch'naya Prom. 1931, No. 11-12, 14 [C. A. 28, 5241 (1934)].

**Benzil** (Coll. Vol. 1, 80): By heating benzoin with aniline and aniline hydrochloride, in 75 per cent yield. PANDALAI, J. Indian Chem. Soc. 11, 511 (1934) [C. A. 28, 7256 (1934)].

**Benzohydrol** (Coll. Vol. 1, 84): In almost quantitative yield by the photochemical reduction of benzophenone in the presence of *iso*-propyl alcohol and sodium *iso*-propoxide. BACHMANN, J. Am. Chem. Soc. 55, 393 (1933).

**Benzophenone** (Coll. Vol. 1, 89): By the rapid addition of phenylmagnesium halides to one equivalent of benzoyl chloride. In one-tenth mole experiments using phenylmagnesium iodide, bromide, and chloride, the yields reported are 68, 55, and 48 per cent, respectively. GILMAN and MAYHUE, Rec. trav. chim. 51, 47 (1932).

**$\beta$ -Benzoylpropionic Acid** (13, 12): From phenylmagnesium bromide and succinic anhydride. KOMPPA and ROHRMAN, Ann. 509, 259 (1934).

**Benzyl Cyanide** (Coll. Vol. 1, 101): Preparation from mandelonitrile in 79 per cent yield by catalytic reduction. ZELINSKY, PACKENDORFF, and LEDER-PACKENDORFF, Ber. 67, 300 (1934).

***p*-Bromodiphenyl** (Coll. Vol. 1, 109): From *p*-dibromobenzene, cyclohexanone, and activated magnesium, by a series of reactions involving the formation and dehydrogenation of 1-bromo-4-cyclohexenylbenzene. v. BRAUN, IRMISCH, and NELLES, Ber. 66, 1471 (1933).

***iso*-Butyl Bromide** (13, 20): Parallel experiments with *iso*-butyl and other alcohols showed that with theoretical amounts of phosphorus tribromide the yield

of alkyl bromide is 10 per cent higher than with corresponding amounts of red phosphorus and bromine. TSENG and HOU, J. Chinese Chem. Soc. 2, 57 (1934).

**n-Butyryl Chloride** (Coll. Vol. 1, 142): Systematic study of the preparation, using phosphorus pentachloride, phosphorus trichloride, and thionyl chloride. CLARK and BELL, Trans. Roy. Soc. Canada [3] 27, 97 (1933).

**o-Chlorobenzoyl Chloride** (Coll. Vol. 1, 148): Preparation from o-chlorobenzoic acid with phosphorus pentachloride, and phosphorus trichloride. CLARK and BELL, Trans. Roy. Soc. Canada, [3] 27, 97 (1933).

Preparation from salicylic acid, pyridine, and phosgene. Brit. pat. 401,643 [Chem. Zentr. 105, II, 2133 (1934)].

**Cyclohexene** (Coll. Vol. 1, 177): In 73 per cent yield by passing cyclohexanol over silica gel at 280-300°. BARTLETT and BERRY, J. Am. Chem. Soc. 56, 2684 (1934).

**Diazomethane** (15, 3): Diazomethane and its homologs are prepared by the action of sodium *iso*-propoxide in *iso*-propyl alcohol upon the products of nitrosation from  $\beta$ -alkylamino-*iso*-butyl methyl ketones (obtained by adding the amine to mesityl oxide). ADAMSON and KENNER, J. Chem. Soc. 1935, 286.

**Diethyl Zinc** (12, 86): Improved apparatus for preparation, purification, and use of zinc ethyl. MCCLEARY and DEGERING, Proc. Indiana Acad. Sci. 43, 127 (1934) [C. A. 28, 7245 (1934)].

**Ethyl Bromide** (Coll. Vol. 1, 27): It is reported that the addition of copper turnings to the reaction mixture of ethyl alcohol, sulfuric acid, water, and sodium bromide raised the yield of ethyl bromide from 57 to 80 per cent, in small-scale preparations. HENDRIXON, Proc. Iowa Acad. Sci. 41, 165 (1934) [C. A. 29, 3650 (1935)].

**Ethyl Oxomalonate** (Coll. Vol. 1, 261): Oxidation of ethyl malonate with selenium dioxide. MÜLLER, Ber. 66, 1668 (1933).

**Fluorobenzene** (13, 46): In 87 per cent yield by stirring aniline with hydrofluoric acid, diazotizing, and warming. Ger. pat. 600,706 [C. A. 28, 7260 (1934)].

**p-Fluorobenzoic Acid** (13, 52): By electrochemical oxidation of *p*-fluorotoluene. FICHTER and ROSENZWEIG, Helv. Chim. Acta 16, 1154 (1933).

**2-Furylcarbinol** (Coll. Vol. 1, 270): A product of high purity is obtained in excellent yields by hydrogenation of furfural at about 175° and 50-100 atm. pressure with copper chromite catalyst. CALINGAERT and EDGAR, Ind. Eng. Chem. 26, 878 (1934).

**Glycine** (Coll. Vol. 1, 292): Glycine esters are hydrolyzed with an organic acid, such as acetic acid, and the mixture is evaporated to dryness. Ger. pat. 594,275 [C. A. 28, 3417 (1934)]. Glycine ethyl ester hydrochloride is converted to the sulfate by silver sulfate, saponified by barium hydroxide, and excess of the latter is removed by conversion to barium sulfate. Ger. pat. 597,305 [C. A. 28, 5078 (1934)].

Glycine is separated from ammonium chloride by acetylation, and the acetyl derivative is hydrolyzed by barium hydroxide. CONTARDI and RAVAZZONI, Rend. ist. lombardo sci. 66, 786 (1933) [C. A. 29, 3309 (1935)].

**Glycine Ethyl Ester Hydrochloride** (14, 46): Cyanofornic esters are reduced with a metal, such as zinc, iron, or aluminum, in the presence of an organic acid. Ger. pat. 594,219 [C. A. 28, 3417 (1934)]. Cyanofornic ester is reduced in alcohol in the presence of concentrated hydrochloric acid, with a platinum catalyst and hydrogen at 40 atm. pressure. Ger. pat. 597,305 [C. A. 28, 5078 (1934)].

**Homoveratric Acid** (15, 31): From veratroyl chloride by treatment with diazomethane, followed by hydrolysis. ARNDT, Ber. 68, 200 (1935).

**Methylene Bromide** (Coll. Vol. 1, 349): Prepared by the bromination of methane, along with methyl bromide. PERELIS, Ind. Eng. Chem. 25, 1160 (1933).

**m-Nitroacetophenone** (10, 74): Solid carbon dioxide is used as cooling medium and is introduced directly into the reaction mixture to obtain a temperature of -20°. BARKENBUS and CLEMENTS, J. Am. Chem. Soc. 56, 1369 (1934).

Prepared by treating *m*-nitrobenzaldehyde with a methylmagnesium halide and oxidizing the resulting carbinol with chromic acid. BERLINGOZZI, Atti accad. Lincei 19, 332 (1934) [C. A. 28, 5053 (1934)].

**m-Nitrobenzoic Acid** (Coll. Vol. 1, 383): In 85 per cent yield by nitration of benzotrithloride and subsequent hydrolysis. SAH, LEI, and WANG, Science Repts. Natl. Tsinghua Univ. A2, 137 (1933) [C. A. 28, 118 (1934)].

**Pentamethylene Bromide** (Coll. Vol. 1, 419): Tetrahydrofurfuryl alcohol passed over alumina at 370-380° gives 1,2-dihydropyran in 44 per cent yield. Hydrogenation in the presence of platinum produces pentamethylene oxide (1,5-epoxypentane), which is converted to the bromide by heating with hydrogen bromide in glacial acetic acid. The yield is 65 per cent, based upon 1,2-dihydropyran. PAUL, Bull. soc. chim. [4] 53, 1489 (1933).

**Phenylacetic Acid** (Coll. Vol. 1, 427): Prepared by catalytic reduction of mandelic acid. ZELINSKY, PACKENDORFF, and LEDER-PACKENDORFF, Ber. 67, 300 (1934).

**Phenylacetylene** (Coll. Vol. 1, 428): Prepared by the action of alcoholic potassium hydroxide on  $\alpha$ -chlorostyrene and by decarboxylation of phenylpropionic acid. OTTO, J. Am. Chem. Soc. 56, 1393 (1934).

By the action of a solution of sodium in liquid ammonia, upon  $\beta$ -bromostyrene or styrene dibromide. VAUGHN, *ibid.* 56, 2069 (1934).

By the action of a solution of sodamide in liquid ammonia upon  $\beta$ -bromostyrene,  $\alpha$ -chlorostyrene, or styrene dibromide. VAUGHN, VOGT, and NIEWLAND, *ibid.* 56, 2120 (1934).

**Phenylethylene** (Coll. Vol. 1, 430): In 75-80 per cent yield by boiling  $\alpha$ -chloroethyl benzene with a small excess of quinoline; in 75 per cent yield by heating  $\alpha$ -phenylethyl alcohol with 3-5 per cent of potassium bisulfate. ZAL'KIND, BERKOVICH, and AMUSIN, Plasticheskie Massui 1934, No. 1, 14 [C. A. 28, 5810 (1934)].

In 93 per cent yield by heating  $\alpha$ -phenylethyl alcohol with 5 per cent of sodium or potassium bisulfite. GAUTHIER and GAUTHIER, Bull. soc. chim. [4] 53, 323 (1933).

**Phenylglyoxal** (15, 67): Preparation and use of selenium dioxide for oxidations. HAHN and SCHALES, Ber. 67, 1823 (1934); RILEY, U. S. pat. 1,955,890 [C. A. 28, 4067 (1934)].

**Platinum Catalyst for Reductions** (Coll. Vol. 1, 452): Directions are given for the preparation of a colloidal platinum (or palladium) catalyst in an anhydrous, alkaline medium. This catalyst is said to be particularly valuable for the reduction of nitriles, oximes, and nitrostyrenes to pure primary amines. SKITA and KEIL, Ber. 65, 424 (1932).

**Quinizarin** (Coll. Vol. 1, 464): From anthraquinone by reaction with nitrosylsulfuric acid in the presence of small amounts of mercury. U. S. pat. 1,963,136 [C. A. 28, 5079 (1934)].

**Quinoline** (Coll. Vol. 1, 456): The Skraup synthesis is carried out with fuming sulfuric acid and copper sulfate catalyst, at 135–154°. KIRKHOFF and ZASOSOV, *Khim. Farm. Prom.* 1934, No. 1, 40 [C. A. 28, 5454 (1934)].

**Trinitrobenzene** (Coll. Vol. 1, 526): Preparation from 2,4,6-trinitrobenzoic acid, or 2,4,6-trinitrobenzaldehyde. SECAREANU, *Bull. soc. chim.* [4] 53, 1395 (1934).

**Veratric Aldehyde** (13, 102): By methylation of vanillin with methyl *p*-toluenesulfonate. KANEVSKA, *Arch. Pharm.* 271, 462 (1933).

## ADDITIONS AND CORRECTIONS FOR PRECEDING VOLUMES

(The numbers in parentheses following the name of the compound refer to the volume and page of *Organic Syntheses*. New methods or changes in procedure have not been checked unless otherwise noted.)

### **Benzyl Cyanide** (Coll. Vol. 1, 101):

Benzyl isocyanide, which gives the product a disagreeable odor, can be removed completely by washing the crude material after the first distillation with an equal volume of warm (60°) 50 per cent sulfuric acid, prepared by adding 275 cc. of concentrated sulfuric acid to 500 cc. of water. The benzyl cyanide is shaken vigorously for about five minutes with the acid, separated, and washed with an equal volume of saturated sodium bicarbonate solution, followed by an equal volume of half-saturated sodium chloride solution. After drying and distilling under reduced pressure, the product is water-white and remains so after standing for several months. The loss in the washing operations is negligible, and the yields are the same as those reported previously.

JOHN R. JOHNSON, private communication.

### **Ethyl Benzoylformate** (Coll. Vol. 1, 236):

By a slight modification of the procedure, crystalline benzoylformic acid (phenylglyoxylic acid) can be isolated. The oxidation of 375 g. (2.5 moles) of mandelic acid by cold alkaline potassium permanganate is performed exactly as described in the first paragraph (p. 236). After removal of the manganese dioxide, the combined filtrates are evaporated to 2500–3000 cc., rather than 800–1000 cc. as given in the second paragraph (p. 237). At this point the solution is acidified carefully, so as to precipitate only benzoic acid, by the addition of 100 cc. (190 g.) of concentrated sulfuric acid (sp. gr. 1.84) previously diluted with an equal volume of water and cooled. The benzoic acid (25–30 g.) which

separates is removed by filtration. The filtrate is made alkaline with 75 g. of sodium hydroxide and concentrated to 800–1000 cc. The subsequent acidification, with 280–300 cc. of concentrated sulfuric acid, and ether extraction are performed as described in the third paragraph (p. 237). After removing the ether about 280 g. of crude, liquid benzoylformic acid remains; at this stage enough water is present to render the acid immiscible with carbon disulfide.

The liquid residue is dried by placing it in a distilling flask with 70–90 cc. of toluene, and distilling off the water and toluene (preferably under slightly reduced pressure). The dried liquid residue is taken up in an equal volume of carbon disulfide; with adequate precautions to exclude moisture, the solution is cooled thoroughly in an ice-salt mixture. The yield of product melting at 58–61° is 190–250 g. (50–67 per cent of the theoretical amount).

CHARLES D. HURD and R. W. McNAMEE, private communication. Checked by REYNOLD C. FUSON and W. E. ROSS.

#### Iodothiophene (12, 44):

A small amount of 2,5-diiodothiophene is formed in the reaction. About 4 g. of crystalline diiodothiophene, m.p. 40–41°, can be isolated from the residue remaining after distillation of the 2-iodothiophene (b.p. 65.5–66.5°/9 mm.).

O. IVAN LEE, private communication.

#### $\beta$ -Naphthylmercuric Chloride (12, 54):

It is unsafe to store the addition complexes of mercuric chloride and diazonium chlorides in a closed vessel. The complex salt should be used as soon as possible, and, if it is to be kept for any length of time, should be placed in a large open dish or a loosely covered container.

In one of a number of preparations, a batch (about 960 g.) of the addition compound from benzenediazonium chloride was air dried and placed in a large bottle with a screw cap. About four

hours later the entire complex decomposed with considerable violence. At the time no heat or strong light was near the bottle.

HENRY GILMAN, private communication.

#### Pentamethylene Bromide (Coll. Vol. 1, 419):

The quantity of bromine given in line 5 is 0.405 mole instead of 0.81 mole.

It is reported that the procedure of v. BRAUN and STEINDORFF, Ber. 38, 2338 (1905), is a more satisfactory method of eliminating benzonitrile from the crude product. The distillate containing the alkylene bromide, benzonitrile, and phosphorus oxybromide is poured carefully into 90–100 cc. of water, with cooling and shaking. The resulting mixture is refluxed for eight to ten hours, with the occasional addition of 3–4 cc. of alcohol to decrease resinification. The product is then removed by steam distillation, washed with sodium carbonate solution, dried, and distilled.

MÜLLER, Ber. 68, 1013 (1935).

#### $\alpha$ -Tetralone (15, 79):

The second reference should read: Chem. Zentr. 93, II, 1141 (1922).

#### Veratric Aldehyde (13, 102):

A product of sufficient purity for most synthetic purposes may be prepared rapidly and conveniently by the method of BARGER and SILBERSCHMIDT, J. Chem. Soc. 133, 2924 (1928). In a 1-l. three-necked, round-bottomed flask (or a wide-mouthed bottle) fitted with a mechanical stirrer, a reflux condenser, and two separatory funnels, 152 g. (1 mole) of vanillin is melted by warming on a steam bath. With vigorous stirring, a solution of 92 g. (1.5 moles) of 90 per cent potassium hydroxide in 150 cc. of water is run in at the rate of two or three drops a second; twenty seconds after this is started, the addition of 160 g. (120 cc., 1.25 moles) of dimethyl sulfate is begun at about the same rate. Just before use, the dimethyl sulfate is washed with an equal volume of ice water, followed by one-third its volume of cold, saturated

sodium bicarbonate solution. The external heating is stopped after a few minutes, and the mixture continues to reflux from the heat of reaction. A turbidity soon develops, and separation into two layers occurs after about one-half of the dimethyl sulfate has been added. The addition of both reagents should be completed in about twenty minutes.

The color of the reaction mixture, which is purplish brown at the beginning, changes abruptly to yellow towards the end. A temporary greenish yellow during the earlier part of the reaction indicates that the solution has become acid, and this condition should be corrected by increasing the rate of addition of the alkali. The final yellow color is permanent, and at the end the reaction mixture is alkaline to litmus.

The reaction mixture is transferred at once to a large beaker, covered with a watch glass, and allowed to cool without disturbance (preferably overnight). The hard, crystalline mass of veratric aldehyde is removed, ground in a mortar with 300 cc. of ice water, filtered with suction, and dried in a vacuum desiccator. The yield is 152-158 g. (92-95 per cent of the theoretical amount) of a product melting at 42.5-43.5°.

JOHN R. JOHNSON and H. B. STEVENSON, private communication.

#### Veratronic nitrile (15, 85):

Crude veratric aldehyde, obtained as described in the preceding paragraph, gives a 90 per cent yield of the oxime (m.p. 89-90°) and an overall yield of 68-70 per cent of veratronic nitrile (m.p. 65-66°). The nitrile thus produced is satisfactory for conversion to veratric amide and 4-aminoveratrole (p. 4) without further purification.

Subsequent preparations have shown that the mixture of the oxime and acetic anhydride requires only twenty minutes of heating, after the initial vigorous reaction, instead of the two-hour period specified. The longer period of heating does not alter the yield.

JOHN R. JOHNSON and H. B. STEVENSON, private communication.

## SUBJECT INDEX

(This Index Comprises Material from Volumes X to XVI of this Series: for Previous Volumes see Collective Volume I.)

(Names in small capital letters refer to the titles of preparations which are given in full detail. A number in ordinary bold face type denotes the volume. A number in bold face italics refers to a page which gives preparative directions for a substance formed either as principal product or as a by-product, or to a product which has been prepared by a method analogous to the one given. Other numbers in ordinary type indicate pages on which a compound is mentioned incidentally or information is given concerning an item other than a compound.)

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