ACETYLBENZOYL

(1,2-Propanedione, 1-phenyl-)

$$CH_3C({=}NOH)COC_6H_5 + H_2O \xrightarrow{H_2SO_4} CH_3COCOC_6H_5 + NH_2OH$$

Submitted by W. W. Hartman and L. J. Roll.
Checked by A. H. Blatt and Lewis Rothstein.

1. Procedure

In a 1-l. flask arranged for steam distillation (Note 1), 50 g. (0.31 mole) of isonitrosopropiophenone (Org. Syn. **16**, 44; Coll. Vol. **2**, **1943**, 363) and 500 g. of 10 per cent sulfuric acid are mixed, and the mixture is distilled with steam until about 2 l. of distillate is collected. During the distillation the flask is heated so that the volume of the reaction mixture is kept roughly constant. The distillation requires about six hours, and at the end of this time the liquid in the flask is clear (Note 2).

The lower, yellow layer of diketone in the distillate is separated; the water layer is then saturated with salt and extracted with ether, using one 80-cc. and two 25-cc. portions for each liter of the aqueous solution. The ether extracts are combined with the diketone proper and dried over sodium sulfate. The ether is removed on the steam bath, and the residual material is distilled from a Claisen flask under reduced pressure. Acetylbenzoyl is collected at 114–116°/20 mm. (Note 3). The yield is 30–32 g. (66–70 per cent of the theoretical amount) (Note 4).

2. Notes

1. A spray trap should be placed between the flask and the condenser; otherwise some isonitrosoketone will be carried over. The checkers used a "Kjeldahl Connecting Bulb, Cylindrical Type," illustrated as item 2020 in the Pyrex Catalog, L.P–21 for 1941.

2. On cooling, the reaction mixture deposits 3 to 7 g. of the dioxime of acetylbenzoyl, m.p. 234–236° dec.[1]

3. Other boiling points reported for acetylbenzoyl are 216–218°, 164–165°/116 mm., and 102–103°/12 mm.

4. According to the submitters the reaction can be carried out with about the same percentage yields using five times the amounts of material specified above.

3. Methods of Preparation

Acetylbenzoyl has been prepared by dehydrogenation of acetylphenylcarbinol over copper at 350°;[2] by oxidation of 1-methyl-2-phenylethylene glycol;[3] by action of amyl nitrite on isonitrosopropiophenone;[4] and by acid hydrolysis of isonitrosopropiophenone[5] or of isonitrosobenzyl methyl ketone.[6] The last-named reaction is reported to furnish quantitative yields of acetylbenzoyl, but the starting material is not easily accessible. Treatment of propiophenone with amyl nitrite (2 moles) without isolating the isonitroso compound has been mentioned as a method of preparing acetylbenzoyl,[4] but the yield of diketone is much better when the isonitroso compound is isolated.[7]

---

[1] Müller and Pechmann, Ber. **22**, 2128 (1889).

[2] Mailhe, Bull. soc. chim. (4) **15**, 326 (1914).

[3] Zincke and Zehn, Ber. **43**, 855 (1910).

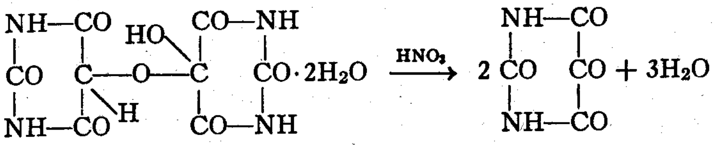
[4] Manasse, Ber. **21**, 2177 (1888).

[5] Pechmann and Müller, Ber. **21**, 2119 (1888).

[6] Kolb, Ann. **291**, 286 (1896); Borsche, Ber. **40**, 740 (1907).

[7] Coles, Manske, and Johnson, J. Am. Chem. Soc. **51**, 2269 (1929).

ALLOXAN



Submitted by W. W. Hartman and O. E. Sheppard.
Checked by C. S. Marvel and B. H. Wojcik.

1. Procedure

In a 500-cc. flask (Note 1), fitted with a mechanical stirrer, are placed 36 cc. of water and 25 g. (0.078 mole) of finely crystalline alloxantin dihydrate (p. 6). The flask and contents are heated on a steam bath to 50°, and 3.6 cc. of fuming nitric acid (sp. gr. 1.62) is added in a fine stream while vigorous stirring is maintained and the temperature is not allowed to rise above 60° (Note 2). After all the fuming nitric acid has been added, the temperature is brought to 55° and the stirrer is stopped. In a few minutes a vigorous reaction begins and large quantities of oxides of nitrogen are evolved. The stirrer is again started and, if the reaction becomes too violent, the mixture is cooled somewhat; otherwise, the reaction is allowed to take its course. The reaction is complete when a current of air, introduced into the flask above the mixture, does not produce much color due to formation of nitrogen tetroxide (Note 3). The mixture is then heated to 60–65° for ten to fifteen minutes, whereupon practically all the solid dissolves. The reaction mixture is poured into a glass (Pyrex) tray and cooled overnight at 0° or below. The large triclinic, colorless crystals of alloxan tetrahydrate are broken up, filtered with suction, washed with ice water, and pressed as dry as possible. The crystals are then added to 25–26 cc. of *hot* water (Note 4), and the mixture is shaken until solution is complete. The solution is filtered immediately, and the filtrate is cooled overnight in a tray at 0°. The crystals are broken up, filtered, washed with ice water, and pressed as dry as possible. These moist crystals of the tetrahydrate, which weigh 22–24 g., are dried to constant weight in a glass tray over concentrated sulfuric acid. The resulting product is a fine white powder (Note 5) which weighs 16 g.

The mother liquor from the recrystallization is placed in a 250-cc. flask and is concentrated to a volume of 8–10 cc. under reduced pressure at not over 30–40° (Note 6). The concentrate, when cooled overnight at 0°, deposits a solid which is filtered, recrystallized from its own weight of boiling water, and dried over sulfuric acid. This solid weighs about 2 g. The mother liquors from the two crystallizations are combined with the original mother liquor from the oxidation, and the whole is evaporated to dryness under diminished pressure at not above 30–40°. This solid residue is somewhat yellow and possesses a strong odor of nitric acid. It is kept on a tray for several days until the odor of nitric acid disappears, and then it is dissolved in its own weight (2–3 g.) of boiling water, and the solution is cooled for several days below 0° (Note 7). The solid is removed, recrystallized from water, and dried over sulfuric acid (Note 8). This crop weighs about 0.5 g. The total yield of alloxan is 18–19 g. (82–87 per cent of the theoretical amount, assuming that the product, after it has been dried over concentrated sulfuric acid [1] (Note 9), contains no water of crystallization).

2. Notes

1. The large flask is necessary because the mixture foams greatly during the reaction.

2. Very little reaction occurs during the addition of the nitric acid, and consequently there is very little rise in temperature. The acid is added during a few minutes.

3. The reaction is complete in about thirty minutes.

4. The water must not be boiled during the addition of the crystals or afterwards as this will cause decomposition of the alloxan to carbon dioxide, parabanic acid, and alloxantin.

---

[1] Abderhalden, Biochemisches Handlexikon, Vol. 4, p. 1160.

5. The tetrahydrate effloresces readily, gradually loses part of its water, and becomes moist when allowed to stand at room temperature. For this reason it is not suitable for keeping. All the water is removed from most of the crystals by drying them over sulfuric acid; but, unless the solid is finely divided or is allowed to stand for weeks over sulfuric acid, probably some monohydrate remains. Drying in an oven is likely to result in local overheating and decomposition, which starts apparently slightly above 100°. Drying in an oven is also likely to result in reddening if even a trace of ammonia or amines is present in the air.

6. A higher temperature is likely to cause oxidation and to result in a violent reaction which may become explosive as the nitric acid becomes concentrated.

7. Alloxan crystallizes from solution much more slowly when it is nearly free of nitric acid and when other soluble substances are present; it is, however, less soluble in nitric acid solution than in water.

8. A little alloxan still remains in solution, for the mother liquor still slowly colors the skin red and on standing deposits alloxantin owing to decomposition of alloxan. The alloxantin can be removed and used in another oxidation. About 0.3–0.5 g. of it may deposit after the filtrate has stood for some time.

9. The submitters obtained the same yields (per cent) when approximately sixty-five times these amounts of materials were used. Thus, carrying out the oxidation of 1610 g. (5 moles) of alloxantin dihydrate in a 22-l. flask, the submitters obtained 1085 g. of the first, 160 g. of the second, and 28 g. of the third crop, a total of 1273 g.

3. Methods of Preparation

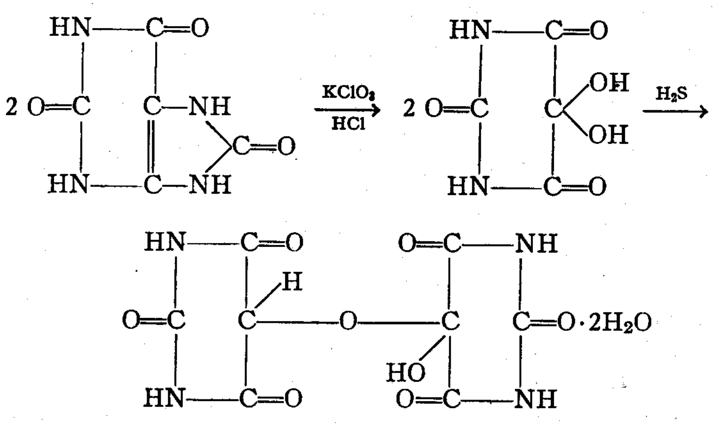
Alloxan has been prepared by slow oxidation of alloxantin with nitric acid at room temperature; [2] by direct oxidation of uric acid with nitric acid; [3] and by oxidation of uric acid with chlorine,[4] chlorine and iodine,[5] or bromine.[6] The preparation of alloxan monohydrate from benzalbarbituric acid has been described.[7]

---

[2] Liebig, Ann. 147, 366 (1868).

[3] Liebig and Wöhler, Ann. 26, 256 (1838).

ALLOXANTIN DIHYDRATE



Submitted by Dorothy Nightingale.
Checked by R. L. Shriner and C. H. Tilford.

1. Procedure

In a 500-cc. three-necked flask, provided with a stirrer, are placed 15 g. (0.09 mole) of finely powdered uric acid, 30 g. (25.2 cc.) of concentrated hydrochloric acid, and 40 cc. of water. The mixture is warmed to 30°, the stirrer is started, and 4 g. (0.014 mole) of finely powdered potassium chlorate is added in small portions during a period of not less than three-fourths of an hour (Note 1). Most of the uric acid dissolves; any undissolved material is removed by filtration through a fritted glass filter. The clear filtrate is diluted with 30 cc. of water, and a rapid stream of hydrogen sulfide is led into it until it is saturated (about ten to fifteen minutes). Sulfur and alloxantin separate, and the mixture is cooled for two to three hours in an ice bath until the separation is complete.

The solid is collected on a Büchner funnel and washed with three 30-cc. portions of cold water. The alloxantin is dissolved by boiling the wet solid for fifteen minutes with 250 cc. of water, and the *hot* solution is filtered to remove the sulfur (Note 2). Alloxantin dihydrate crystallizes from the filtrate in glistening plates which should be pressed as dry as possible on a Büchner filter, washed with about 30 cc. of ether, and dried in a vacuum desiccator (Note 3). The yield is 8–10 g. (55–69 per cent of the theoretical amount) (Note 4). The product melts with decomposition at 234–238° (Note 5), and is pure enough for most purposes.

2. Notes

1. It is important that the temperature of the reaction mixture be kept near 30°. The potassium chlorate must be added slowly.

2. Since alloxantin is difficultly soluble, it is desirable to make a second extraction of the sulfur to be certain that all the alloxantin has been removed.

3. The compound gradually turns pink on standing in the air. It should be stored in a tightly stoppered bottle or kept in a vacuum desiccator over calcium chloride.

4. If larger amounts of material are desired it is best to oxidize several 15-g. portions of uric acid and to combine the sulfur-alloxantin mixtures for the extraction.

5. The water of crystallization may be removed by heating the dihydrate at 120–150° under reduced pressure for two hours. The melting points reported in the literature vary considerably. The anhydrous material turns yellow at about 225–230° and decomposes at temperatures ranging from 238–242° to 253–255°, depending on the rate of heating. The instantaneous decomposition temperatures determined on the Maquenne block were 270–275°.

---

[4] Biltz and Hehn, Ann. **413**, 60 (1916).

[5] Brugnatelli, Ann. chim. phys. (2) **8**, 201 (1818).

[6] Hardy, Ann. chim. phys. (4) **2**, 372 (1864).

[7] Speer and Dabovich, Org. Syn. **21**, 5.

3. Methods of Preparation

The above procedure is essentially that described in the laboratory manual by Fischer and Helferich.[1]

Alloxantin has been obtained by the oxidation of uric acid with nitric acid, followed by reduction with hydrogen sulfide;[2] by oxidation of uric acid with potassium chlorate, followed by reduction with stannous chloride;[3] by condensation of alloxan with dialuric acid in aqueous solution;[4] and by oxidation of dialuric acid.[5]

BROMOACETAL

(Acetaldehyde, bromo-, diethyl acetal)

$$\mathrm{CH_3CO_2CH{=}CH_2 + Br_2 \longrightarrow CH_3CO_2CHBrCH_2Br}$$

$$\mathrm{CH_3CO_2CHBrCH_2Br + C_2H_5OH \longrightarrow BrCH_2CHO + CH_3CO_2C_2H_5 + HBr}$$

$$\mathrm{BrCH_2CHO + 2C_2H_5OH \xrightarrow{HBr} BrCH_2CH(OC_2H_5)_2 + H_2O}$$

Submitted by S. M. McElvain and D. Kundiger.
Checked by R. L. Shriner and C. H. Tilford.

1. Procedure

An apparatus is assembled as shown in Fig. 1. The 3-l. three-necked round-bottomed flask A is equipped with a mechanical stirrer sealed with a well-lubricated rubber sleeve. In one neck of the flask are fitted a thermometer and a glass tube leading through a safety trap B to a water pump. In the other neck a 7-mm. glass tube, extending to the bottom of the flask, is attached to a 500-cc. bottle C in which is placed 255 cc. (5 moles) of bromine (Note 1). This bottle is connected to a 500-cc. wash bottle D containing 250 cc. of sulfuric acid. The inlet tube of D is connected to a calcium chloride tube.

---

[1] Fischer and Helferich, "Anleitung zur Darstellung organischer Präparate," 10th Ed., pp. 66, 67, Braunschweig, 1922; Doja and Mokeet, J. Indian Chem. Soc., **13**, 542 (1936).

[2] Deniges, Bull. soc. pharm. Bordeaux, **66**, 8–12 (1928) [C. A. **23**, 4160 (1929)].

[3] Davidson and Epstein, J. Org. Chem. **1**, 305 (1936).

[4] Wöhler and Liebig, Ann. **26**, 279 (1838); Behrend and Friederichs, Ann. **344**, 1 (1906).

[5] Baeyer, Ann. **127**, 11 (1863).

A solution of 430 g. (5 moles) of vinyl acetate (Note 2) in 1.5 l. (26 moles) of absolute ethyl alcohol is placed in the flask A. The solution is cooled to about −10° by an ice-salt mixture, and stirring is started. Gentle suction is applied at the outlet tube of B, and the bromine is introduced into A by a rapid current of air. The rate of introduction of the bromine, controlled by adjustment of the clamp E, should be regulated so that eight to ten hours is required to volatilize all the bromine. Stirring is stopped, and the reaction mixture is allowed to stand overnight and to come to the temperature of the room. The mixture is poured into 1.7 l. of ice water (Note 3); the lower layer of bromoacetal and ethyl acetate is separated (Note 4), washed twice with 300-cc. portions of cold water, once with 300 cc. of cold 10 per cent sodium carbonate solution, and dried over two successive 25-g. portions of anhydrous calcium chloride for thirty minutes. The crude product weighs 990–1010 g.; it is purified by distillation under diminished pressure (water pump) through a 6-inch Widmer column or a 20-cm. Vigreux column. The first fraction consists of ethyl acetate; this is followed by the pure bromoacetal which boils at

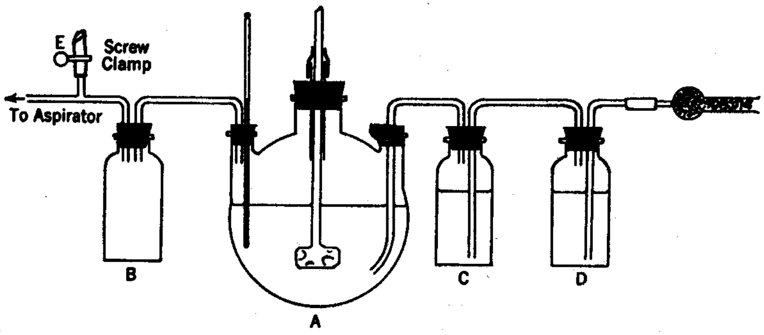


Fig. 1.

62–63°/15 mm. (84–85°/30 mm.) and which amounts to 610–625 g. (62–64 per cent of the theoretical amount) (Note 5).

2. Notes

1. The bromine is previously washed with 100 cc. of concentrated sulfuric acid.

2. The vinyl acetate (Eastman Kodak Company) is distilled from the added preservative; the first turbid portion containing water is discarded; and the fraction boiling at 69–71°/740 mm. is used.

3. If an emulsion forms at this point, 320 g. of hydrated sodium sulfate is added.

4. Bromoacetal is a fairly strong lachrymator and is best handled under a hood.

5. A yield of 78 per cent of bromoacetal has been obtained by a slight modification of the procedure described above. One-half of the amounts of materials specified above were used, and, after the bromination was complete, the reaction mixture was allowed to stand for sixty-four hours before it was processed. The yield of bromoacetal was 380 g.[1]

3. Methods of Preparation

The procedure given above is essentially a large-scale adaptation of that of Filachione.[2] Bromoacetal has been prepared by the bromination of acetal directly,[3] or in the presence of calcium carbonate;[4] by action of sodium ethoxide on α,β-dibromodiethyl ether;[5] by bromination of paraldehyde followed by action of ethyl alcohol;[6] and by the action of ethyl alcohol on bromoacetaldehyde.[7]

[1] Private communication, C. F. H. Allen.

[2] Filachione, J. Am. Chem. Soc. **61**, 1705 (1939).

[3] Pinner, Ber. **5**, 149 (1872).

[4] Fischer and Landsteiner, Ber. **25**, 2551 (1892).

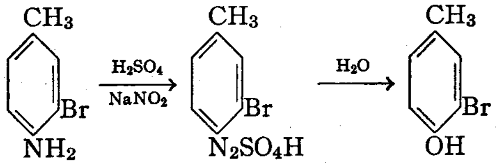
[5] Wislicenus, Ann. **192**, 112 (1878).

[6] Freundler and Ledru, Bull. soc. chim. (4) **1**, 75 (1907).

[7] Rotbart, Ann. chim. (11) **1**, 451 (1934).

3-BROMO-4-HYDROXYTOLUENE

(*p*-Cresol, 2-bromo-)



Submitted by H. E. Ungnade and E. F. Orwoll
Checked by C. F. H. Allen and Alan Bell.

1. Procedure

In a 2-l. beaker is placed 75 g. (0.4 mole) of 3-bromo-4-aminotoluene (Note 1), and to it is added the hot diluted acid obtained by adding 72 cc. of concentrated sulfuric acid to 200 cc. of water. The clear solution is stirred and cooled to about 15°, after which 180 g. of ice is added; the amine sulfate usually separates. As soon as the temperature has dropped below +5°, a solution of 32.2 g. (0.47 mole) of sodium nitrite in 88 cc. of water is added from a dropping funnel, the stem of which extends below the surface of the liquid. The temperature of the solution is kept below +5° during the addition, which requires about fifteen minutes. The solution is stirred for five minutes after the addition of all the sodium nitrite, and 300 g. of cold water, 3 g. of urea, and 300 g. of cracked ice are then added successively. The solution is kept in an ice bath until used.

A 1-l. Claisen flask fitted with a dropping funnel and a thermometer dipping into the liquid is attached to a condenser set for downward distillation. In the flask are placed 150 g. of anhydrous sodium sulfate, 200 g. (108 cc.) of concentrated sulfuric acid, and 100 cc. of water. The flask is heated over a wire gauze, and while the internal temperature is maintained at 130–135°, the diazonium solution, in 25-cc. portions, is added at the same rate as the distillate is collected (Note 2). When this operation has been completed, 200 cc. of water, in 25-cc. portions, is introduced and the distillation is continued until an additional 200 cc. of distillate has been collected. The complete distillation requires three to three and one-half hours.

The distillate is extracted with two 150-cc. portions of ether, and the combined extracts are washed successively with 100 cc. of water and 150 cc. of 10 per cent sodium bicarbonate solution. The phenol is then extracted from the ether layer by use of one 200-cc. and two 50-cc. portions of 10 per cent sodium hydroxide solution. The combined alkaline solutions are acidified, with cooling, by addition of 100 cc. of concentrated hydrochloric acid. The phenol is extracted with one 200-cc. and two 100-cc. portions of ether, and the combined extracts are washed with 100 cc. of water and dried over 50 g. of anhydrous sodium sulfate. The mixture is filtered, and the ether is removed from the filtrate by distillation on a water bath. The residue, 65–72 g. of a brown oil (Note 3), is then distilled from a Claisen flask with modified side arm (Org. Syn. **22,** 11); b.p. 102–104°/20 mm. The yield is 60–69 g. (80–92 per cent of the theoretical amount) (Note 4).

2. Notes

1. The 3-bromo-4-aminotoluene may be purchased, or prepared according to Org. Syn. Coll. Vol. **1, 1941,** 111. The material used melted at 12–13°.

2. If the diazonium solution is added too rapidly, and the temperature of the liquid falls, the addition is interrupted until the temperature again exceeds 130°.

3. This crude product serves for most purposes, e.g., conversion to *o*-bromo-*p*-methylanisole.

4. The procedure has been used by the submitters for the conversion of *m*-bromoaniline into *m*-bromophenol, b.p., 234–237°/742 mm.; 105–107°/11 mm. The yield was 66 per cent of the theoretical amount.

3. Methods of Preparation

o-Bromo-*p*-cresol has been prepared by the direct bromination of *p*-cresol in chloroform solution;[1,2] by bromination of dry sodium *p*-cresoxide;[3] and by decomposition of the diazonium sulfate of 3-bromo-4-aminotoluene;[4] the last is a general method.[5,6]

CARBOBENZOXY CHLORIDE AND DERIVATIVES

(Formic acid, chloro-, benzyl ester)

$$C_6H_5CH_2OH + COCl_2 \rightarrow C_6H_5CH_2OCOCl + HCl$$

$$C_6H_5CH_2OCOCl + 2NH_3 \rightarrow C_6H_5CH_2OCONH_2 + NH_4Cl$$

$$C_6H_5CH_2OCOCl + H_2NCH_2CO_2H + NaOH \rightarrow C_6H_5CH_2OCONHCH_2CO_2H + NaCl + H_2O$$

Submitted by H. E. Carter, R. L. Frank, and H. W. Johnston.
Checked by Nathan L. Drake and Charles M. Eaker.

1. Procedure

(*A*) *Benzyl Chloroformate.*—A 3-l. round-bottomed flask is fitted with a rubber stopper carrying an exit tube and a delivery tube extending to the bottom of the flask. The tubes are equipped with stopcocks so that the reaction flask may be disconnected. In the flask is placed 500 g. of dry toluene (Note 1), and the apparatus is weighed. The flask is then cooled in an ice bath, and phosgene (Note 2) is bubbled into the toluene until 109 g. (1.1 moles) has been absorbed (Note 3). The exit gases are passed through a flask containing toluene to remove any phosgene and then through a calcium chloride tube to a gas trap (Org. Syn. **14,** 2; Coll. Vol. **2, 1943,** 4).

---

[1] Vogt and Henninger, Ber. **15,** 1081 (1882).

[2] Zincke and Wiederhold, Ann. **320,** 202 (1902).

[3] Schall and Dralle, Ber. **17,** 2530 (1894).

[4] Cain and Norman, J. Chem. Soc. **89,** 24 (1906).

[5] Kalle and Company, Ger. pat. 95,339 [Frdl. **4,** 124 (1894–97)].

[6] Niemann, Mead, and Benson, J. Am. Chem. Soc. **63,** 609 (1941).

After the absorption of phosgene is completed, the connection to the phosgene tank is replaced by a separatory funnel. The reaction flask is gently shaken while 108 g. (104 cc., 1 mole) of redistilled benzyl alcohol is added rapidly through the separatory funnel. The flask is allowed to stand in the ice bath for one-half hour and at room temperature for two hours. The solution is then concentrated under reduced pressure, at a temperature not exceeding 60°, in order to remove hydrogen chloride, excess phosgene (Note 4), and the major portion of the toluene. The residue weighs 200–220 g. and contains 155–160 g. of benzyl chloroformate (91–94 per cent of the theoretical amount based on the benzyl alcohol) (Note 5). The amount of benzyl chloroformate present in this solution may be estimated by preparing the amide from a small aliquot portion or it may be safely calculated by assuming a minimum yield of 90 per cent of the theoretical amount based on the benzyl alcohol used.

(*B*) *Benzyl Carbamate.*—A measured aliquot (suitably 10 cc.) of the solution of benzyl chloroformate, prepared as described above, is added slowly and with vigorous stirring to five volumes of cold concentrated ammonium hydroxide (sp. gr. 0.90), and the reaction mixture is allowed to stand at room temperature for thirty minutes. The precipitate is filtered with suction, washed with cold water, and dried in a vacuum desiccator. The yield of practically pure benzyl carbamate, melting at 85–86°, is 7.0–7.2 g. (91–94 per cent of the theoretical amount based on the benzyl alcohol used in *A*). Pure benzyl carbamate melting at 87° is obtained by recrystallizing the slightly impure material from two volumes of toluene.

(*C*) *Carbobenzoxyglycine.*—A solution of 7.5 g. (0.1 mole) of glycine in 50 cc. of 2 *N* sodium hydroxide is placed in a 200-cc. three-necked flask fitted with a mechanical stirrer and two dropping funnels. The flask is cooled in an ice bath, and 17 g. (0.1 mole) of benzyl chloroformate (21–24 g. of the solution obtained in *A*) and 25 cc. of 4 *N* sodium hydroxide are added simultaneously to the vigorously stirred solution over a period of twenty to twenty-five minutes. The mixture is stirred for an additional ten minutes. The toluene layer is separated, and the aqueous layer is extracted once with ether. The aqueous solution is cooled in an ice bath and acidified to Congo red with concentrated hydrochloric acid (Note 6). The precipitate is filtered, washed with small portions of cold water, and dried in the air. It is practically pure carbobenzoxyglycine; it weighs 18–19 g. (86–91 per cent of the theoretical amount) and melts at 119–120°. The material may be recrystallized from chloroform; it then melts at 120° (Note 7).

2. Notes

1. The toluene may be dried by distillation.

2. Commercial phosgene was used; it was obtained in a tank from the Ohio Chemical Company.

3. The phosgene is absorbed rapidly for some time, then more slowly as the concentration increases. About one hour is required for this step. The amount of phosgene absorbed is checked by weighing the flask and delivery tubes occasionally.

4. In order to prevent the escape of phosgene, a toluene trap is inserted between the apparatus and the water pump. For this purpose it is convenient to use a 2-l. flask immersed in an ice bath and containing about 1 l. of toluene. The flask is fitted with an inlet tube reaching almost to the bottom.

5. It is not practical to remove the toluene completely; moreover, toluene does not interfere in the preparation of the derivatives.

6. The derivative may precipitate as an oil. However, crystallization is readily induced by cooling and scratching.

7. Carbobenzoxyalanine (m.p. 114–115°) is obtained in 80–90 per cent yield from alanine and benzyl chloroformate by the same procedure.

3. Methods of Preparation

Benzyl chloroformate has been prepared by action of phosgene on benzyl alcohol.[1, 2] The methods described here for the preparation of benzyl chloroformate and the carbobenzoxy deriva-

---

[1] Thiele and Dent, Ann. **302**, 257 (1898).

[2] Bergmann and Zervas, Ber. **65**, 1192 (1932).

acetate. The yield of pure 1,1-cyclobutanedicarboxylic acid melting at 156–158° is 30–34 g. (21–23 per cent of the theoretical amount).

(*B*) *Cyclobutanecarboxylic Acid.*—The above dibasic acid is placed in a 75-cc. distilling flask carrying a thermometer and attached to a 75-cc. Claisen flask as a receiver. The receiver is cooled with running water while the flask containing the dibasic acid is heated in a metal or oil bath (bath temperature, 160–170°) until no more carbon dioxide is evolved. Then the temperature of the bath is raised to 210–220°, and the material which boils at 189–195° is collected. The crude cyclobutanecarboxylic acid (19–22 g.) is redistilled from the Claisen flask in which it was collected. The pure acid boils at 191.5–193.5°/740 mm. (Note 5) and weighs 18–21 g. (18–21 per cent of the theoretical amount based on malonic ester). There is a small higher-boiling fraction, which comes over at 193.5–196°/740 mm.

2. Notes

1. The submitters and the checkers prepared the sodium ethoxide in the conventional manner. However, sodium ethoxide and sodium methoxide are very conveniently prepared by the "inverse" procedure, as described by Tishler in Fieser, "Experiments in Organic Chemistry," 2nd Ed., 1941, D. C. Heath and Company, New York, p. 385 (bottom): The metal is placed in the flask, and the alcohol is added through the condenser at such a rate that rapid refluxing is maintained. It is necessary, as a precautionary measure, to clamp the flask and not to trust to the friction between a rubber stopper and the flask to hold the flask in place. When this precaution is taken, a cooling bath may be used with safety. It is necessary to cool the flask; the metal must not be allowed to melt, as this will result in the formation of one large mass with a greatly decreased metallic surface. (Private communication, C. F. H. ALLEN.)

2. The steam distillation separates ethyl malonate and ethyl 1,1-cyclobutanedicarboxylate from ethyl pentane-1,1,5,5-tetracarboxylate, formed in a side reaction between malonic ester (2 moles) and trimethylene bromide (1 mole). The tetraethyl ester remains in the residue from the steam distillation. In several test experiments, in which about two-thirds of the amounts specified above were used, the yield of tetraethyl ester was 30–40 per cent of the theoretical amount, based upon the sodium ethoxide used.

3. If this extraction with ether is omitted the yield of 1,1-cyclobutanedicarboxylic acid is 3–4 g. less.

4. The submitters used 55 cc. of hydrochloric acid at this point; the checkers stated that this amount was insufficient to neutralize the mixture. The purpose of acidification at this point is not to liberate the cyclobutanedicarboxylic acid, but merely to remove carbonates and excess potassium hydroxide. After the carbon dioxide has been expelled, the solution is made alkaline with ammonia; hence a great excess of hydrochloric acid should be avoided. The submitters used only enough hydrochloric acid to make the solution acid to litmus. After the solution has been made basic with ammonia, barium chloride solution is added until there is no further precipitation of barium malonate.

5. This acid is quite pure. The checkers distilled 52.5 g. of it through an analytical column; except for a fore-run of 1.5–2.0 g., all the material had a constant boiling point and index of refraction.

3. Methods of Preparation

1,1-Cyclobutanedicarboxylic acid has been prepared by hydrolysis of the ethyl ester,[1] or of the half nitrile, 1-cyano-1-carboxycyclobutane.[2] The ethyl ester has been prepared by condensation of ethyl malonate with trimethylene bromide [1] or chlorobromide.[3] The half nitrile has been prepared by condensation of trimethylene bromide with ethyl cyanoacetate followed by hydrolysis of the ester to the acid.[2]

---

[1] Perkin, J. Chem. Soc. **51**, 1 (1887); Rupe, Ann. **327**, 183 (1903).

[2] Carpenter and Perkin, J. Chem. Soc. **75**, 930 (1899).

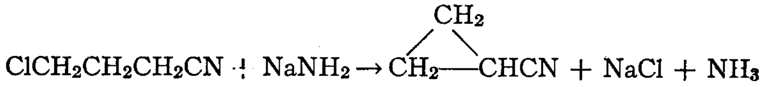
[3] Kishner, J. Russ. Phys.-Chem. Soc. **37**, 507 (1905) [Chem. Zentr. **1905**, II, 761].

Cyclobutanecarboxylic acid has been prepared by decarboxylation of the 1,1-dibasic acid,[1,4] and by decarboxylation of 1-cyano-1-carboxycyclobutane followed by hydrolysis of the cyano group.[2]

CYCLOPROPYL CYANIDE

(Cyclopropane, cyano-)

$$2Na + 2NH_3 \rightarrow 2NaNH_2 + H_2$$



$$ClCH_2CH_2CH_2CN + NaNH_2 \rightarrow \overset{CH_2}{CH_2\text{—}CHCN} + NaCl + NH_3$$

Submitted by M. J. Schlatter.
Checked by R. L. Shriner and Chris Best.

1. Procedure

The apparatus shown in Fig. 2 is assembled in a good hood. One liter of liquid ammonia and 0.5 g. of hydrated ferric nitrate are placed in the 2-l. three-necked flask A, which is equipped with a stirrer and a special reflux condenser cooled with Dry Ice. This condenser is attached to a soda-lime tower which is connected to a source of compressed air through the T-tube C. Over a period of about forty-five minutes, 92 g. (4 gram atoms) of clean sodium shavings is added to the liquid ammonia, and the mixture is stirred until the blue color disappears (one to two hours).

In the similarly equipped 5-l. three-necked flask B are placed 1.5 l. of liquid ammonia and 440 g. (4.25 moles) of γ-chlorobutyronitrile (Org. Syn. Coll. Vol. **1**, **1941**, 156). The flasks are connected by means of the 12-mm. glass tube D reaching to the bottom of the sodamide flask A and extending 1 cm. through the rubber stopper in one neck of flask B. Vigorous stirring is maintained in both flasks while the sodamide suspension is slowly forced over into the reaction flask in small portions (*Caution!* Note 1) by means of air pressure applied through C; the rate of addition is controlled by placing the finger over the bypass in the T-tube. At first the reaction is violent and only small amounts of the sodamide solution should be added. The addition is continued at such a rate that the total time required for addition of all the sodamide solution is one to one and one-half hours. The sodamide flask is rinsed with 300 cc. of liquid ammonia and the washings are added to the reaction mixture, after which stirring is continued for two hours. During the second hour, addition of Dry Ice to the reflux condenser is discontinued, and the ammonia is permitted to evaporate slowly. At the end of the two-hour stirring period, the inlet tube is replaced by a dropping funnel and 1 l. of dry ether is slowly added (Note 2). The reaction mixture is quickly filtered through a sintered glass funnel, and the filter cake is washed with two 200-cc. portions of dry ether (Note 3). The ammonia and ether are removed by distillation on a water bath through a packed column (Note 4). The residue is then distilled through the column under the pressure of a water pump (Note 5). The yield of cyclopropyl cyanide boiling at 69–70°/80 mm. (75–76°/95 mm.) is 149–152 g. (52–53 per cent of the theoretical amount based upon γ-chlorobutyronitrile) (Notes 6 and 7). The pressure is then reduced, and the unchanged

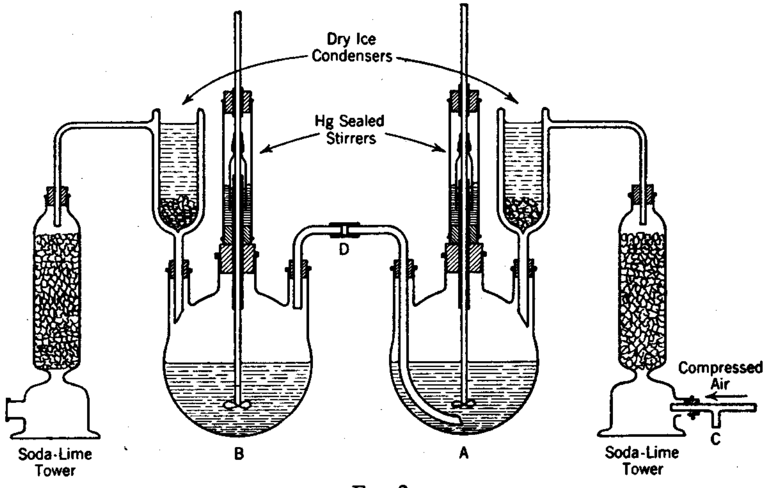


Fig. 2.

---

[4] Perkin and Sinclair, J. Chem. Soc. **61**, 40 (1892).

γ-chlorobutyronitrile is collected at 93–96°/26 mm. It amounts to 52–62 g.

2. Notes

1. The reaction is very vigorous, and addition of the sodamide solutions in large portions must be avoided. The use of stopcocks or pinch clamps to regulate the addition is not recommended.

2. Very little cyclopropyl cyanide is obtained unless the ether is added *before* complete evaporation of the ammonia.

3. The mixture may be permitted to stand at this point and the ammonia allowed to evaporate spontaneously under a hood.

4. The Carborundum column described in Org. Syn. **20,** 96, is quite satisfactory.

5. It is desirable to interpose a Dry Ice trap between the receiver and the pump in order to prevent loss of the nitrile, and too low a pressure should not be used.

6. The submitter reports that an equivalent number of moles of γ-bromobutyronitrile or a mixture of γ-chloro- and γ-bromobutyronitrile may be substituted for γ-chlorobutyronitrile. If the bromo compound is used the reaction mixture should be refluxed six hours and it is necessary to filter off the sodium bromide just before the final vacuum distillation.

7. This yield is based upon the γ-chlorobutyronitrile taken. When the recovered γ-chlorobutyronitrile (52–62 g.) is taken into account, the yield of cyclopropyl cyanide is about 60 per cent of the theoretical amount.

3. Methods of Preparation

Cyclopropyl cyanide has been prepared by the repeated distillation of γ-chlorobutyronitrile over powdered potassium hydroxide,[1,2,3,4,5] or over a mixture of sodium hydroxide and alumina.[6]

---

[1] Henry, Rec. trav. chim. **18,** 228 (1898).

[2] Dalle, Bull. acad. roy. Belg. **1902,** 36–79 [Chem. Zentr. **1902,** I, 913].

[3] Bruylants and Strassens, Bull. acad. roy. Belg. **1921,** 702–19 [C. A. **17,** 2872 (1923)].

[4] von Braun, Fussgänger, and Kühn, Ann. **485,** 210 (1925).

[5] Nicolet and Sattler, J. Am. Chem. Soc. **49,** 2068 (1927).

[6] Cloke, J. Am. Chem. Soc. **51,** 1180 (1929).

The preparation, on a small scale, of cyclopropyl cyanide from γ-chlorobutyronitrile by action of sodium in liquid ammonia, or of sodium suspended in ether, has been described.[7] The present directions are based upon those given by Schlatter.[8]

β-DI-*n*-BUTYLAMINOETHYLAMINE

(Ethylenediamine, *N,N*-dibutyl-)

$$(C_4H_9)_2NCH_2CH_2Br\cdot HBr + 2NH_3 \rightarrow (C_4H_9)_2NCH_2CH_2NH_2\cdot HBr + NH_4Br$$

$$(C_4H_9)_2NCH_2CH_2NH_2\cdot HBr + NaOH \rightarrow (C_4H_9)_2NCH_2CH_2NH_2 + NaBr + H_2O$$

Submitted by Lawrence H. Amundsen, Karl W. Krantz, and James J. Sanderson.
Checked by R. L. Shriner and John L. Rendall.

1. Procedure

A rubber tube from an inverted cylinder of liquid ammonia is attached to a glass tube which extends beneath the surface of 325 cc. of 90 per cent ethyl alcohol in a 500-cc. Erlenmeyer flask. Ammonia is passed into the alcohol until the weight increases by 41 g. (2.4 moles). The flask is cooled in ice water occasionally in order to hasten the absorption of the ammonia.

The alcoholic ammonia is added to 49 g. (0.16 mole) of di-*n*-butylaminoethyl bromide hydrobromide (Org. Syn. Coll. Vol. **2, 1943,** 92) (Note 1) in a 1-l. round-bottomed flask. The flask is stoppered tightly and allowed to stand for six days at room temperature. The solution is then transferred to an evaporating dish and stirred while it is evaporated to a crystalline paste under a hood. The crystalline paste is transferred to a 400-cc. beaker, and to it is added a solution of 16 g. of sodium hydroxide in 18 cc. of water. The solution separates into an upper layer of brown oil and a lower layer which contains a considerable amount of undissolved sodium bromide. About 10 cc. of water is added to dissolve most of the precipitate. The whole is then extracted with three 50-cc. portions of benzene. The combined extracts are placed in a 250-cc. flask over 15 g. of potassium carbonate and set aside to dry overnight.

---

[7] Cloke, Anderson, Lachman, and Smith, J. Am. Chem. Soc. **53,** 2791 (1931).

[8] Schlatter, J. Am. Chem. Soc. **63,** 1733 (1941).

The dried benzene extract is placed in a 250-cc. flask fitted with a 30-cm. fractionating column, and the benzene is removed by distillation at atmospheric pressure. Fractionation of the residue is carried out under reduced pressure using a 50-cc. Claisen flask with a built-in 12- to 15-cm. Vigreux column. The fraction boiling at 100–103°/13 mm. is collected; it weighs 11 to 14.7 g. (41–55 per cent of the theoretical amount) (Note 2).

2. Notes

1. It is not necessary to isolate the di-*n*-butylaminoethyl bromide hydrobromide. The crude di-*n*-butylaminoethyl bromide hydrobromide prepared from 405 g. (2.34 moles) of di-*n*-butylaminoethanol is taken up in 600 cc. of water, and the tarry impurities are removed by extraction with three 200-cc. portions of benzene. About 400 cc. of water is evaporated from this solution, and to it is then added 2.8 l. of alcoholic ammonia prepared from absolute ethyl alcohol; the concentration of the alcohol in the reaction mixture should be 90 per cent with respect to water. The yield is 114 g. (28 per cent of the theoretical amount based on 405 g. of the aminoethanol). The over-all yield obtained by the procedure described above is 27 per cent, based on the aminoethanol.

2. The submitter reports that diethylaminoethylamine and di-*n*-propylaminoethylamine have also been prepared by this method.

3. Method of Preparation

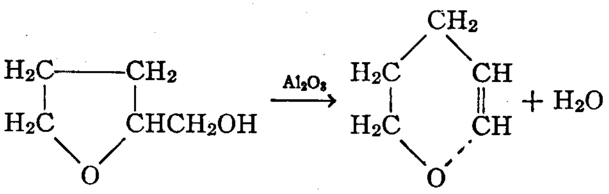
Di-*n*-butylaminoethylamine has been prepared by the action of alcoholic ammonia on di-*n*-butylaminoethyl bromide hydrobromide.[1]

---

[1] Amundsen and Krantz, J. Am. Chem. Soc. **63**, 305 (1941).

2,3-DIHYDROPYRANE

(Pyran, dihydro-)



Submitted by R. L. Sawyer and D. W. Andrus.
Checked by Nathan L. Drake and Charles M. Eaker.

1. Procedure

The reaction is carried out in a heated tube similar to that described by Herbst and Manske (Org. Syn. **16**, 47; Coll. Vol. **2, 1943,** 389) except that the receiving chamber B (*loc. cit.*, Fig. 2) does not have a side arm, and that a 10-cm. water-cooled condenser is attached to the exit end of the tube leading directly to the receiver. The tube is packed with activated alumina (Note 1) held in place at the ends by plugs of glass wool.

The furnace is heated to 300–340° (Note 2), and 204 g. (195 cc., 2 moles) of tetrahydrofurfuryl alcohol (Note 3) is introduced from the dropping funnel at the rate of 50 cc. per hour. The product, collected in an Erlenmeyer flask which contains 30 g. of anhydrous potassium carbonate, consists of a light brown oil and a lower aqueous layer. When the reaction tube has drained, the lower aqueous layer is separated and discarded. The upper layer is fractionated through a short column, and a fraction boiling at 70–86° is collected. This consists of a mixture of water and dihydropyrane, most of which distils at 83–86°. The residue (25–35 g.) is mainly unchanged tetrahydrofurfuryl alcohol (Note 4).

The water-dihydropyrane fraction separates into two layers. The lower aqueous layer is separated and discarded. The upper layer, consisting of fairly pure dihydropyrane, is dried over 5–6 g.

of anhydrous potassium carbonate, decanted, refluxed for one hour with 2–3 g. of metallic sodium, and then distilled from sodium (Note 5). The yield is 110–118 g. of dihydropyrane, boiling at 84–86° (66–70 per cent of the theoretical amount).

2. Notes

1. Several varieties of technical activated alumina were used. After three or four runs the catalyst becomes covered with a brown tar and the yield of dihydropyrane decreases. The catalyst may be regenerated by igniting it at red heat until the tar is burned off. The checkers used 8–14 mesh activated alumina from the Aluminum Ore Company of America. The catalyst was reactivated at 450° by drawing a slow stream of air through it until the tar was burned off.

2. The temperature of the furnace is measured by a thermometer placed alongside the glass tube inside the furnace. The temperature should be 330–340° except in the regions about 10 cm. from each end of the furnace; here the temperatures will be 300–340°, depending on the construction of the furnace.

3. According to the submitters, Eastman's practical grade of tetrahydrofurfuryl alcohol must be purified by distillation; the fraction boiling at 79–80°/20 mm. was used. The checkers used, without purification, tetrahydrofurfuryl alcohol obtained from the Quaker Oats Company. The yields were equally good.

4. The recovered tetrahydrofurfuryl alcohol turns yellow on standing and is unsuitable for further runs. If it is used, the yield of dihydropyrane drops to 36–38 per cent, and the catalyst must be regenerated after each run.

5. Dihydropyrane is very difficult to dry. Even after this treatment the product often contains traces of water.

3. Methods of Preparation

The procedure given above is essentially the method of Paul.[1] The interaction of tetrahydrofurfuryl bromide and sodium amide gives chiefly 1,4-epoxy-4-pentene and a small amount of dihydropyrane. 1,4-Epoxy-4-pentene will undergo rearrangement at 380° in the presence of alumina to yield dihydropyrane.[2]

---

[1] Paul, Bull. soc. chim. (4) **53**, 1489 (1933).

[2] Paul, Bull. soc. chim. (5) **2**, 745 (1935).

β,β-DIMETHYLACRYLIC ACID

(Senecioic acid)

$$(CH_3)_2C{=}CHCOCH_3 + 3KOCl \rightarrow (CH_3)_2C{=}CHCO_2K + CHCl_3 + 2KOH$$

$$2(CH_3)_2C{=}CHCO_2K + H_2SO_4 \rightarrow 2(CH_3)_2C{=}CHCO_2H + K_2SO_4$$

Submitted by Lee Irvin Smith, W. W. Prichard, and Leo J. Spillane.
Checked by Nathan L. Drake and Harry D. Anspon.

1. Procedure

A 5-l. round-bottomed three-necked flask is equipped with a Kyrides sealed stirrer (Org. Syn. **21**, 40, Note 1) and two long condensers, and the apparatus is so arranged that, if necessary, the exit water from the condensers may be quickly used to cool the flask.

In the flask are placed 200 cc. of dioxane, 100 g. (1.02 moles) of mesityl oxide, and a solution of 4.6 moles of potassium hypochlorite in 3 l. of water (Note 1), and the stirrer is started. The mixture becomes warm immediately, and within five minutes chloroform begins to reflux. When the reaction becomes very vigorous the stirrer is stopped and the flask is cooled with running water (Note 2). The stirring is resumed as soon as feasible and is continued for three or four hours, when the temperature of the mixture will have dropped to that of the room. Sodium bisulfite (about 5 g.) is then added to react with the excess hypochlorite (Note 3).

One of the condensers is then replaced by a dropping funnel, and enough 50 per cent sulfuric acid (about 200 cc.) is added, with stirring and cooling, to make the solution acid to Congo red paper. When the solution has cooled, it is extracted with eight 400-cc. portions of ether (Note 4). The ether extract is *carefully* distilled on a steam bath until the ether and chloroform are removed.

The residue is then placed in a modified Claisen flask (Org. Syn. **22,** 11) and distilled under reduced pressure. Dimethylacrylic acid distils at 100–106°/20 mm. The yield of white solid is 49–53 g. (49–53 per cent of the theoretical amount). This product melts at 60–65°. It may be further purified by recrystallization from petroleum ether (b.p., 60–70°) or water (Note 5).

2. Notes

1. The hypochlorite is prepared according to Org. Syn. **17,** 66; Coll. Vol. **2, 1943,** 429, Note 2. It is cooled to 10° before it is placed in the flask.

2. The flask is cooled only as much as is necessary to keep the chloroform refluxing gently. After a half hour the reaction will have subsided enough so that no further cooling is necessary.

3. When a few cubic centimeters of the solution no longer liberate iodine from a slightly acid potassium iodide solution, enough sodium bisulfite has been added.

4. It is important that the ether be *well shaken* with the solution during the extractions.

5. For recrystallization from water, 48–50 g. of the acid is dissolved in 450 cc. of hot water. The solution is cooled in ice for several hours, and the crystalline precipitate is filtered with suction and dried overnight in a desiccator. The yield of pure dimethylacrylic acid melting at 66–67.5° is 35–40 g., a recovery of 70–83 per cent.

3. Methods of Preparation

This acid has been prepared from various α-haloisovaleric acid derivatives by elimination of the halogen together with one of the β-hydrogen atoms;[1,2,3,4] from β-hydroxyisovaleric acid derivatives by elimination of water;[5,6,7,8] by the action of sodium isobutoxide on iodoform;[9] by the condensation of malonic acid with acetone;[10,11,12] by the action of alkali upon 2,4-dibromo-2-methylbutanone;[13] by the incomplete ozonolysis of phorone;[14] by the action of alcoholic potassium hydroxide upon 2,5,5,7-tetramethylocta-2,6-diene-4-one;[15] by the action of aluminum chloride on α,α-dimethylsuccinic anhydride;[16] by condensation of acetoacetic ester with acetone and action of barium hydroxide upon the product, isopropylideneacetoacetic ester;[17] and by the action of hypohalites on mesityl oxide.[18,19,20]

---

[1] Duvillier, Compt. rend. **88**, 913 (1879); Ann. chim. phys. (5) **19**, 428 (1880); Bull. soc. chim. (3) **3**, 507 (1890); (3) **5**, 848 (1891).

[2] Weinig, Ann. **280**, 252 (1894).

[3] Perkin, J. Chem. Soc. **69**, 1470 (1896).

[4] Sernow, J. Russ. Phys. Chem. Soc. **32**, 804 (1900) [Chem. Zentr. **1901**, **I**, 665].

[5] Friedmann, Beitr. Chem. Physiol. Path. **11**, 374 (1908) [C.A. **4**, 3094 (1910)].

[6] Semljanitzin and Saytzeff, Ann. **197**, 72 (1879).

[7] v. Miller, Ann. **200**, 261 (1880).

[8] Neubauer, Ann. **106**, 63 (1858).

[9] Gorbow and Kessler, Ber. **17**, Ref. 67 (1884); **20**, Ref. 776 (1887).

[10] Dutt, J. Indian Chem. Soc. **1**, 297 (1924).

[11] Massot, Ber. **27**, 1225 (1894).

[12] Knoevenagel, Chem. Zentr. **1905**, **II**, 726.

[13] Favorski and Wanscheidt, J. prakt. Chem. (2) **88**, 665 (1913).

[14] Harries and Türk, Ann. **374**, 347 (1910).

[15] Deux, Compt. rend. **208**, 522 (1939).

[16] Desfontaines, Compt. rend. **134**, 293 (1902).

[17] Pauly, Ber. **30**, 481 (1897).

[18] Kohn, Monatsh. **24**, 770 (1903).

[19] Barbier and Leser, Bull. soc. chim. (3) **33**, 815 (1905).

[20] Cuculescu, Bull. Fac. Stiinte Cernauti **1**, 53 (1927) [C. A. **26**, 1897 (1932)].

β-DIMETHYLAMINOPROPIOPHENONE HYDROCHLORIDE

(Propiophenone, β-dimethylamino-)

$$C_6H_5COCH_3 + CH_2O + (CH_3)_2NH_2Cl \rightarrow C_6H_5COCH_2CH_2N(CH_3)_2 \cdot HCl + H_2O$$

Submitted by Charles E. Maxwell.
Checked by C. F. H. Allen and J. Van Allan.

1. Procedure

In a 500 cc. round-bottomed flask attached to a reflux condenser are placed 60 g. (58.5 cc., 0.5 mole) of acetophenone (Note 1), 52.7 g. (0.65 mole) of dimethylamine hydrochloride, and 19.8 g. (0.22 mole) of paraformaldehyde. After the addition of 1 cc. of concentrated hydrochloric acid (sp. gr. 1.19) in 80 cc. of 95 per cent ethyl alcohol, the mixture is refluxed on a steam bath for two hours (Note 2). The yellowish solution is filtered, if it is not clear (Notes 3 and 4), and is transferred to a 1-l. wide-mouthed Erlenmeyer flask. While still warm, it is diluted by the addition of 400 cc. of acetone (Note 5), allowed to cool slowly to room temperature, and then chilled overnight in the refrigerator. The large crystals are filtered and washed with 25 cc. of acetone. After it has been dried for two and one-half hours at 40–50°, this crude product weighs 72–77 g. (68–72 per cent of the theoretical amount) and melts at 138–141° (Notes 6 and 7); it is suitable for many reactions.

It may be recrystallized by dissolving it in 85–90 cc. of hot 95 per cent ethyl alcohol and slowly adding 450 cc. of acetone to the solution. The recovery is about 90 per cent. The purified material, dried at 70°, melts at 155–156° (Notes 8 and 9).

2. Notes

1. Acetophenone, m.p. 19–20°, and a practical grade of dimethylamine hydrochloride were used.

2. The reaction mixture, which at first forms two layers, soon becomes homogeneous, and the paraformaldehyde dissolves.

3. The filtration must be done rapidly, preferably through a preheated funnel. Any material which crystallizes in the receiver is brought into solution again by warming on the steam bath.

4. Alternatively, the reaction mixture may be cooled at once and the solid product removed. The filtrate is successively concentrated and chilled three times, each crop of crystals being rinsed with acetone. For example, in a run using 480 g. of acetophenone, the amounts obtained were 297, 92, 53, and 16 g. respectively, and 42 g. from the acetone washings, making a total of 500 g. or 66 per cent of the theoretical amount.

5. The excess dimethylamine hydrochloride is held in solution by the acetone.

6. The material is somewhat hygroscopic and holds traces of water tenaciously. The melting point is lowered by the presence of moisture; a preliminary shrinking is usually observed.

7. After it has been dried for an additional four hours, the product melts at 152–153°. The product melts at this same temperature after it has been kept for sixty hours in a vacuum desiccator, except that then there is no preliminary shrinking.

8. These directions are applicable equally well for runs of larger size.

9. The diethylamino homolog results when diethylamine hydrochloride is used.

3. Method of Preparation

The procedure described is an example of a general reaction,[1,2] the Mannich reaction, a review of which, from the experimental point of view, has recently been published.[3]

[1] Mannich and Heilner, Ber. 55, 359 (1922).

[2] Blicke and Burckhalter, J. Am. Chem. Soc. 64, 453 (1942).

[3] Blicke, Organic Reactions 1, 303 (1942), New York, John Wiley & Sons.

β-ETHOXYETHYL BROMIDE

(Ethane, 1-bromo-2-ethoxy-)

$$3C_2H_5OCH_2CH_2OH + PBr_3 \rightarrow 3C_2H_5OCH_2CH_2Br + P(OH)_3$$

Submitted by GEORGE C. HARRISON and HARVEY DIEHL.
Checked by R. L. SHRINER and C. H. TILFORD.

1. Procedure

IN a 2-l. three-necked flask, fitted with a mechanical stirrer (Note 1), a reflux condenser, and a dropping funnel, is placed 630 g. (670 cc., 7 moles) of β-ethoxyethyl alcohol (Note 2). The stirrer is started, and 600 g. (210 cc., 2.2 moles) (Note 3) of phosphorus tribromide is added from the dropping funnel over a period of one and one-half to two hours. The temperature is permitted to rise until the reaction mixture refluxes gently.

The mixture is then distilled, and the distillate boiling below 150° is collected in a 2-l. flask containing 1 l. of water. The lower layer of crude β-ethoxyethyl bromide is separated and dried over 10 g. of calcium chloride. The liquid is decanted and distilled through a 25-cm. fractionating column, and the fraction boiling at 125–127°/760 mm. is collected (Note 4). The yield of pure product is 660–670 g. (65–66 per cent of the theoretical amount based on the phosphorus tribromide).

2. Notes

1. A rubber sleeve lubricated with a drop of oil provides an effective seal for the stirrer.

2. Technical β-ethoxyethyl alcohol is marketed commercially as Cellosolve; it should be dried over calcium oxide and distilled.

3. A slight excess of β-ethoxyethyl alcohol gives the best results.

4. The first fraction, boiling at 38–40°, is ethyl bromide, and it weighs 120–130 g. Lower yields (56–59 per cent) of β-ethoxyethyl bromide are obtained by distillation without a fractionating column. The residue, however, should not be overheated, for at high temperatures phosphorous acid decomposes to give phosphine and perhaps even elementary phosphorus, and then, when air is admitted to the apparatus, an explosion may occur. A minor explosion in connection with this preparation has been reported (N. L. DRAKE, private communication), and a similar situation has been observed in reactions with phosphorus trichloride.[1]

3. Methods of Preparation

β-Ethoxyethyl bromide has been prepared by the action of sodium ethoxide upon ethylene bromide;[2] by the action of bromine upon β-ethoxyethyl iodide;[3] and by the procedure adopted here, which was first used by Chalmers.[4] The action of sodium bromide and sulfuric acid on β-ethoxyethyl alcohol cleaves the ether linkage.

β-ETHOXYPROPIONITRILE

(Propionitrile, β-ethoxy-)

$$C_2H_5OCH_2CH_2Br + NaCN \rightarrow C_2H_5OCH_2CH_2CN + NaBr$$

Submitted by GEORGE C. HARRISON and HARVEY DIEHL.
Checked by R. L. SHRINER amd C. H. TILFORD.

1. Procedure

IN a 3-l. three-necked flask, equipped with a Hershberg stirrer (Org. Syn. **17**, 31; Coll. Vol. **2**, **1943**, 117), a reflux condenser, and a dropping funnel, are placed 175 g. (3.6 moles) of sodium cyanide and 125 cc. of distilled water (Note 1). The mixture is stirred until the sodium cyanide is dissolved, and then, while vigorous stirring is continued, 535 g. (360 cc., 3.5 moles) of β-ethoxyethyl bromide (p. 32) in 260 cc. of 95 per cent ethyl alcohol is added over a period of fifteen minutes. The separatory funnel is replaced by a 360° thermometer, and the mixture is stirred and gently refluxed for ten hours.

---

[1] Coghill, J. Am. Chem. Soc. **60**, 488 (1938); see also Org. Syn. Coll. Vol. **2**, **1943**, Note 5, p. 40.

[2] Foran, J. Soc. Chem. Ind. **44**, 173–4 (1925).

[3] Henry, Jahresb. **1885**, 1163.

[4] Chalmers, Can. J. Research **7**, 464–471 (1932).

The mixture is then fractionally distilled until the temperature reaches 140°. The first fraction boiling at 75–95° consists mostly of alcohol and water, and is discarded. The fraction boiling between 95° and 140° contains water and 25–30 g. of β-ethoxypropionitrile. This is extracted twice with 50-cc. portions of benzene, and the benzene extracts are added to the cooled residue in the distilling flask. The mixture is filtered (Note 2), the solid material is washed with 75 cc. of benzene, which is added to the filtrate, and the whole is distilled. The fraction boiling at 169–174° is collected; it weighs 178–200 g. (52–58 per cent of the theoretical amount).

2. Notes

1. The reaction should be carried out under the hood.

2. Direct distillation without filtration may result in clogging the condenser by ammonium bromide.

3. Method of Preparation

β-Ethoxyethyl cyanide has been prepared by the action of potassium cyanide on β-ethoxyethyl bromide.[1]

---

[1] Henry, Bull. soc. chim. (2) **44**, 458 (1885).

ETHYL BENZOYLACETATE

(Acetic acid, benzoyl-, ethyl ester)

$$CH_3COCH_2CO_2C_2H_5 + C_2H_5ONa \rightarrow [CH_3COCHCO_2C_2H_5]Na + C_2H_5OH$$

$$[CH_3COCHCO_2C_2H_5]Na + C_6H_5CO_2C_2H_5 \rightarrow [C_6H_5COCHCO_2C_2H_5]Na + CH_3CO_2C_2H_5$$

$$[C_6H_5COCHCO_2C_2H_5]Na + H_2SO_4 \rightarrow C_6H_5COCH_2CO_2C_2H_5 + NaHSO_4$$

Submitted by S. M. McElvain and K. H. Weber.
Checked by R. L. Shriner and C. H. Tilford.

1. Procedure

A 2-l. three-necked flask is mounted on a steam bath and fitted with a reflux condenser, a separatory funnel, and an efficient sealed stirrer. In the flask is placed 600 cc. of absolute alcohol, and to this is added gradually 46 g. (2 gram atoms) of clean sodium cut into small pieces.[1] The sodium ethoxide solution is stirred and cooled to room temperature, after which 267 g. (260 cc., 2.05 moles) of ethyl acetoacetate (Note 1) is added slowly through the separatory funnel. The reflux condenser is then replaced by a short still head, and the alcohol is removed by distillation at approximately room temperature and under the pressure of a water pump. When approximately half the alcohol has been removed, sufficient sodium enolate precipitates so that stirring has to be discontinued. When the residue appears dry (after about two hours) the last traces of alcohol are removed by heating for an hour on the steam bath under a pressure of 2 mm. The flask is allowed to cool to room temperature under reduced pressure.

To the cooled residue of sodium enolate is added 600 g. (570 cc., 4 moles) of ethyl benzoate. The steam bath is replaced by an oil bath, and the temperature of the bath is raised to 140–150° and maintained there for six hours. Then, over a period of another hour, the temperature of the bath is gradually raised to 180° (Note 2). The distillate that is collected during this period of heating amounts to 200–210 g. and consists chiefly of ethyl acetate and ethyl alcohol.

---

[1] For a more convenient method of preparing sodium ethoxide, see Note 1, p. 18.

The reaction mixture is cooled, 250 cc. of water is added, and the mixture is made acid to litmus by addition of a cooled solution of 100 g. of concentrated sulfuric acid in 200 cc. of water. Chipped ice is added if necessary to keep the mixture cool. The upper ester layer is separated, and the aqueous layer is extracted with 200 cc. of ether. The combined ether and ester layers are shaken with 350 cc. of a saturated sodium bicarbonate solution until no more carbon dioxide is evolved, and then the organic layer is washed with 200 cc. of water. The water layer is combined with the sodium bicarbonate solution and extracted with 400 cc. of ether. The combined ether and ester layers are dried over sodium sulfate. The ether is removed by distillation on the steam bath, and the excess ethyl benzoate and acetoacetic ester (Note 3) are then removed by distillation under reduced pressure through a 15-cm. fractionating column. Finally, the ethyl benzoylacetate is distilled (Note 3) at 101–106°/1 mm. (130–135°/3 mm.). The yield of ester boiling over a 5° range is 190–210 g. (50–55 per cent of theoretical amount based on the ethyl acetoacetate).

2. Notes

1. Commercial ethyl acetoacetate was distilled, and the fraction boiling at 68–69°/11 mm. was used.

2. During the last hour of heating about 20 g. of the ethyl acetate-alcohol mixture distilled.

3. A mixture of ethyl acetoacetate and ethyl benzoate (100–150 g.) was collected at 75–90°/12 mm., after which 250–300 g. of pure ethyl benzoate, b.p. 90–93°/12 mm., was recovered. These products were removed through a 15-cm. fractionating column. The remaining ethyl benzoylacetate was distilled through a short still head without a fractionating column.

3. Methods of Preparation

Methods of preparation are given in Org. Syn. **18,** 33; Coll. Vol. **2, 1943, 266.**

ETHYL BROMOACETATE

(Acetic acid, bromo-, ethyl ester)

$$CH_3COOH + Br_2 \xrightarrow[(CH_3CO)_2O]{\text{Pyridine}} BrCH_2COOH + HBr$$

$$BrCH_2COOH + C_2H_5OH \xrightarrow{H_2SO_4} BrCH_2COOC_2H_5 + H_2O$$

Submitted by Samuel Natelson and Sidney Gottfried.
Checked by Nathan L. Drake and Stuart Haywood.

1. Procedure

(*A*) *Bromoacetic Acid.*—(Note 1) A mixture of 1 l. (17.5 moles, excess) of glacial acetic acid, 200 cc. of acetic anhydride, and 1 cc. of pyridine is placed in a 3-l. flask fitted with a dropping funnel and a reflux condenser, the end of which is protected with a drying tube (Note 2); the tip of the dropping funnel should reach below the level of the liquid. Some glass beads are added, and the mixture is heated to boiling. The flame is then removed, approximately 1 cc. of bromine is added, and the reaction is allowed to proceed until the liquid becomes colorless (Note 3). Then the remainder of 1124 g. (360 cc., 7.03 moles) of bromine (Note 4) is added as rapidly as it will *react* (Note 5); during this period (about two and one-half hours), the acid is kept boiling *gently* by means of a flame. After about half the bromine has been added, the liquid assumes a cherry color which is retained throughout the remainder of the bromination. After all the bromine has been added, the mixture is heated until it becomes colorless.

The mixture is allowed to cool, and 75 cc. of water is added slowly to destroy the acetic anhydride. Excess acetic acid and water are now removed on a boiling water bath under a pressure of approximately 35 mm. When the evaporation is complete, the residue will crystallize on cooling; this residue, which is almost pure bromoacetic acid, weighs 845–895 g. (Note 6).

(*B*) *Ethyl Bromoacetate.*—For the esterification, an apparatus similar to that used in the preparation of anhydrous oxalic acid (Org. Syn. Coll. Vol. **1, 1941,** 422) may be used, but with the outlets from the trap reversed so that the lighter liquid returns to the mixture and the heavier liquid (water) is drawn off at the bottom. A somewhat simpler apparatus may be built using the water trap shown in Fig. 3 (Note 7). The crude bromoacetic acid is placed in a 3-l. flask, together with 610 cc. of alcohol (9.9 moles, excess) and 950 cc. of benzene. About 1.5 cc. of concentrated sulfuric acid is added to hasten the reaction (Note 8), and the mixture is refluxed on a boiling water bath while the water is separated and measured. Approximately 296 cc. of liquid (whose composition is approximately 50 per cent alcohol and water) separates from the benzene; this includes all the water formed in the reaction, together with the excess alcohol. When no more water separates from the benzene, 75 cc. of alcohol is added to the reaction mixture and heating is continued for thirty minutes. If the reaction has been completed, there will not be a second phase in the distillate. The end of the reaction is also indicated when the benzene flowing through the side tube becomes clear and the rate of refluxing decreases considerably. At this point, 150 cc. of benzene is condensed and removed through the trap.

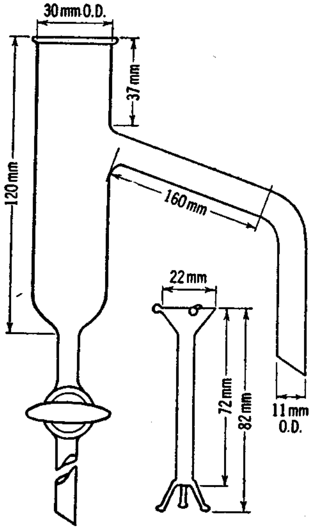


FIG. 3.

The mixture is transferred to a separatory funnel and washed once with 1.5 l. of water, once with 1.5 l. of 1 per cent sodium bicarbonate solution, and finally with 1.5 l. of water. It is then dried over anhydrous sodium sulfate and fractionated at atmospheric pressure from an oil bath using a Vigreux column 1 foot in length (Note 9). The fraction boiling at 154–155°/759 mm. is collected (Note 10). The yield is approximately 818 g. (65–70 per cent of the theoretical amount).

2. Notes

1. The vapors of ethyl bromoacetate are extremely irritating to the eyes. Care should be taken to keep the material in closed containers and to manipulate it in open vessels only in a good hood.

2. An all-glass apparatus is advisable. If it is not available, one-holed asbestos stoppers may be made by soaking strips of asbestos in water, wrapping them around pieces of glass tubing of suitable size until the desired diameter has been reached, and then allowing them to dry at 110°.

3. At the beginning there is a lag of about ten minutes before the reaction starts and the color of the bromine disappears.

4. If C.P. bromine is available it may be used directly. Technical bromine should be dried with concentrated sulfuric acid.

5. The bromine should not be added so rapidly that loss occurs through the condenser.

6. Pure bromoacetic acid may be obtained by distillation of this crude product from a Claisen flask immersed in an oil bath and fitted with an 8-inch insulated Vigreux column. The fraction boiling at 108–110°/30 mm. is collected. The yield is 775–825 g. (80–85 per cent of the theoretical amount).

7. The trap shown in Fig. 3 is a modification of the moisture trap designed by Dean and Stark.[1] The dimensions may be varied to suit individual purposes, for the size is largely a matter of convenience. The trap may be used without the inner funnel, but with this funnel (C. F. Koelsch, private communication) the condensate separates into two layers rapidly and completely, and

---

[1] Dean and Stark, Ind. Eng. Chem. **12,** 486 (1920).

the liquid falling from the condenser does not agitate the two phases in the trap. The funnel tube must be of such a length that the top of the funnel is above the side arm of the trap. The tube of the trap may be graduated, but this is not necessary. Suitable traps are listed in the catalog of Pyrex glassware, supplement 1, August 20, 1942, p. 4, items 3582 and 3622.

8. In the absence of a catalyst the reaction proceeds more slowly and smaller yields are obtained. Phosphoric acid may be substituted for sulfuric acid, but the use of sulfuric acid results in the best yield in the shortest time.

9. If a fractionating column is not used, as much as 15–20 per cent of the product may be lost in the fore-run.

10. The fraction boiling over a one-degree range is collected. The boiling point has been observed to range from 154–155° to 158–159° on different days.

3. Methods of Preparation

Bromoacetic acid has been prepared by direct bromination of acetic acid at elevated temperatures and pressures,[2,3,4] or with dry hydrogen chloride as a catalyst;[5] and with red phosphorus as a catalyst with the formation of bromoacetyl bromide.[6,7,8,9,10] Bromoacetic acid has also been prepared from chloroacetic acid and hydrogen bromide at elevated temperatures;[6] by oxidation of ethylene bromide with fuming nitric acid;[7] by oxidation of an alcoholic solution of bromoacetylene by air;[8] and from ethyl α,β-dibromovinyl ether by hydrolysis.[9] Acetic acid has been converted into bromoacetyl bromide by action of bromine in the presence of red phosphorus, and ethyl bromoacetate has been obtained by action of alcohol upon the acid bromide.[10,11,12,13,14] Ethyl bromoacetate has also been prepared by direct bromination of ethyl acetate at elevated temperatures;[15,16] by action of alcohol upon bromoacetic anhydride;[17] by action of phosphorus tribromide upon ethyl glycollate;[18] and by action of hydrogen bromide upon ethyl diazoacetate.[19] The method described above is based upon the procedure of Natelson and Gottfried.[20]

[2] Perkin and Duppa, Ann. **108**, 106 (1858).

[3] Michael, Am. Chem. J. **5**, 202 (1883).

[4] Hell and Muhlhauser, Ber. **11**, 241 (1878); **12**, 735 (1879).

[5] Lapworth, J. Chem. Soc. **85**, 41 (1904).

[6] Demole, Ber. **9**, 561 (1876).

[7] Kachler, Monatsh. **2**, 559 (1881).

[8] Gloeckner, Ann. Suppl. **7**, 115 (1870).

[9] Imbert and Konsort. Electrochem. Ind., Ger. pat. 216,716 [Frdl. **9**, 28 (1908–10); C. A. **4**, 952 (1910)].

[10] Ward, J. Chem. Soc. **121**, 1161 (1922).

[11] Naumann, Ann. **129**, 268 (1864).

[12] Auwers and Bernhardi, Ber. **24**, 2218 (1891).

[13] Lassar-Cohn, Ann. **251**, 341 (1889).

[14] Volhard, Ann. **242**, 161 (1887).

[15] Crafts, Compt. rend. **56**, 707 (1863); Ann. **129**, 50 (1864).

[16] Schutzenberger, Ber. **6**, 71 (1873).

[17] Gal, Compt. rend. **71**, 274 (1870).

[18] Henry, Ann. **156**, 176 (1870).

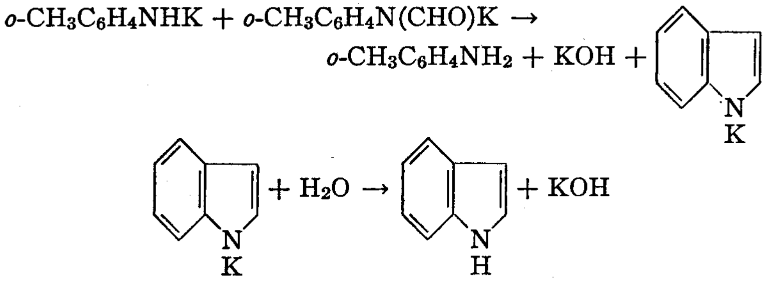
[19] Curtius, J. prakt. Chem. (2) **38**, 430 (1888).

[20] Natelson and Gottfried, J. Am. Chem. Soc. **61**, 970 (1939).

INDOLE

$$o\text{-}CH_3C_6H_4NHCHO + (CH_3)_3COK \rightarrow o\text{-}CH_3C_6H_4N(CHO)K + C_4H_9OH$$

$$o\text{-}CH_3C_6H_4N(CHO)K \rightarrow o\text{-}CH_3C_6H_4NHK + CO$$



Submitted by F. T. Tyson.
Checked by R. L. Shriner and C. H. Tilford.

1. Procedure

A 2-l. three-necked round-bottomed flask is fitted with a reflux condenser and a glass inlet tube connected to a cylinder of nitrogen. The third opening of the flask is closed by a stopper. The top of the condenser is connected to an air trap which consists of two 500-cc. suction flasks joined in series. The first suction flask is empty; the second contains 100 cc. of paraffin oil, and the inlet tube of this flask extends slightly below the surface of the oil.

In the reaction flask is placed 600 cc. of commercial *tert.*-butyl alcohol (Note 1), and the air in the flask is displaced by dry nitrogen gas. Then 29 g. (0.75 gram atom) of metallic potassium is added, in portions, to the alcohol. The mixture is heated on a water bath until all the potassium has dissolved, and then 68 g. (0.5 mole) of *o*-formotoluide (Note 2) is added and brought into solution. The condenser is set for distillation with a filter flask as the receiver; this flask is protected from the air by connecting it to the trap used in the initial operation. The reaction flask is surrounded by a metal bath, and the excess alcohol is removed by distillation. The residue is heated to 350–360° for about twenty minutes (Note 3) and then is allowed to cool in a stream of nitrogen. The residue is decomposed by addition of 300 cc. of water, and the mixture is steam-distilled to remove the indole. The distillate is extracted successively with 300 cc. and 100 cc. of ether, and the combined ether extracts are shaken with cold dilute 5 per cent hydrochloric acid to remove small amounts of *o*-toluidine. The ether extract is washed with 100 cc. of water, followed by 100 cc. of 5 per cent sodium carbonate solution, and is dried over 20 g. of sodium sulfate. The ether is removed by distillation, and the residue is distilled under reduced pressure. Indole distils at 142–144°/27 mm. (128°/10 mm.; 121°/5 mm.) as a pale yellow oil which solidifies and then melts at 52–53°. The yield is 23 g. (79 per cent of the theoretical amount) (Note 4).

2. Notes

1. Alcohols other than *tert.*-butyl alcohol, such as methyl, ethyl, butyl, or isobutyl alcohol, may be used, but with a decrease in yield. If methyl or ethyl alcohol is substituted for *tert.*-butyl alcohol, the potassium should be added in smaller portions and the more vigorous reaction must be controlled by external cooling. Furthermore, if methyl alcohol is used the amount of potassium should be decreased from 0.75 gram atom to 0.5 gram atom.

2. *o*-Formotoluide can be prepared by heating a mixture of 856 g. (8 moles) of *o*-toluidine and 403 g. (8.4 moles) of 90 per cent formic acid on a steam bath for about three hours and allowing the reaction mixture to stand overnight. The mixture is fractionated under reduced pressure; there is obtained 920–963 g. (85–89 per cent of the theoretical amount) of *o*-formotoluide, b.p. 173–5°/25 mm., m.p. 55–58°. This product is a pale yellow solid which contains traces of toluidine and possesses an odor indicating the presence of traces of an isocyanide. However, the material is sufficiently pure for conversion to indole. By use of 99 per cent formic acid, a quantitative yield may be obtained. If a purer product is desired, the original reaction mixture is mixed

with about a liter of water, the crude formotoluide is filtered, washed with 1 per cent hydrochloric acid and with water. After drying, the crude formotoluide is recrystallized from benzene-petroleum ether. The yield is practically the same as that obtained by direct distillation, and the product melts at 61°. In order to assure freedom from moisture, the recrystallized product may be distilled under reduced pressure; the loss in this distillation is negligible.

3. During this interval combustible gases, chiefly carbon monoxide and hydrogen, are evolved, and a liquid, which is principally *o*-toluidine, distils.

4. The product is pale yellow. The color may be removed by crystallizing the material from a mixture of 100 cc. of petroleum ether and about 10 cc. of ethyl ether. The recovery is 21 g. (91 per cent).

3. Methods of Preparation

Indole has been obtained through many syntheses which have little value as methods of preparation. In addition to these syntheses it has been prepared by heating 2-amino-ω-chlorostyrene with sodium methoxide;[1] by pyrolysis of 2,2′-diaminostilbene hydrochloride under reduced pressure;[2] by reduction of indoxyl with zinc dust and alkali;[3] by reduction of 2-aminoindole with sodium and alcohol;[4] by reduction of 2-nitrophenylacetaldehyde;[5] by heating *o*-formylphenylglycine with acetic anhydride and sodium acetate;[6] by passing a mixture of acetylene and aniline through an iron tube at 700°;[7] and by reduction of ω,2-dinitrostyrene with iron and acetic acid.[8] The method described above is related to the Madelung synthesis of 2-alkylindoles,[9] and has been published.[10] The methods for preparation of indole have recently been examined experimentally.[11] The authors recommend the method of Reissert,[12] which involves condensation of *o*-nitrotoluene with ethyl oxalate, followed by reduction to indole-2-carboxylic acid and decarboxylation of the latter.

[1] Lipp, Ber. **17**, 1072 (1884).

[2] Thiele, Ber. **28**, 1413 (1895).

[3] Vorländer, Ber. **37**, 1134 (1904).

[4] Pschorr, Ber. **43**, 2550 (1910).

[5] Weerman, Ann. **401**, 12 (1913).

[6] Gluud, Ber. **48**, 422 (1915).

[7] Majima, Ber. **55**, 3854 (1922).

[8] Nenitzescu, Ber. **58**, 1063 (1925).

[9] Madelung, Ber. **45**, 1130 (1912); cf. Verley, Bull. soc. chim. (4) **35**, 1039 (1924).

[10] Tyson, J. Am. Chem. Soc. **63**, 2024 (1941).

[11] Shorygin and Polyakova, C. A. **36**, 3802 (1942).

[12] Reissert, Ber. **30**, 1045 (1897).

KETENE DIETHYLACETAL

(Ketene, diethyl ketal)

$$\mathrm{BrCH_2CH(OC_2H_5)_2 + (CH_3)_3COK \rightarrow CH_2{=}C(OC_2H_5)_2 + KBr + (CH_3)_3COH}$$

Submitted by S. M. McElvain and D. Kundiger.
Checked by R. L. Shriner and C. H. Tilford.

1. Procedure

In a 2-l. round-bottomed flask, preferably fitted with an interchangeable ground-glass joint, are placed 650 g. (820 cc.) of absolute *tert.*-butyl alcohol (Note 1) and 39.1 g. (1 gram atom) of potassium (Note 2). A reflux condenser is attached to the flask and the mixture is refluxed until all the potassium is dissolved (about eight hours). The solution is allowed to cool slightly, and 198 g. (1 mole) of bromoacetal (p. 8), together with some boiling-chips (Note 3), is quickly added. A cream-colored precipitate of potassium bromide begins to deposit immediately. The flask is attached at once to a closely indented 46-cm. Vigreux column, equipped with a glass insulating jacket and a total reflux, partial take-off still head[1] (Note 4), and the *tert.*-butyl alcohol is distilled from an oil bath (about 120–130°) at the rate of 25 drops per minute with a reflux ratio at the still head of about 6 : 1. This operation requires sixteen to eighteen hours (Note 5), and at the

---

KETENE DIETHYLACETAL

[1] Whitmore and Lux, J. Am. Chem. Soc. **54**, 3451 (1932).

end of this time the temperature of the oil bath is raised to 160° and maintained there until no more alcohol comes over. The bath is then lowered and allowed to cool while the pressure within the fractionating system is very gradually reduced to 200 mm. and held there by a barostat (Note 6).

A small amount of the alcohol comes over at 51–52°/200 mm and then, after the heating bath is replaced, 4–6 cc. of an intermediate fraction distils. This is followed by a fraction which boils at 83–86°/200 mm. and which is collected as pure ketene acetal. A total of 78–87 g. is obtained (67–75 per cent of the theoretical amount). The major portion is collected while the temperature of the bath is 120–140°, and the remainder is obtained by raising the bath temperature to 170–180°.

Ketene acetal is best stored in a bottle made of alkaline glass which is preferably new and dusted with sodium *tert.*-butoxide (Note 7). The glass stopper should be very well greased. Even with these precautions a small amount of a voluminous precipitate of the white polymer will develop.

2. Notes

1. The *tert.*-butyl alcohol is refluxed over quicklime, distilled, and then redistilled over 1 g. of potassium per 100 g. of the alcohol. Improved yields of ketene acetal are obtained from *tert.*-butyl alcohol that has been recovered from a previous preparation of the acetal.

2. The potassium should be cut into pieces sufficiently small to pass through the neck of the flask. Sodium in *tert.*-butyl alcohol can be used, but it is necessary to carry out the subsequent reaction at 125° in sealed tubes. The amount of *tert.*-butyl alcohol specified is sufficient to provide for complete solution of the potassium as the *tert.*-butoxide.

3. An ebullator tube through which dry nitrogen was drawn has been used for the subsequent distillation under reduced pressure, but it is far more advantageous to use about six boiling-chips. Because of its rapid reaction with water, ketene acetal must be protected from moisture of the air.

4. The still head described by Whitmore and Lux [1] is most satisfactory for controlling this distillation. The tube leading from the take-off of the column is attached to the receiver through a fraction cutter protected from moisture by a large tube of calcium chloride. The checkers replaced the Vigreux column by a 50-cm. column filled with glass helices and surrounded by a heating jacket. With this column the removal of the *tert.*-butyl alcohol was complete in five to six hours.

5. A slower rate of fractionation does not result in an increased yield, but interrupted fractionation results in a decreased yield.

6. A good barostat is necessary. Control of the reduced pressure by adjusting a "leak" in the system is entirely unsatisfactory, for as a result of a small increase in pressure, the liquid ceases to boil, the column drains, and the boiling-chips are rendered ineffective. The barostat used by the submitters is essentially that described by Ellis [2] in which the relay is replaced by the thermionic relay described by Waddle and Saeman.[3]

7. The column and apparatus should not be washed with acid cleaning solution because the glass surface is left acidic and it then catalyzes the polymerization of ketene acetal.[4] A thin coating of the polymer on the walls of the apparatus is not detrimental. If polymer must be removed, it is best done by dissolving it in a 10 per cent solution of hydrochloric acid in acetone; a deep red solution results.

3. Method of Preparation

Ketene acetal may be prepared by the action of potassium *tert.*-butoxide on iodoacetal [5] or bromoacetal.[4]

---

[2] Ellis, Ind. Eng. Chem., Anal. Ed. **4**, 318 (1932).

[3] Waddle and Saeman, Ind. Eng. Chem., Anal. Ed. **12**, 225 (1940); Ferry, ibid. **10**, 647 (1938).

[4] Johnson, Barnes, and McElvain, J. Am. Chem. Soc. **62**, 964 (1940).

[5] Beyerstedt and McElvain, J. Am. Chem. Soc. **58**, 529 (1936).

MANDELIC ACID

$$C_6H_5COCH_3 + 2Cl_2 \rightarrow C_6H_5COCHCl_2 + 2HCl$$

$$C_6H_5COCHCl_2 + 3NaOH \rightarrow C_6H_5CHOHCO_2Na + 2NaCl + H_2O$$

$$C_6H_5CHOHCO_2Na + HCl \rightarrow C_6H_5CHOHCO_2H + NaCl$$

Submitted by J. G. Aston, J. D. Newkirk, D. M. Jenkins, and Julian Dorsky.
Checked by R. L. Shriner amd C. H. Tilford.

1. Procedure

(*A*) *Dichloroacetophenone.*—A 3-l. round-bottomed flask is fitted with a three-holed rubber stopper through which are passed an inlet tube extending to the bottom of the flask, an outlet tube, and a thermometer. The inlet tube is connected to a cylinder of chlorine through a bubble counter consisting of a 500-cc. wash bottle which contains about 200 cc. of concentrated sulfuric acid. The outlet tube is connected with a gas absorbing apparatus (Org. Syn. **14,** 2; Coll. Vol. **2, 1943,** 4) in which the evolved hydrochloric acid is absorbed by running water. It is best to set up the apparatus under a good hood.

In the flask are placed 240 g. (2 moles) of acetophenone and 1 l. of glacial acetic acid. The thermometer is adjusted so that it extends considerably below the surface of the solution, and chlorine is admitted at such a rate that the temperature does not exceed 60° (Note 1). Chlorination is continued until an excess of the halogen has been absorbed. This requires about five hours; completion of the reaction is indicated by the development of a yellow color. The reaction mixture is poured over 6 l. of crushed ice in a 2-gal. jar. The mixture is stirred several times (Note 2) and allowed to stand until the ice has melted. The dichloroacetophenone, which separates as a heavy lachrymatory oil, is removed. The yield is 340–370 g. (90–97 per cent of the theoretical amount). This product, containing only a few per cent of water and acetic acid, is pure enough for the preparation of mandelic acid. It may be purified by adding about 100 cc. of benzene, removing the water and benzene by distillation, and fractionally distilling the residual oil under reduced pressure. There is obtained 302–356 g. (80–94 per cent of the theoretical amount) of a colorless oil boiling at 132–134°/13 mm. (142–144°/25 mm.).

(*B*) *Mandelic Acid.*—In a 2-l. three-necked round-bottomed flask, fitted with an efficient mechanical stirrer, a dropping funnel, and a thermometer, is placed 156 g. (3.9 moles) of sodium hydroxide dissolved in 1.4 l. of water. The solution is warmed to 60° (Note 3), vigorous stirring is begun, and 200 g. (1.06 moles) of dichloroacetophenone (either crude or distilled) is added from the dropping funnel. The dichloroacetophenone is added slowly at first so that the temperature does not exceed 65°. The addition requires about two hours (Note 4). Stirring is continued for one hour longer, while the temperature is maintained at 65° by means of a water or steam bath. After addition of 170 cc. of 12*M* hydrochloric acid (Note 5), the solution is extracted with ether. The continuous extractor shown in Fig. 4 is very useful for this purpose. About 250–300 cc. of ether is used, and the extraction is continued until no more material is obtained. With this apparatus, about 130 g. of crude mandelic acid is recovered after twenty-four hours, and 150 g. after forty-eight hours. The volume of liquid in the larger flask must be great enough so that,

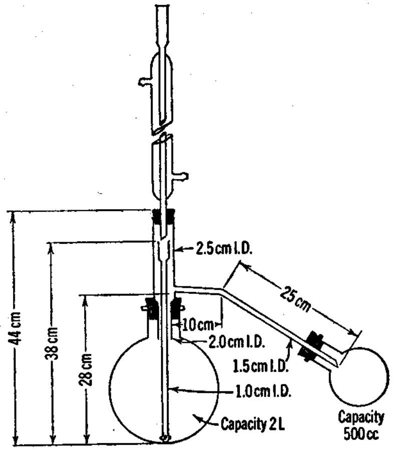


Fig. 4.

when 250–300 cc. of ether is used for the extraction, there will be a continuous overflow from the larger to the smaller flask; the latter serves as the "boiler."

The ether extracts are transferred to a 1-l. round-bottomed flask, the ether is removed by distillation, and the residue of crude mandelic acid is dried by warming it on a steam bath under the vacuum of a water pump. About 400 cc. of benzene is added, and the mixture is distilled until 100 cc. of distillate is collected. The acid in the residual mixture is brought completely into solution by the addition of 6–10 cc. of ethyl alcohol. The hot solution is then filtered through a warm Büchner funnel, and the filtrate is cooled overnight at 6°. The first crop of pure mandelic acid weighs 100–120 g. A second crop is obtained by evaporation of the mother liquor to about one-fourth its volume; this weighs 20–40 g. The total yield is 136–144 g. (85–90 per cent of the theoretical amount based on the dichloroacetophenone, or 76–87 per cent based on the acetophenone). The white crystalline product melts at 115–117° (Note 6).

2. Notes

1. According to Beilstein (**VII,** 283) trichloroacetophenone is obtained by chlorination of acetophenone at elevated temperatures.[1] However, at 60° less than 1 per cent of trichloroacetophenone is formed.
2. Stirring results in a better separation of acetic acid from the oil and prevents the formation of an emulsion.
3. At lower temperatures, hydrolysis is slow.
4. If the temperature becomes much higher, side reactions occur and loss in yield and purity results. The heat of reaction is sufficient to maintain the required temperature.
5. If the reaction mixture is cooled at this point, some of the mandelic acid may crystallize. If this happens, the precipitate should not be filtered, as it is contaminated with sodium chloride.
6. The submitters report that when 1 kg. of acetophenone is used yields of 0.98–1.06 kg. of mandelic acid are obtained.

---

[1] Gautier, Ann. chim. phys. (6) **14**, 348, 379, 385, 396 (1888).

3. Methods of Preparation

Dichloroacetophenone has been prepared by chlorination of acetophenone with and without aluminum chloride;[1] by action of dichloroacetyl chloride upon benzene and aluminum chloride;[1] by action of hypochlorous acid upon phenylacetylene;[2] by heating trichloromethylphenylcarbinol;[3] and by chlorination of phenylacetylene in alcohol.[4]

Mandelic acid has been prepared by hydrolysis of mandelonitrile (prepared in turn from benzaldehyde and hydrogen cyanide or from benzaldehyde, sodium bisulfite, and sodium cyanide);[5] by action of water at 180° upon trichloromethylphenylcarbinol;[6] by action of potassium carbonate upon a heated mixture of benzaldehyde and chloroform;[7] by action of warm, dilute alkali upon dibromoacetophenone;[8] and by action of warm, dilute sodium hydroxide upon phenylglyoxal.[9]

---

[2] Wittorf, J. Russ. Phys. Chem. Soc. **32**, 88 (1900) [Chem. Zentr. **1900**, II, 29].

[3] Kötz, J. prakt. Chem. (2) **90**, 299, 304 (1914).

[4] Jackson, J. Am. Chem. Soc. **56**, 977 (1934).

[5] Org. Syn. Coll. Vol. **1**, **1941**, 336; Spiegel, Ber. **14**, 239 (1881); Ultee, Rec. trav. chim. **28**, 254 (1909); Müller, Ber. **4**, 980 (1871).

[6] Jocicz, J. Russ. Phys. Chem. Soc. **29**, 100 (1897) [Chem. Zentr. **1897**, I, 1013].

[7] Savariau, Compt. rend. **146**, 297 (1908).

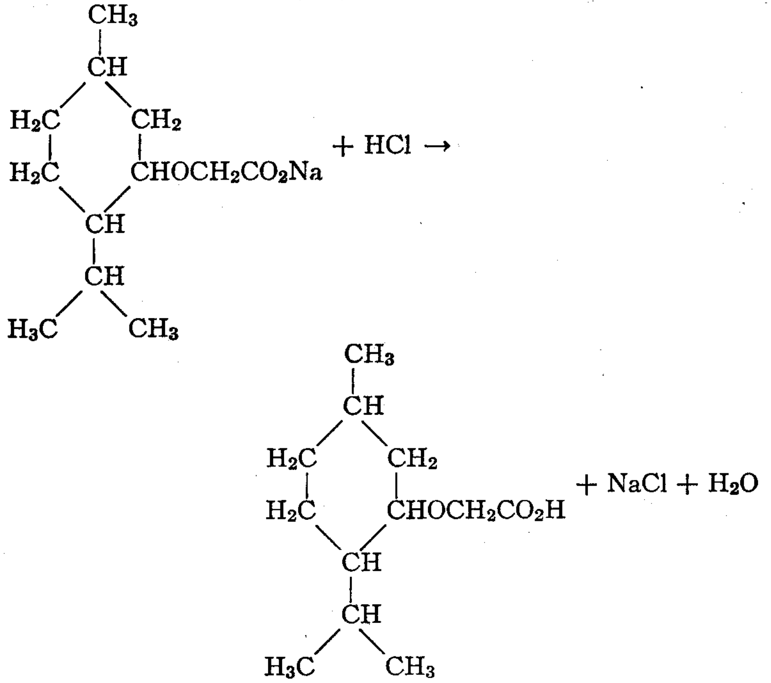
[8] Engler and Wöhrle, Ber. **20**, 2202 (1887).

[9] Pechmann, Ber. **20**, 2905 (1887).

l-MENTHOXYACETIC ACID

$$2C_{10}H_{19}OH + 2Na \rightarrow 2C_{10}H_{19}ONa + H_2$$

$$2C_{10}H_{19}ONa + ClCH_2CO_2H \rightarrow C_{10}H_{19}OCH_2CO_2Na + C_{10}H_{19}OH + NaCl$$



Submitted by M. T. Leffler and A. E. Calkins.
Checked by R. L. Shriner and C. H. Tilford.

1. Procedure

A 5-l. three-necked round-bottomed flask is fitted with a mechanical stirrer (Note 1) and a reflux condenser bearing a calcium chloride tube. A solution of 400 g. (2.56 moles) of *l*-menthol (crystals, m.p. 41–42°) in 1 l. of dry toluene (Note 2) is placed in the flask, and to it is added 70 g. (3.04 gram atoms) of clean sodium. The third neck of the flask is then tightly closed with a cork stopper, and the flask is heated in an oil bath until the toluene refluxes gently. As soon as the sodium has melted, stirring is begun and is maintained at such a rate that the sodium is broken into fine globules.

After the reaction mixture has been refluxed for fifteen hours, the stirrer is stopped, the reaction mixture is allowed to cool, and the excess sodium (Note 3) is carefully removed. The apparatus is then assembled as before (Note 1), but with a 1-l. separatory funnel fitted into the third neck of the flask (Note 4). The temperature of the oil bath is raised to 85–90°, and with continued stirring, a solution of 95 g. (1.01 moles) of monochloroacetic acid (Note 5) in 800 cc. of warm dry toluene is added from the separatory funnel at such a rate that refluxing is not too vigorous. A heavy precipitate of sodium chloroacetate forms immediately. After all the chloroacetic acid has been added, the mixture is refluxed and stirred for forty-eight hours. During this period, the stirring must be as thorough as possible; it is necessary to add 1-1.5 l. of dry toluene, and the stirrer must be stopped at frequent intervals while the solid material is removed from the side of the flask.

When the reaction is complete, the flask is removed from the oil bath and the cooled reaction mixture is transferred to a 5-l. separatory funnel and extracted with three 1-l. portions of water (Note 6). The water extract is carefully acidified with 20 per cent hydrochloric acid, and the crude menthoxyacetic acid, which collects on top as a brown oil, is extracted with three 200-cc. portions of benzene. The benzene extracts are combined, and the solvent is removed by distillation on a steam cone. The residue is then fractionally distilled under reduced pressure. The fraction boiling below 100°/20 mm. is mainly water and toluene. The second fraction boiling at 100–115°/8–10 mm. is impure *l*-menthol and may be saved for redistillation (Note 6). The yield of *l*-menthoxyacetic acid, boiling at 134–137°/2 mm. (150–155°/4 mm.), $[\alpha]_D^{25} = -92.4°$, amounts to 166–180 g. (78–84 per cent of the theoretical amount).

2. Notes

1. The success of the reaction depends largely on the type of agitation used. A stainless-steel stirrer of the anchor type with a gas-tight rubber or metal-graphite bearing serves well because of its strength. It should be operated at high speed in the first part of the reaction in order to powder the sodium; in the second stage vigorous stirring is not so essential, but the solid and liquid phases should be mixed efficiently.

2. The toluene may be dried by refluxing it over metallic sodium for several hours. It is distilled from the sodium into a receiver protected from the air by a calcium chloride tube.

3. The excess sodium should amount to about 11 g. If the sodium remains divided, it is removed by filtering the hot mixture through glass wool.

4. It is not advisable to leave the separatory funnel attached to the flask during the long period of stirring which follows, as the constant, heavy vibration tends to loosen the connection. As soon as it has been used, the funnel should be replaced by a tightly fitting cork stopper.

5. The commercial grade (m.p. 61–63°) of monochloroacetic acid should be ground and thoroughly dried over concentrated sulfuric acid in a vacuum desiccator for two days. The yield was lowered by about 10 per cent when the chloroacetic acid was used without previous drying.

6. The toluene layer, containing the menthol formed in the reaction, is saved for the recovery of both the toluene and the menthol, which are separated by distillation under atmospheric pressure. The *l*-menthol collected at 210–212° (corr.) amounts to 150–225 g.

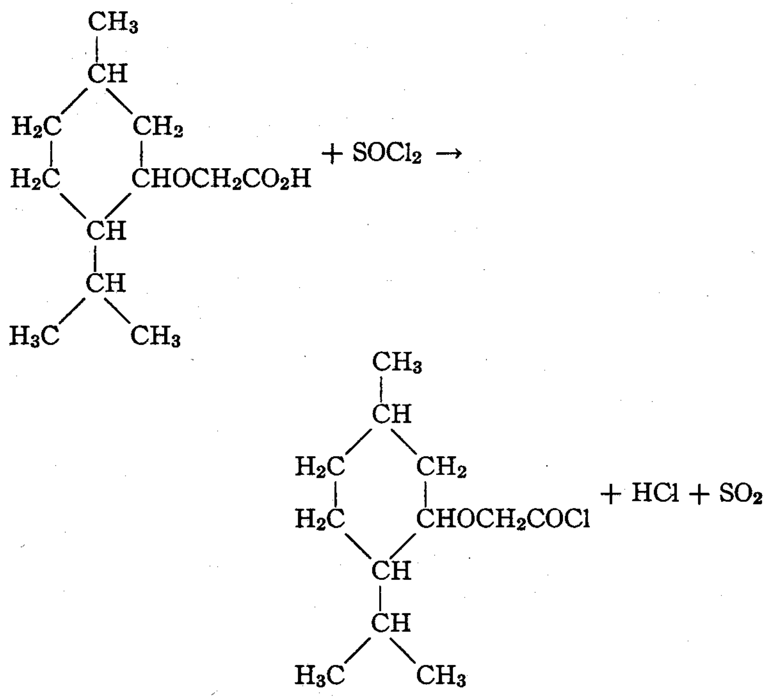
3. Method of Preparation

l-Menthoxyacetic acid has been prepared only by the action of sodium menthoxide upon monochloroacetic acid.[1]

---

[1] Frankland and O'Sullivan, J. Chem. Soc. **99**, 2325 (1911); Rule and Todd, ibid. **1931**, 1929.

l-MENTHOXYACETYL CHLORIDE



Submitted by M. T. Leffler and A. E. Calkins.
Checked by R. L. Shriner and C. H. Tilford.

1. Procedure

A 1-l. three-necked round-bottomed flask is mounted on a steam cone and is fitted with a 250-cc. separatory funnel and a reflux condenser connected to a trap (Note 1) for absorbing gases. In the flask is placed 325 g. (198 cc., 2.73 moles) of thionyl chloride (Note 2), and to it is added, during the course of one hour, 125 g. (0.58 moles) of *l*-menthoxyacetic acid (p. 52). The flask is shaken frequently during the addition of the acid and, if necessary, is warmed to start the reaction. When all the acid has been added

(Note 3), the reaction mixture is refluxed gently for five hours. After the reaction is complete, the excess of thionyl chloride is removed by distillation on the steam bath (Note 4) and the residue is distilled under reduced pressure. The yield of *l*-menthoxyacetyl chloride boiling at 117–120°/3 mm. (120–125°/5 mm.), $[\alpha]_D^{25} = -89.6°$, amounts to 115–118 g. (Note 5) (85–87 per cent of the theoretical amount). The product turns dark on standing; it should be stored in a glass-stoppered amber bottle.

2. Notes

1. The gas absorption trap shown in Org. Syn. Coll. Vol. **1**, **1941**, 97, may be used.

2. The commercial grade (b.p. 74–78°) of thionyl chloride was used.

3. Owing to the high viscosity of the acid, it is desirable to rinse the separatory funnel with a little thionyl chloride which is then added to the reaction mixture.

4. The recovered thionyl chloride may be redistilled for future runs. It is best to remove the last traces of thionyl chloride by heating the crude product to about 140° under the vacuum of the water pump.

5. The submitters report the same yields (per cent) when twice the amounts of materials are used.

3. Method of Preparation

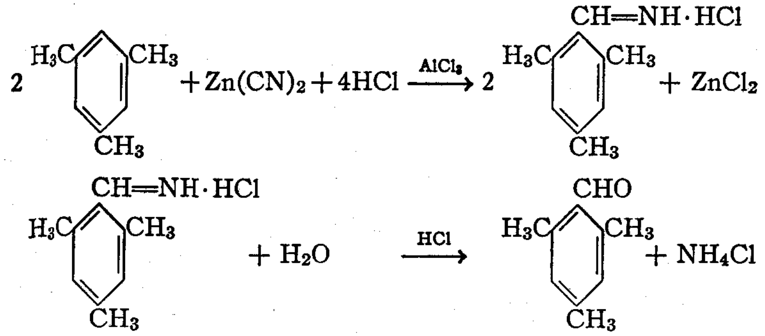
The procedure given above is adapted from that described by Read and Grubb.[1] No other methods for the preparation of *l*-menthoxyacetyl chloride have been described.

---

[1] Read and Grubb, J. Soc. Chem. Ind. **51**, 330T (1932).

MESITALDEHYDE

(β-Isodurylaldehyde)



Submitted by R. C. Fuson, E. C. Horning, S. P. Rowland, and M. L. Ward.
Checked by C. F. H. Allen and J. Van Allan.

1. Procedure

In a 1-l. three-necked round-bottomed flask, fitted with an efficient stirrer, a reflux condenser, an inlet tube, and a thermometer (Notes 1 and 2), are placed 102 g. (118 cc., 0.85 mole) of mesitylene (Org. Syn. Coll. Vol. **1**, **1941**, 341), 147 g. (1.25 moles) of zinc cyanide (Note 3), and 400 cc. of tetrachloroethane (Note 4). The inlet tube is connected to a source of hydrogen chloride (Note 5), and the mixture is stirred at room temperature while a rapid stream of dry hydrogen chloride is passed through it. This is continued until the zinc cyanide is decomposed; usually about three hours is required. The flask is then immersed in an ice bath, the inlet tube is removed, and 293 g. (2.2 moles) of finely ground anhydrous aluminum chloride is added to the mixture (Notes 6 and 7), with *very vigorous* stirring. The ice bath is then removed, and the passage of hydrogen chloride is resumed for the remainder of the reaction period. The heat of reaction is sufficient to warm the mixture slowly, and a temperature of about 70° is reached at the end of an hour. A temperature of 67–72° is maintained for an additional two and a half hours. The cooled mixture is decomposed by pouring it cautiously, with stirring by hand, into a 4-l. container about half full of crushed ice, to which has been added 100 cc. of concentrated hydrochloric acid. After the mixture has stood overnight, it is transferred to a 3-l. round-bottomed flask and refluxed for three hours. The organic layer is then separated, and the aqueous layer is extracted once with 50 cc. of tetrachloroethane. The combined tetrachloroethane solutions are washed with 150 cc. of a 10 per cent solution of sodium carbonate and distilled with steam. The first 800–900 cc. of distillate is set aside for recovery of the solvent (Notes 8 and 9), and the second portion is collected as long as oily drops are observed (Note 10). This distillate is extracted with 500 cc. of benzene, the solvent is removed on the steam bath, and the residue is distilled from a 250-cc. modified Claisen flask (Org. Syn. **22,** 11). After a small fore-run, the mesitaldehyde distils at 118–121°/16 mm. The yield is 95–102 g. (75–81 per cent of the theoretical amount) (Notes 11 and 12).

2. Notes

1. Because of the toxic nature of tetrachloroethane and hydrogen cyanide, *all operations* as far as the final distillation should be carried out in a *good* hood.

2. It is convenient to place the thermometer in the gas inlet tube. The bulb should be immersed in the liquid, but the inlet tube need extend only just below the liquid surface.

3. The zinc cyanide may be commercial material, or it may be prepared as directed by Adams and Levine.[1] However, the zinc cyanide does not react well if it is too carefully purified.[2]

4. Tetrachloroethane is a toxic substance; it should be handled with due care.

5. Commercial cylinders of hydrogen chloride, now available, are most convenient. However, the gas may be readily prepared (Org. Syn. Coll. Vol. **1, 1941,** 293, 534).

---

[1] Adams and Levine, J. Am. Chem. Soc. **45,** 2375 (1923).

[2] Arnold and Sprung, J. Am. Chem. Soc. **60,** 1699 (1938).

6. Although it is more convenient to add the zinc cyanide and aluminum chloride together, the procedure results in lower yields.

7. The apparatus shown in Fig. 5 is most convenient. A 250-cc. Erlenmeyer flask is connected to the side neck of the flask by a 13-cm. length of 20-mm. thin-walled rubber tubing.[3]

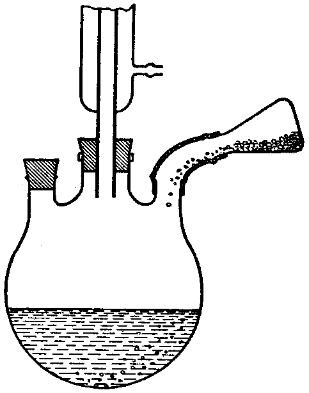


FIG. 5.

8. If difficulty is experienced in separating the organic layer, the entire solution may be subjected to steam distillation.

9. The first portion of the distillate consists almost entirely of tetrachloroethane and water. The solvent may be recovered by separating the organic layer, drying it with calcium chloride, and distilling.

10. About 9 l. of water is obtained; the time required is about four hours.

11. If a smaller yield of mesitaldehyde is acceptable and time is of importance, the preparation may be carried out without a solvent, and with other changes as follows: The zinc cyanide and aluminum chloride are mixed by shaking, the mesitylene is added, and the flask is immersed in an oil bath at 100°. The stirrer is started, and a fairly rapid current of dry hydrogen chloride is passed into the mixture, below the surface of the liquid, for four hours; at the end of this time, the current of gas is discontinued, but stirring and heating are maintained for two hours longer. The reaction mixture is decomposed and processed as already described. The fraction which boils at 110–120°/9–10 mm. is taken as mesitaldehyde; the yield is 73 per cent of the theoretical amount. (Private communication, D. B. GLASS.)

12. 2,4,6-Triethylbenzaldehyde and 2,4,6-triisopropylbenzaldehyde may be prepared in yields of 69 and 65 per cent, respec-

---

[3] Fieser, "Experiments in Organic Chemistry," p. 311, New York, 1941. Reprinted by special permission of D. C. Heath and Company.

tively, by the procedure described above, with a reaction time of eight hours and the following modifications:

	TRIETHYLBENZALDEHYDE	TRIISOPROPYLBENZALDEHYDE
Hydrocarbon	100 g. (0.62 mole)	100 g. (0.49 mole)
Zinc cyanide	115 g. (0.97 mole)	102 g. (0.74 mole)
Aluminum chloride	215 g. (1.60 moles)	134 g. (1.0 mole)
Boiling point	146–149°/21 mm.	123–126°/4 mm.

3. Methods of Preparation

Most of the methods for preparing mesitaldehyde have been given previously.[4] The procedure described here has been recently published.[5, 6, 7]

β-METHYLGLUTARIC ACID

(Glutaric acid, β-methyl-)

$$\mathrm{2CNCH_2CONH_2 + CH_3CHO \rightarrow CH_3CH[CH(CN)CONH_2]_2 + H_2O}$$

$$\mathrm{CH_3CH[CH(CN)CONH_2]_2 + 6H_2O + 4HCl \rightarrow HO_2CCH_2CH(CH_3)CH_2CO_2H + 4NH_4Cl + 2CO_2}$$

Submitted by ROBERT E. KENT and S. M. MCELVAIN.
Checked by LEE IRVIN SMITH and G. A. BOYACK.

1. Procedure

(*A*) *α,α′-Dicyano-β-methylglutaramide.*—In a 6-l. flask, 520 g. (6.2 moles) of recrystallized cyanoacetamide (Org. Syn. Coll. Vol. **1**, **1941**, 179) (Note 1) is dissolved in 3.4 l. of water, and the solution is cooled to 10° and filtered if it is not clear (Note 2). While the flask is shaken constantly, 137.5 g. (3.1 moles) of freshly distilled acetaldehyde and 20 cc. of piperidine are added *successively* to the solution. After the mixture has stood at room temperature for two hours, the flask is transferred to an ice-salt bath and the mixture is partially frozen. During this operation, the flask should be shaken frequently. After thirty minutes, α,α′-dicyano-β-methylglutaramide begins to deposit, and when the precipitation is complete (about one hour), the mixture is allowed to come to room temperature in order to melt the ice which is present. The precipitate is then filtered with suction and washed thoroughly with cold distilled water. The yield is 420–425 g. (71 per cent of the theoretical amount) of a white, powdery solid which melts at 152–157° (Note 3).

(*B*) *β-Methylglutaric Acid.*—In a 5-l. flask are placed 400 g. of the amide and 1 l. of concentrated hydrochloric acid; the mixture is warmed on a steam bath until solution is complete, after which it is diluted with 1 l. of water and refluxed for eight hours. The amber-colored solution is saturated with sodium chloride and extracted with five 600-cc. portions of ether. The combined ether extracts are dried for one hour over phosphorus pentoxide, and the solvent is removed by distillation. The residue, crude β-methylglutaric acid, weighs 238–240 g. (80 per cent of the theoretical amount) and melts at 79–82° with previous softening. This product is recrystallized from about 250 cc. of 10 per cent hydrochloric acid. The recovery is about 90 per cent (Note 4), and the purified product melts at 85–86°.

2. Notes

1. Ammonia exerts a hindering effect on this condensation, and the yield is greatly reduced when crude cyanoacetamide is used.
2. At 10°, cyanoacetamide sometimes crystallizes. The mixture should not be filtered until it is certain that the precipitate contains no cyanoacetamide. Any cyanoacetamide which separates redissolves quickly after the acetaldehyde and piperidine have been added.

---

[4] Barnes, Org. Syn. **21**, 110.

[5] Fuson, Horning, Ward, Rowland, and Marsh, J. Am. Chem. Soc. **64**, 31 (1942).

[6] Hinkel, Ayling, and Morgan, J. Chem. Soc. **1932**, 2797.

[7] Hinkel, Ayling, and Beynon, J. Chem. Soc. **1936**, 342.

3. This amide is insoluble in the usual solvents, but it may be further purified, if desired, by trituration with dilute hydrochloric acid, followed by washing with hot absolute alcohol. It then melts sharply at 160–161°.

4. The checkers used one-tenth of the specified amounts of reagents. They obtained, in two runs, the following average yields of products: crude α,α′-dicyano-β-methylglutaramide, m.p. 152–157°, 75 per cent; crude β-methylglutaric acid, m.p. 79–82°, 78 per cent; purified β-methylglutaric acid, m.p. 84–85°, 80 per cent (recovery). In the second run, however, the yields (except for the recovery in the recrystallization) were slightly higher than those given for the larger runs.

3. Methods of Preparation

The above method is adapted from the procedure of Day and Thorpe.[1] β-Methylglutaric acid has been prepared by hydrolysis of β-methylglutaronitrile;[2] by condensation of crotonic ester with ethyl sodiocyanoacetate,[3] and with sodiomalonic ester;[4] and by condensation of acetaldehyde with malonic ester.[5]

[1] Day and Thorpe, J. Chem. Soc. 117, 1465 (1920).

[2] Blaise and Gault, Bull. soc. chim. (4) 1, 88 (1907).

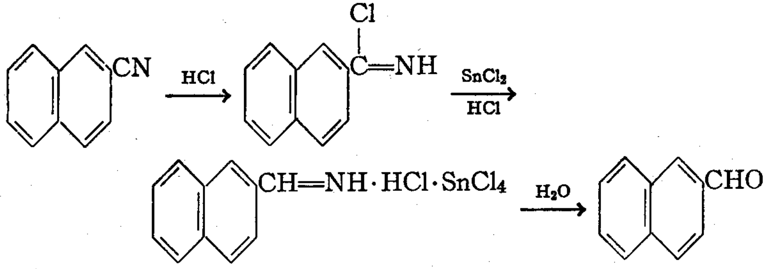
[3] Howles, Thorpe, and Udall, J. Chem. Soc. 77, 948 (1900); Darbishire and Thorpe, ibid. 87, 1716 (1905).

[4] Auwers, Köbner, and v. Meyenburg, Ber. 24, 2887 (1891).

[5] Knoevenagel, Ber. 31, 2585 (1898).

β-NAPHTHALDEHYDE

(2-Naphthaldehyde)



Submitted by Jonathan W. Williams.
Checked by C. F. H. Allen and J. Van Allan.

1. Procedure

In a 2-l. three-necked round-bottomed flask, provided with a mechanical stirrer, a reflux condenser carrying a drying tube, and an inlet tube reaching nearly to the bottom of the flask, are placed 76 g. (0.4 mole) of anhydrous stannous chloride (Note 1) and 400 cc. of anhydrous ether. The mixture is then saturated with dry hydrogen chloride, while it is slowly stirred; this requires two and one-half to three hours, during which time the stannous chloride forms a viscous lower layer.

The inlet tube is replaced by a dropping funnel, and a solution of 30.6 g. (0.2 mole) of β-naphthonitrile, m.p. 60–62° (Note 2), in 200 cc. of dry ether is added rapidly. Hydrogen chloride is again passed into the mixture until it is saturated, and the mixture is then stirred rapidly for one hour and allowed to stand overnight while the yellow aldimine-stannichloride separates completely.

The ethereal solution is decanted, and the solid is rinsed with two 100-cc. portions of ether. The solid is transferred to a 5-l. flask fitted for steam distillation and immersed in an oil bath, the temperature of which is maintained at 110–120° (Note 3). Dry steam is passed through the mixture (Note 4) until the aldehyde is completely removed; this requires eight to ten hours, and 8-10 l. of distillate is collected.

The white solid is filtered and allowed to dry in the air; it amounts to 23–25 g. (73–80 per cent of the theoretical amount) and melts at 53–54°. For further purification, it is distilled under reduced pressure (Note 5); the water-clear distillate (b.p. 156–158°/15 mm.) is poured into a mortar while hot and is pulverized when cool. The recovery is 93–95 per cent, and the melting point is 57–58°.

2. Notes

1. The success of this type of reaction depends on the quality of the catalyst. The most active and dependable form of anhydrous stannous chloride[1] is prepared as follows: In a 600-cc. beaker is placed 204 g. (189 cc., 2 moles) of acetic anhydride (99–100 per cent) and, while the liquid is stirred by hand, 226 g. (1 mole) of commercial c.p. crystalline stannous chloride dihydrate is added. This operation should be performed in a hood, for the heat of the reaction is sufficient to cause the acetic anhydride to boil. After about one and a half hours, the anhydrous stannous chloride is filtered on a large Büchner funnel, rinsed with two 50-cc. portions of dry ether, and dried overnight in a vacuum desiccator. The yield is quantitative (189 g.). The product may be kept in a tightly closed bottle until it is wanted. The product secured by dehydrating crystalline stannous chloride in an oil bath at 195–200° is satisfactory in many instances but is not dependable.

2. β-Naphthonitrile is prepared by the procedure described under *o*-Tolunitrile, in Org. Syn. Coll. Vol. **1, 1941**, 514.

3. The use of dry, slightly superheated steam reduces the time of distillation but is not essential.

4. A superheater obtained from the Fisher Scientific Company was used. It was preceded by the usual steam trap to remove the condensed water. The thermometer in the superheater recorded 260°.

5. It is convenient to combine the material from several runs.

---

[1] Stephen, J. Chem. Soc. **1930**, 2786.

3. Methods of Preparation

Most of the methods for preparation of β-naphthaldehyde have been given previously.[2] A recent procedure describes the preparation of β-naphthaldehyde from 2-bromomethylnaphthalene and hexamethylenetetramine in boiling acetic acid.[3] The method of reduction of nitriles by stannous chloride was discovered by Stephen.[4]

p-NITROBENZOYL PEROXIDE

[Peroxide, bis(*p*-nitrobenzoyl)-]

$$2\ p\text{-}O_2NC_6H_4COCl + Na_2O_2 \rightarrow [p\text{-}O_2NC_6H_4COO]_2 + 2NaCl$$

Submitted by Charles C. Price and Edwin Krebs.
Checked by R. L. Shriner and C. H. Tilford.

1. Procedure

A 600-cc. beaker containing 100 cc. of water and equipped with an efficient stirrer, a thermometer, and a 200-cc. separatory funnel is immersed in an ice-water bath. When the temperature of the water has fallen to 0–5°, 10 g. (0.13 mole) of sodium peroxide (Note 1) is added. Then, with vigorous stirring, a solution of 37 g. (0.2 mole) of *p*-nitrobenzoyl chloride in 100 cc. of dry toluene is added dropwise over a period of about thirty minutes. After the mixture has been stirred for an additional one and one-half hours, the precipitate is filtered and washed with 200 cc. of cold water (Note 2). The yield of *p*-nitrobenzoyl peroxide is 28.5–29 g. (86–88 per cent of the theoretical amount). It melts at 155–156°.

The product may be recrystallized most conveniently by dissolving it as rapidly as possible (Note 3) in 500 cc. of dry toluene which has been preheated to 80–85°. As soon as the solid is completely dissolved (two to three minutes of stirring), the solution is filtered through a warm Büchner funnel and the filtrate is immediately cooled in an ice-water bath. The yield of very pale yellow glistening needles is 25 to 26 g. (86–89 per cent recovery); they melt at 156° with vigorous decomposition (Note 4).

---

[2] Org. Syn., **21**, 88.

[3] Badger, J. Chem. Soc. **1941**, 536.

[4] Stephen, J. Chem. Soc. **127**, 1874 (1925).

2. Notes

1. In a parallel experiment in which 25 g. of sodium peroxide was used, the precipitate was not the peroxide but evidently consisted of sodium *p*-nitroperbenzoate.

2. *p*-Nitrobenzoic acid may be recovered by acidification of the filtrate.

3. Excessive heating during recrystallization leads to extensive decomposition of the peroxide.

4. By a procedure similar to that described for *p*-nitrobenzoyl peroxide, the following peroxides have been prepared: *m*-nitrobenzoyl peroxide (m.p. 136–137°) in 90 per cent yield; anisoyl peroxide (m.p. 126–127°) in 86–89 per cent yields; *p*-bromobenzoyl peroxide (m.p. 144°) in 73 per cent yield; and 3,4,5-tribromobenzoyl peroxide (m.p. 186°) in 40 per cent yield.[1] The procedure is not satisfactory for preparation of acetylsalicylyl peroxide, which is more conveniently prepared by action of hydrogen peroxide upon an acetone solution of the acid chloride.

3. Methods of Preparation

p-Nitrobenzoyl peroxide,[2] as well as *m*-nitrobenzoyl peroxide [2] and anisoyl peroxide,[3] have been prepared in about 50 per cent yields from the acid chlorides and an acetone solution of hydrogen peroxide, in the presence of a basic substance such as pyridine, sodium acetate, or sodium hydroxide. *m*-Nitrobenzoyl peroxide has also been prepared by nitration of benzoyl peroxide with cold

---

[1] Price, Kell, and Krebs, J. Am. Chem. Soc. **64**, 1104 (1942).

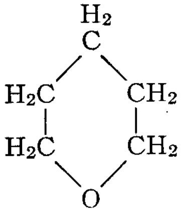
[2] Vanino and Uhlfelder, Ber. **33**, 1046 (1900).

[3] Vanino and Uhlfelder, Ber. **37**, 3624 (1904).

concentrated nitric acid,[4] or with a cold [5] or hot [2] mixture of nitric and sulfuric acids.

PENTAMETHYLENE BROMIDE

(Pentane, 1,5-dibromo-)



$+ 2HBr \xrightarrow{H_2SO_4} BrCH_2CH_2CH_2CH_2CH_2Br + H_2O$

Submitted by D. W. Andrus.
Checked by Nathan L. Drake and Charles M. Eaker.

1. Procedure

A hydrobromic acid solution (Org. Syn. Coll. Vol. 1, **1941**, 26) is prepared in a 500-cc. round-bottomed flask by passing sulfur dioxide into a mixture of 120 g. (37.7 cc., 0.75 mole) of bromine, 50 cc. of water, and 150 g. of crushed ice. This is equivalent to a mixture of 253 g. (1.5 moles) of 48 per cent hydrobromic acid and 74 g. of concentrated sulfuric acid. To the mixture 21.5 g. (0.25 mole) of tetrahydropyrane (p. 90) is added, a reflux condenser is attached to the flask, and the light brown homogeneous mixture is refluxed for three hours (Note 1).

The heavy lower layer is separated (Note 2), washed once with a saturated solution of sodium bicarbonate, once with water, and then dried over 4–5 g. of anhydrous calcium chloride. The crude product is decanted from the calcium chloride, and the drying agent is rinsed once or twice with a small quantity of ethyl bromide which is added to the main product. The mixture is distilled under reduced pressure, and the pentamethylene bromide, which weighs 46–47 g. (80–82 per cent of the theoretical amount), is collected at 104–106°/19 mm.

---

[4] Brodie, J. Chem. Soc. **17**, 271 (1864).

[5] Vanino, Ber. **30**, 2004 (1897); Gelissen and Hermans, Ber. **58**, 285 (1925).

2. Notes

1. The submitter refluxed the mixture for ten hours, but the checkers obtained equally good yields in three hours.

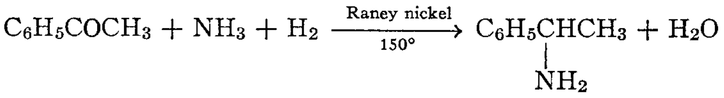
2. The upper aqueous layer contains considerable unchanged hydrobromic acid. If this layer is distilled, about 150 g. (0.9 mole) of constant-boiling hydrobromic acid (b.p. 123–124°/748 mm.) may be recovered.

3. Methods of Preparation

The methods of preparing pentamethylene bromide are given in Org. Syn. Coll. Vol. **1, 1941,** 428, where the preparation of the dihalide from benzoylpiperidine and phosphorus pentabromide is described in detail. The procedure given above is based upon the work of Paul.[1]

α-PHENYLETHYLAMINE

(Benzylamine, α-methyl-)



$$C_6H_5COCH_3 + NH_3 + H_2 \xrightarrow[150°]{\text{Raney nickel}} \underset{\displaystyle NH_2}{C_6H_5\overset{}{C}HCH_3} + H_2O$$

Submitted by JOHN C. ROBINSON, JR., and H. R. SNYDER.
Checked by NATHAN L. DRAKE and DANIEL DRAPER.

1. Procedure

IN a 2-l. bomb are placed 720 g. (6 moles) of pure acetophenone and 1 tablespoon of Raney nickel catalyst (Org. Syn. **21, 15**). After the cap and gauge block are securely fastened, 700 cc. (30 moles) of liquid ammonia is introduced (Note 1). The mixture is hydrogenated at 150° under 5000–3500 lb. (Note 2). The reaction is allowed to continue as long as hydrogen is absorbed, generally four to six hours. The bomb is cooled, the excess ammonia is allowed to escape, and the contents are filtered from the catalyst. The mixture is cooled in an ice bath, acidified to Congo red with concentrated hydrochloric acid (200–300 cc.), and steam-distilled for ten to twelve hours to remove excess acetophenone (Note 3). The residue is then cooled and added slowly to 200 g. of solid sodium hydroxide in a flask surrounded by an ice bath. The amine is separated, and the aqueous layer is extracted with three 150-cc. portions of benzene. The extracts and amine are combined and dried over solid sodium hydroxide. After removal of the benzene, the residue is fractionated under diminished pressure. The yield of α-phenylethylamine (Note 4), b.p. 80–81°/18 mm., is 320–380 g. (Note 5) (44–52 per cent of the theoretical amount).

2. Notes

1. Liquid ammonia is introduced into the large bomb as follows: The cap and gauge block of the large bomb are tightened in place. The inner gas inlet tube is removed from the cap assembly of a smaller bomb (capacity about 250 cc.). This bomb is equipped with a test tube type liner which is kept chilled in a bath of Dry Ice while it is filled with liquid ammonia. This test tube is then placed in the small bomb, and the cap and gauge block are quickly (fifteen to thirty seconds) tightened. The bomb is then filled with hydrogen under high pressure and connected with the larger bomb by means of a short length of the conventional steel pressure tubing. The smaller bomb is inverted, and the valves are opened. This operation will introduce about 150 cc. of liquid ammonia at one time and may be repeated as often as necessary.

2. A booster pump is required, for it is quite important to keep the pressure above the minimum value of about 3500 lb. The temperature of the reduction is above the critical temperature of ammonia, and the pressure will not fall much below 3500

---

[1] Paul, Bull. soc. chim. (4) **53**, 1489 (1933).

lb. At this point hydrogen must be pumped into the bomb until the pressure is about 5000 lb.; this process is repeated until the reaction is complete. If a safety disk is to be incorporated into the line, it *must not* be made of *copper*, as ammonia, even under 2–3 atm., rapidly attacks copper. A *special* disk of steel, nickel, or other suitable material is required.

3. It is necessary to heat the flask externally with a flame or the volume of the solution will greatly increase during the lengthy steam distillation.

4. According to the submitters, methyl amyl ketone (800 g.) and ammonia (600 cc.) have been converted to 2-aminoheptane, b.p. 139–141°, in exactly the same manner, in 50–55 per cent yields. A slightly modified procedure was used in the preparation of *n*-heptylamine and furfurylamine. Heptaldehyde (320 g.) was dissolved in 500 cc. of methanol, and 150 cc. of liquid ammonia was added; the reduction was conducted as above. *n*-Heptylamine, b.p. 57–58°/23 mm., was obtained in yields of 53–63 per cent. Freshly distilled furfural (290 g.) was dissolved in 500 cc. of methanol, 150 cc. of liquid ammonia was introduced, and the reduction carried out as usual. The product was removed, filtered, and fractionated directly. Furfurylamine, b.p. 144–146°, was obtained in 50 per cent yield.

5. The yields are based upon the amount of acetophenone initially used and do not make allowances for the material recovered from the steam distillation. A small amount of di-(α-phenylethyl)-amine, b.p. 61–62°/2 mm., may be recovered from the residues.

3. Methods of Preparation

The methods for preparation of α-phenylethylamine are reviewed in Org. Syn. Coll. Vol. **2, 1943,** 506, where detailed directions are given for the preparation of this amine from acetophenone and ammonium formate. The procedure given above is based upon that of Schwoegler and Adkins.[1]

---

[1] Schwoegler and Adkins, J. Am. Chem. Soc. **61**, 3499 (1939).

β-PHENYLETHYLAMINE

(Phenethylamine)

$$C_6H_5CH_2CN + 2H_2 \xrightarrow{\text{Raney nickel}} C_6H_5CH_2CH_2NH_2$$

Submitted by John C. Robinson, Jr., and H. R. Snyder.
Checked by Nathan L. Drake and Daniel Draper.

1. Procedure

In a 2-l. bomb are placed 1 kg. (8.55 moles) of pure (Note 1) benzyl cyanide and 1 tablespoon of Raney nickel catalyst (Org. Syn. **21,** 15). After the cap is securely fastened down, 150 cc. of liquid ammonia is introduced (Note 2). Hydrogen is introduced until the pressure is about 2000 lb. The bomb is then heated to 120–130° and shaking is begun. The reduction is complete well within an hour (Note 1). The bomb is cooled, opened, and the contents are removed. The bomb is rinsed with a little ether, and the combined liquids are filtered from the catalyst. The ether is removed, and the residue is fractionated under reduced pressure. The yield is 860–890 g. (83–87 per cent of the theoretical amount) of β-phenylethylamine, b.p. 90–93°/15 mm. (Notes 3, 4, and 5).

2. Notes

1. Benzyl cyanide, prepared according to Org. Syn. Coll. Vol. **1, 1941,** 107, should be distilled from Raney nickel. Minute traces of halide has a strong poisoning effect on the catalyst. If the reduction does not occur within an hour, the contents of the bomb should be removed and filtered. New catalyst is then added and the process is repeated.

2. The presence of ammonia in the reduction mixture reduces the amount of secondary amine formed. For directions for introducing the liquid ammonia, see Note 1 to the preparation of α-phenylethylamine (p. 69).

3. If several runs are made, a small amount of the secondary amine may be recovered from the combined residues. Di-(β-phenylethyl)-amine boils at 155–157°/4 mm.

4. Similarly *n*-amyl cyanide has been converted to *n*-hexylamine, b.p. 128–130°, in 67–70 per cent yields.

5. It has been reported (R. N. Icke and C. E. Redemann, private communication) that β-phenylethylamine, as well as several substituted β-phenylethylamines, may be prepared in excellent yields by catalytic reduction of the corresponding cyanides in 10 *N* methanolic ammonia. An example of this procedure follows. Commercial anhydrous methanol is saturated with ammonia gas at 0°; this solution is approximately 10 *N*. A solution of 58.5 g. (0.5 mole) of benzyl cyanide in 300 cc. of 10 *N* methanolic ammonia (the ratio of ammonia to benzyl cyanide should be at least 5 : 1 in order to minimize the formation of the secondary amine) is placed in a high-pressure hydrogenation bomb, 5–10 cc. of settled Raney nickel catalyst (Org. Syn. **21,** 15) is added, the bomb is closed, and hydrogen is introduced until the pressure is 500–1000 lb. The bomb is shaken and heated to 100–125° until absorption of hydrogen ceases (about two hours). The bomb is cooled and opened, and the contents are removed. The bomb is rinsed with two or three 100-cc. portions of methanol, and the combined liquids are poured through a fluted filter to remove the catalyst. (*Caution!* If the catalyst becomes dry, it is likely to ignite.) The solvent and the ammonia are removed by distillation, and the residue is fractionated through a short column. The yield of β-phenylethylamine boiling at 92–93°/19 mm. (62–63°/4 mm.) is 51–54.5 g. (84–90 per cent of the theoretical amount). The hydrochloride, after crystallization from dry ethyl alcohol, melts at 218–219°. This procedure has also been used for preparation of the following β-phenylethylamines from the cyanides; the yields of amines were uniformly high: 3,4-dimethoxyphenylethylamine, b.p. 119–119.5°/1 mm.; *o*-methylphenylethylamine, b.p. 67°/0.5 mm.; *m*-methylphenylethylamine, b.p. 68°/2 mm.; *p*-methylphenylethylamine, b.p. 71°/2 mm.; and 3,4-methylenedioxyphenylethylamine, b.p. 109°/2 mm.

3. Methods of Preparation

β-Phenylethylamine has been made by a number of reactions, many of which are unsuitable for preparative purposes. Only the most important methods, from a preparative point of view, are given here. The present method is adapted from that of Adkins,[1] which in turn was based upon those of Mignonac,[2] von Braun and coworkers,[3] and Mailhe.[4] Benzyl cyanide has been converted to the amine by catalytic reduction with palladium on charcoal,[5] with palladium on barium sulfate,[6] and with Adams' catalyst;[7] by chemical reduction with sodium and alcohol,[8] and with zinc dust and mineral acids.[9] Hydrocinnamic acid has been converted to the azide and thence by the Curtius rearrangement to β-phenylethylamine;[10] also the Hofmann degradation of hydrocinnamide has been used successfully.[11] β-Nitrostyrene,[12] phenylthioacetamide,[13] and the benzoyl derivative of mandelonitrile[14] all yield β-phenylethylamine upon reduction. The amine has also been prepared by cleavage of *N*-(β-phenylethyl)-phthalimide[15] with hydrazine; by the Delépine synthesis from β-phenylethyl iodide and hexamethylenetetramine;[16] by the hydrolysis of the corresponding urethan and urea,[17] and by the reduction of phenylacetaldoxime.[18]

---

[1] Adkins, "The Reaction of Hydrogen with Organic Compounds over Copper-Chromium Oxide and Nickel Catalysts," Univ. of Wisconsin Press, Madison, Wis., 1937, pp. 53–54.

[2] Mignonac, French pat. 638,550 [C. A. **23**, 154 (1929)]; British pat. 282,038 [C. A. **22**, 3668 (1928)].

[3] von Braun, Blessing, and Zobel, Ber. **56**, 1988 (1923).

[4] Mailhe, Bull. soc. chim. (4) **23**, 237 (1918).

[5] Strack and Schwaneberg, Ber. **65**, 710 (1932).

[6] Rosenmund and Pfannkuch, Ber. **56**, 2258 (1923).

[7] Carothers and Jones, J. Am. Chem. Soc. **47**, 3051 (1925).

[8] Wohl and Berthold, Ber. **43**, 2184 (1910).

[9] Bernthsen, Ann. **184**, 304 (1877).

[10] Sah and Kao, Science Repts. Natl. Tsing Hua Univ. (A) **3**, 525 (1936) [C. A. **31**, 3889 (1937)].

[11] McRae and Vining, Can. J. Research **6**, 409 (1932).

[12] Kindler, Brandt, and Gehlhaar, Ann. **511**, 209 (1934).

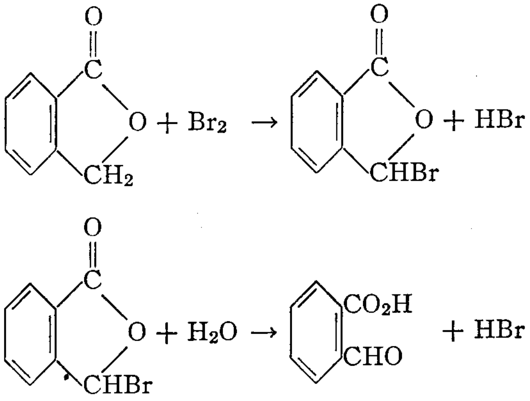
[13] Kindler, Ber. **57**, 775 (1924).

[14] Hartung, J. Am. Chem. Soc. **50**, 3373 (1928).

[15] Ing and Manske, J. Chem. Soc. **1926**, 2348.

[16] Galat and Elion, J. Am. Chem. Soc. **61**, 3585 (1939).

PHTHALALDEHYDIC ACID



Submitted by R. L. Shriner and F. J. Wolf.
Checked by Lee Irvin Smith, R. T. Arnold, and Walter Frajola.

1. Procedure

(*A*) *2-Bromophthalide.*—The apparatus shown in Fig. 6 is used for the bromination. Flasks A and B are of 200-cc. capacity. Bromine is introduced by means of a current of carbon dioxide, which passes through mineral oil or sulfuric acid in the bubble counter, then through the bromine in flask B, and finally through the drying tower. The tower is conveniently made from a condenser jacket and is filled with anhydrous calcium chloride. Flask A is surrounded by an oil bath and is equipped with a thermometer, an outlet tube of wide bore connected to a gas absorption trap, and a gas inlet tube having an inside diameter of 2 mm. The inlet tube reaches to the bottom of the flask.

---

[17] Curtius and Jordan, J. prakt. Chem. (2) **64**, 308 (1901).

[18] Bischler and Napieralski, Ber. **26**, 1905 (1893).

In the reaction flask A is placed 134 g. (1 mole) of phthalide (Note 1). In flask B is placed 160 g. (53.5 cc., 1 mole) of bromine. The oil bath is maintained at 140–155°, and the stream of carbon dioxide is started when the temperature of the phthalide has reached 140°. The temperature inside flask A is maintained at 135–150° (oil bath 140–155°) during the course of the reaction (Note 2). Carbon dioxide is introduced at such a rate that no bromine vapor is observed in the outlet tube (5–8 bubbles per second). The stream of carbon dioxide is continued for thirty minutes after all the bromine color has disappeared from the train. The reaction is complete in ten to thirteen hours, depending upon the rate at which the bromine has been introduced into the reaction mixture.

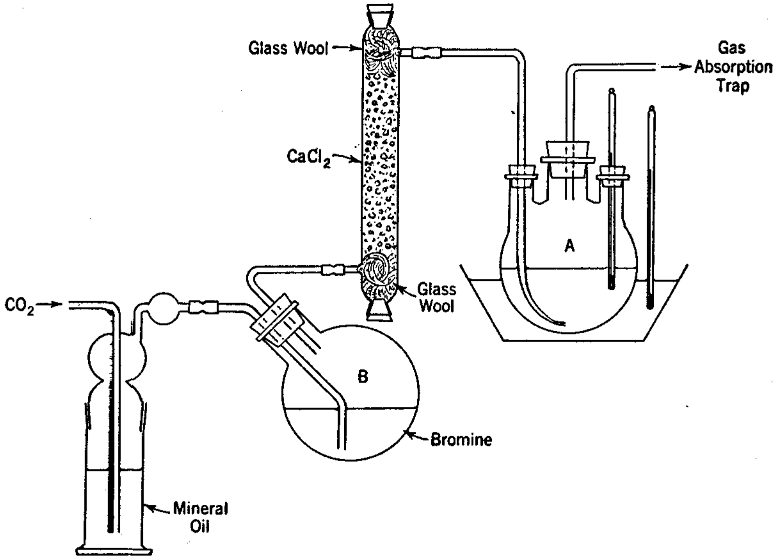


Fig. 6.

While still warm, the reaction mixture is transferred to a 250-cc. modified Claisen flask (Org. Syn. Coll. Vol. **1, 1941,** 130) fitted for distillation under reduced pressure. Any hydrogen bromide remaining in the reaction mixture is removed by heating at 120° under the vacuum of a water pump. The product is then distilled under reduced pressure. The fore-run of less than 15 g.

is largely phthalide (Note 3). The 2-bromophthalide, which distils at 138–142°/4 mm. (128–132°/2 mm.), weighs 175–178 g. (82–83 per cent of the theoretical amount based on the phthalide) (Note 4). It is water-clear and solidifies to a solid which melts at 69–73°.

The distilled product is pure enough for use in the subsequent hydrolysis, but it may be purified by recrystallization from 100 cc. of carbon tetrachloride. Upon cooling, 100 g. of pure 2-bromophthalide melting at 75° is obtained. An additional 30 to 40 g. of slightly yellow material is obtained by concentrating the mother liquor.

(*B*) *Phthalaldehydic Acid.*—The entire distillate is placed in a 500-cc. flask and covered with 230 cc. of water. The flask is equipped with a mechanical stirrer and is heated on a steam cone. The hydrolysis is complete when the layer of 2-bromophthalide has disappeared (about thirty minutes). The reaction mixture is then placed in a refrigerator overnight, during which time the entire mass solidifies. The product is filtered, washed with two 50-cc. portions of ice water, and dried in the air. The yield of crude product melting at 60–65° (Note 5) is 140–160 g.

The crude product is recrystallized from 400 cc. of hot water and dried in the air. The recrystallized product is white, melts at 95–96°, and weighs 97–102 g. (78–83 per cent of the theoretical amount based on the bromo compound or 65–68 per cent based on the phthalide).

2. Notes

1. The phthalide used by the submitters and by the checkers was a commercial product, obtained from E. I. du Pont de Nemours and Company, Wilmington, Delaware. This product is no longer available. Phthalide may be prepared in 82.5 per cent yields by hydrogenation of phthalic anhydride in benzene at 270° under 3000 lb. pressure in the presence of copper chromite [1] or, in yields of 61–71 per cent, from phthalimide according to the procedure given in Org. Syn. **16,** 71; Coll. Vol. **2, 1943,** 526.

---

[1] Austin, Bousquet, and Lazier, J. Am. Chem. Soc. **59**, 864 (1937).

2. At a temperature below 135°, bromination does not take place readily. Above 155°, the reaction mixture becomes considerably darker, and the yield is lower.

3. A change in crystalline structure of the distillate is observed when all the phthalide has been removed.

4. The checkers consistently obtained yields of at least 87 per cent, and in one run the yield of product melting at 78° was 95 per cent.

5. In one run, the checkers obtained 180 g. of product which melted at 67°. This, after recrystallization, melted at 94.5–95° and weighed 121 g. This yield is 84.9 per cent of the theoretical amount based on the bromo compound, or 80 per cent based on the phthalide. The crude product holds water tenaciously, but this is removed by allowing the product to stand in a vacuum desiccator over Drierite.

3. Methods of Preparation

To the methods listed in Org. Syn. **16,** 68 (Coll. Vol. **2, 1943,** 523), may be added the hydrolysis of 2-chlorophthalide; [2] and the action of carbon dioxide and sodium, under pressure, upon *o*-chlorobenzaldehyde.[3] The procedure described is essentially that of Racine.[4]

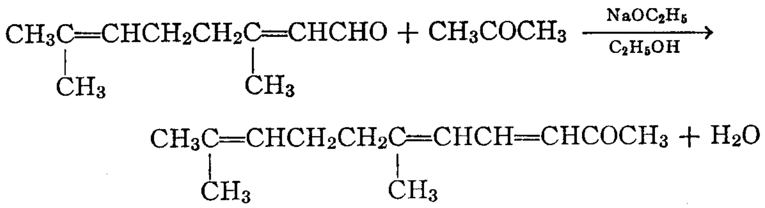
---

[2] Austin and Bousquet, U. S. pat. 2,047,946 [C. A. **30**, 6011 (1936)].

[3] Morton, Le Fevre, and Hechenbleikner, J. Am. Chem. Soc. **58**, 754 (1936).

[4] Racine, Ann. **239**, 79 (1887).

PSEUDOIONONE



$$CH_3\underset{\underset{CH_3}{|}}{C}{=}CHCH_2CH_2\underset{\underset{CH_3}{|}}{C}{=}CHCHO + CH_3COCH_3 \xrightarrow[C_2H_5OH]{NaOC_2H_5}$$

$$CH_3\underset{\underset{CH_3}{|}}{C}{=}CHCH_2CH_2\underset{\underset{CH_3}{|}}{C}{=}CHCH{=}CHCOCH_3 + H_2O$$

Submitted by Alfred Russell and R. L. Kenyon.
Checked by Lee Irvin Smith, W. B. Renfrow, Jr., and Louis E. DeMytt.

1. Procedure

(*A*) *Purification of Citral.*—In a 4-l. bottle are placed 1 l. of water, 1 kg. of crushed ice, 450 g. of anhydrous sodium sulfite (or an equivalent amount of hydrated sodium sulfite), 320 g. of sodium bicarbonate, and 270 g. (304 cc., 1.78 moles) of commercial citral (Note 1). A tightly fitting stopper is securely wired into place, and the bottle is shaken thoroughly for five to six hours. The solution, which contains very little unchanged citral, is extracted twice with 300-cc. portions of ether (Note 2).

A 5-l. round-bottomed flask is fitted with a 1-l. dropping funnel, the mouth of which is connected to a tube passing through the stopper of the flask, and the whole apparatus is rigidly attached to a shaker (Note 3). About one-half of the sulfite solution is placed in the flask and covered with 800 cc. of ether. In the dropping funnel is placed 800 cc. of 10 per cent aqueous sodium hydroxide. Shaking is begun, and when the contents of the flask are thoroughly mixed, the sodium hydroxide solution is admitted in a thin continuous stream over a period of about one hour. After all the sodium hydroxide solution is added, shaking is continued for not longer than five minutes, and the mixture is then poured into a large separatory funnel. The aqueous layer is drawn off and the ether layer is set aside. The aqueous layer is returned to the separatory funnel, covered with 300 cc. of ether, and shaken with

an additional 200 cc. of 10 per cent aqueous sodium hydroxide. After separation, the aqueous layer is extracted once with 150 cc. of ether, and the combined ether extracts are then dried over anhydrous sodium sulfate.

The remaining half of the sulfite solution is subjected to the same treatment, and the total ether extract, after drying, is evaporated on a water bath. The residue is then distilled under reduced pressure, yielding 200–215 g. of almost colorless citral which boils at 84–85°/2 mm. (93–95°/5 mm.).

(*B*) *Pseudoionone.*—In a 2-l. round-bottomed flask, fitted with a mechanical stirrer, a dropping funnel, and a thermometer, are placed 203 g. (230 cc., 1.33 moles) of pure citral and 800 g. (1010 cc., 13.8 moles) of acetone (C.P., dried over anhydrous potassium carbonate). The mixture is cooled to −5° (or below) in an ice-salt bath, vigorous stirring is begun, and there is added through the dropping funnel a cold solution of 9.2 g. (0.4 mole) of sodium in 200 cc. of absolute alcohol. The solution of sodium ethoxide is added at the maximum rate which will permit maintenance of the temperature at −5° or below (rapid dropping). After the addition is complete, stirring is continued for three or four minutes. A solution of 30 g. (0.2 mole) of tartaric acid in 200 cc. of water is added, and the mixture is *immediately* steam-distilled to remove the excess acetone. A white precipitate may form when the tartaric acid is added, but this disappears during the steam distillation (Note 4). The mixture in the distilling flask is cooled in an ice bath, and the upper layer (about 380 cc.) is then removed and refluxed vigorously for five to six hours with three times its volume of 25 per cent aqueous sodium bisulfite.

After cooling, the mixture is extracted twice with 200-cc. portions of ether to remove any material that has not reacted with the bisulfite. One-half of the aqueous solution is placed in the shaking extractor together with 650 cc. of ether. The calculated amount of 10 per cent aqueous sodium hydroxide (one mole of sodium hydroxide per mole of sodium bisulfite used) is now added as described for purification of the citral. Shaking is continued for fifteen minutes after the addition of the alkali is complete

(Note 5). The layers are separated (Note 6); the aqueous layer is returned to the separatory funnel and covered with 200 cc. of ether. After 100 cc. of 10 per cent sodium hydroxide has been added, the mixture is vigorously shaken, and then the aqueous layer is removed and extracted with another 200-cc. portion of ether. The two ether extractions, one with addition of sodium hydroxide and one without, are repeated. The second half of the bisulfite solution is subjected to the same treatment as the first half, and all the ether extracts are combined (Note 7) and dried over anhydrous sodium sulfate. The ether is removed on the water bath, and the residual yellow-green oil is distilled under reduced pressure, yielding 120–130 g. (45–49 per cent of the theoretical amount, based upon 210 g. of pure citral) of pale yellow pseudoionone, boiling at 114–116°/2 mm. (124–126°/4 mm.).

2. Notes

1. Unless a pure pseudoionone free from isomers is wanted, it is not necessary to perform the elaborate purification of citral, or the elaborate purification of pseudoionone. The checkers, using commercial citral obtained from the Florasynth Laboratories, Inc., New York, found 90 per cent of it to boil over a three-degree range between 100 and 103°/7 mm. Using a solution of 203 g. of this distilled citral in 1 l. of commercial acetone, the checkers proceed as follows: The citral solution is cooled in an ice-salt bath to $-10°$, and one-fourth of the solution is forced, by dry compressed air, into a 500-cc. round-bottomed, three-necked flask, fitted with a stirrer, dropping funnel, and an adjustable outlet tube long enough to reach to the bottom of the flask. The temperature is maintained at 0° to $-5°$ while one-fourth of a solution of 9.2 g. of sodium in 200 cc. of absolute alcohol is added dropwise. After all the base is added, stirring is continued for three minutes, and then the reaction mixture is forced over into one-fourth of a solution of 33 g. of tartaric acid in 200 cc. of water. The elapsed time, from the addition of the first drop of base until the mixture is forced into the acid, is fourteen minutes. The condensation is repeated three times more, and the combined acidified mixture is steam-distilled until 1 l. of distillate is obtained. It is important that the solution should remain slightly acid during steam distillation. The material remaining in the flask is cooled, the layers are separated, and the aqueous layer is extracted with ether. The combined organic layers are dried over sodium sulfate and then distilled. The yield of pseudoionone boiling at 123–124°/2.5 mm. is 177.8 g. (70 per cent of the theoretical amount based upon the citral). By carrying out the condensation in small batches, the temperature is much more easily controlled and the yields are greatly improved. This pseudoionone, when catalytically reduced in a bomb, gave hexahydropseudoionol, boiling at 124–128°/10 mm., in a yield of more than 90 per cent of the theoretical amount.

2. In handling these large quantities, much better results are obtained if extractions, etc., are carried out in portions.

3. A pressure outlet may be used, but the arrangement outlined here is quite sufficient. Citral and pseudoionone are both rapidly polymerized by contact with aqueous sodium hydroxide. This apparatus continuously provides an intimate mixture of the sulfite solution with the ether. On decomposition, the free carbonyl compound is immediately extracted and prolonged contact with sodium hydroxide is thus avoided.

4. From the completion of addition of the sodium ethoxide solution to the steam distillation, fast work is advantageous, and all equipment should be in readiness before the addition is started. Allowing the solution to stand before addition of the tartaric acid may cause darkening and formation of gummy material. It is important that the solution should remain slightly acid during the steam distillation.

5. The pseudoionone bisulfite addition product, unlike that of citral, apparently decomposes rather slowly; if the separation is made too soon, some undecomposed bisulfite compound is left in solution. This is later decomposed and, in contact with the alkali, polymerizes to a dark red gum.

6. The checkers obtained three layers at this point—a lower aqueous layer, a dark red oily layer, and the upper ether layer. The ether layer was removed and the other two layers were re-

turned for further treatment. The dark oily layer gradually disappeared during the subsequent extractions.

7. The checkers washed these ether extracts with a little water to ensure removal of any basic material.

3. Methods of Preparation

Pseudoionone has been prepared by the condensation of citral and acetone, using as condensing agent a saturated solution of barium hydroxide,[1] a solution of sodium ethoxide in alcohol,[2,3] or metallic sodium.[4] Impure products have been obtained from citral and acetone, using alcoholic sodium hydroxide as the condensing agent,[4] and by treatment of oil of lemon grass and acetone with bleaching powder, cobalt nitrate, and alcohol.[5,6,7]

---

[1] Tiemann and Krüger, Ber. **26**, 2692 (1893).

[2] Stiehl, J. prakt. Chem. (2) **58**, 84 (1898).

[3] Tiemann, Ber. **32**, 115 (1899).

[4] Hibbert and Cannon, J. Am. Chem. Soc. **46**, 119 (1924).

[5] Ziegler, J. prakt. Chem. (2) **57**, 493 (1898).

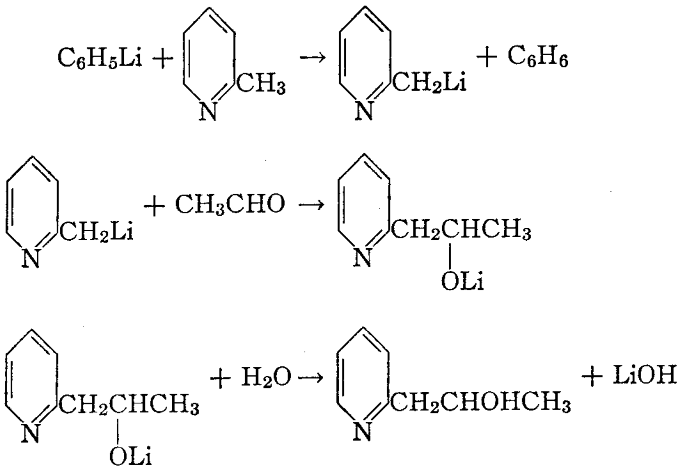
[6] Tiemann, Ber. **31**, 2313 (1898).

[7] Haarmann and Reimer Company, Ger. pat. 73,098 [Frdl. **3**, 889 (1890–94)].

1-(α-PYRIDYL)-2-PROPANOL

[2-(β-Hydroxypropyl)-pyridine]

$$C_6H_5Br + 2Li \rightarrow C_6H_5Li + LiBr$$



Submitted by L. A. Walter.
Checked by C. F. H. Allen and James Van Allan.

1. Procedure

While a current of dry nitrogen is passed through the apparatus, 400 cc. of dry ether and 6.9 g. (1 gram atom) of lithium (in small pieces) (Note 1) are placed in a 1-l. three-necked flask fitted with a dropping funnel, mechanical stirrer, and reflux condenser protected from moisture. The stirrer is started, and 10–15 cc. of a solution of 79 g. (0.5 mole) of dry bromobenzene in 100 cc. of dry ether is added from the dropping funnel. The reaction usually starts immediately; if not, the flask may be warmed, and the remainder of the mixture is then added at such a rate that the ether refluxes gently. The mixture is stirred until the lithium disappears (Note 2).

Forty-six grams (0.5 mole) of α-picoline (Note 3) is then added, and the mixture is stirred at room temperature for one hour, during which time the dark red solution of picolyllithium is formed. The flask is then immersed in an ice-salt bath, and when the mixture is thoroughly chilled the nitrogen train is disconnected. Then 20 g. of dry acetaldehyde in 50 cc. of dry ether (Note 4) is slowly dropped into the mixture over a period of twenty minutes. The red color entirely disappears. After fifteen minutes, 100 cc. of water is slowly added and then 100 cc. of concentrated hydrochloric acid (sp. gr. 1.2). The aqueous layer is removed and poured, with stirring, into a warm solution of 300 g. of sodium carbonate decahydrate in 100 cc. of water (Note 5). The crude reaction product separates as an oil and is taken up in 300 cc. of chloroform. The precipitated lithium carbonate is filtered, transferred to a beaker, and stirred with four 200-cc. portions of chloroform. The chloroform extracts are decanted or filtered, and all the chloroform solutions are combined (Note 6). The chloroform is removed by distillation, and the residue is fractionated under reduced pressure through a good column. The 1-(α-pyridyl)-2-propanol boils sharply at 116–117°/17 mm. (124–125°/20 mm.). A small fore-run and a considerable amount of high-boiling residue are discarded. The yield is 30–34 g. (44–50 per cent of the theoretical amount based on the α-picoline) (Notes 7 and 8). This product darkens on exposure to light, and it should be preserved in a brown glass bottle.

2. Notes

1. The most unsatisfactory operation of this preparation is cutting the lithium. It may be finely divided by rubbing the metal against a coarse wood rasp and allowing the filings to drop through a large paper funnel directly into the ether while a rapid stream of dry nitrogen is passed through the flask. This procedure is most convenient when a large piece of lithium is available and the amount of filings can be determined by the loss in weight. Larger pieces, cut with a knife (Org. Syn. **18,** 71; Coll. Vol. **2, 1943,** 518), can be used equally well (Note 2). Bartlett, Swain, and Woodward [1] have published a convenient method for the preparation of lithium sand.

2. The time depends upon the size of the pieces; the solution may be stirred for twenty-four hours without affecting the yield.

3. The submitters used α-picoline, b.p. 128–130°, obtained from the Barrett Company. The checkers used practical α-picoline, b.p. 128–134°, freshly distilled under reduced pressure. Samples of picoline containing water should be carefully fractionated to remove the water as the α-picoline-water azeotrope, b.p. 93°.

4. Alternatively, the acetaldehyde may be distilled into the flask through the nitrogen inlet. During this operation, the outlet must be kept well above the surface, to prevent clogging. The introduction of aldehyde is stopped when the red color has disappeared.

5. A solution of 111 g. of anhydrous sodium carbonate in 150 cc. of water may be substituted.

6. If sodium hydroxide is used to liberate the amino alcohol from its salt, extraction with chloroform produces unworkable emulsions.

7. Equally good yields of 1-(α-pyridyl)-3-propanol, b.p. 116–118°/4 mm., may be obtained by using ethylene oxide in place of acetaldehyde.

8. The submitters obtained yields as high as 43 g. (60 per cent of the theoretical amount).

3. Methods of Preparation

This procedure is based upon that of Ziegler.[2] 1-(α-Pyridyl)-2-propanol has also been prepared in poor yields (4–6 per cent) by heating α-picoline with aqueous acetaldehyde in sealed tubes.[3,4]

---

[1] Bartlett, Swain, and Woodward, J. Am. Chem. Soc. **63**, 3230 (1941).

[2] Ziegler and Zeiser, Ann. **485**, 174 (1931).

[3] Ladenburg, Ann. **301**, 140 (1898).

[4] Meisenheimer and Mahler, Ann. **462**, 308 (1928).

trans-STILBENE

$$C_6H_5CHOHCOC_6H_5 + 4H \xrightarrow[HCl]{Zn(Hg)_x} C_6H_5CH{=}CHC_6H_5 + 2H_2O$$

Submitted by R. L. Shriner and Alfred Berger.
Checked by W. E. Bachmann and Charles E. Maxwell.

1. Procedure

In a 4-l. beaker, equipped with a powerful mechanical stirrer which reaches nearly to the bottom, are placed 500 cc. of water and 50 g. of mercuric chloride. The stirrer is started, and 200 g. (3.06 gram atoms) of zinc dust (Note 1) is rapidly sifted into the suspension. Stirring is continued until the mercuric chloride dissolves (about twenty to thirty minutes). The zinc is then allowed to settle, the supernatant liquid is removed by decantation, and the amalgam is filtered and washed with 200 cc. of water. The zinc amalgam is returned to the beaker, which is now surrounded by an ice bath, and 500 cc. of 95 per cent ethyl alcohol and 100 g. (0.48 mole) of benzoin (Org. Syn. Coll. Vol. **1**, **1941**, 94) are added. The stirrer is started, and 500 cc. of concentrated hydrochloric acid is added through a dropping funnel at such a rate that addition is complete in about two hours; throughout the reaction the temperature is maintained below 15°. Stirring is continued for about two hours more.

About 2 l. of cold water is added to the reaction mixture, and the insoluble material is collected on a Büchner funnel. The precipitate is transferred to a 2-l. beaker and extracted with two 600-cc. portions of hot ethyl alcohol. The combined extracts, on cooling, deposit long needles of stilbene which weigh 55–59 g. and melt at 116–121°. These are filtered with suction and are recrystallized from 600 cc. of 95 per cent ethyl alcohol. The yield is 45–48 g. (53–57 per cent of the theoretical amount) of colorless needles melting at 123–124°.

2. Note

1. The zinc dust used was obtained from J. T. Baker and Company.

3. Methods of Preparation

The procedure described is essentially that of Ballard and Dehn.[1] Stilbene has also been prepared by reduction of desoxybenzoin,[2a] benzaldehyde,[2b] and benzil; [2a, 2c] by dehydrogenation of ethyl benzene,[3a] toluene,[3a, 3b, 3c] and bibenzyl; [3b, 3d] by alkaline reduction of phenylnitromethane,[4a] phenylnitroacetonitrile,[4a] and desoxybenzoin; [4b] by distillation of benzyl sulfone,[5a] benzyl sulfide,[5a, 5b] calcium cinnamate,[5c] cinnamic acid,[5d] phenyl cinnamate,[5e, 5f] and diphenyl fumarate; [5e] by dehydrohalogenation of α,α′-dichlorobibenzyl [6a] and benzyl chloride; [6b] by dehalogenation of α,α,α′,α′-tetrachlorobibenzyl [7a] and benzal chloride; [7b] by the coupling of cinnamic acid and phenyldiazonium chloride; [8] by dehydration of benzylphenylcarbinol,[6a, 9a] benzyl ether,[9b] and benzyl alcohol.[9b, 9c] The diazonium coupling reaction [8] appears to have the widest applicability for the synthesis of substituted stilbenes.

---

[1] Ballard and Dehn, J. Am. Chem. Soc. **54**, 3969 (1932).

[2] (*a*) Irvine and Weir, J. Chem. Soc. **91**, 1384 (1907); (*b*) Williams, Jahresb. **1867**, 672; Barbaglia and Marquardt, Gazz. chim. ital. **21**, 195 (1891); Baumann and Klett, Ber. **24**, 3307 (1891); Law, J. Chem. Soc. **91**, 748 (1907); Schepps, Ber. **46**, 2564 (1913); (*c*) Jena and Limpricht, Ann. **155**, 89 (1870); Blank, Ann. **248**, 1 (1888).

[3] (*a*) Meyer and Hofmann, Monatsh. **37**, 681 (1916); (*b*) Behr and van Dorp, Ber. **6**, 753 (1873); Aronstein and van Nierop, Rec. trav. chim. **21**, 448 (1902); (*c*) Lorenz, Ber. **7**, 1096 (1874); Ber. **8**, 1455 (1875); Lange, Ber. **8**, 502 (1875); Michaelis and Lange, Ber. **8**, 1313 (1875); Michaelis and Paneck, Ann. **212**, 203 (1882); (*d*) Dreher and Otto, Ann. **154**, 171 (1870); Barbier, Compt. rend. **78**, 1769 (1874); Radziszewski, Ber. **8**, 756 (1875); Kade, J. prakt. Chem. (2) **19**, 461 (1879).

[4] (*a*) Wislicenus and Endes, Ber. **36**, 1194 (1903); (*b*) Sudborough, J. Chem. Soc. **67**, 601 (1895).

[5] (*a*) Fromm and Achert, Ber. **36**, 534 (1903); (*b*) Märcker, Ann. **136**, 75 (1865); Limpricht and Schwanert, Ann. **145**, 330 (1868); Forst, Ann. **178**, 370 (1875); (*c*) Engler and Leist, Ber. **6**, 254 (1873); (*d*) von Miller, Ann. **189**, 338 (1877); (*e*) Anschütz, Ber. **18**, 1945 (1885); (*f*) Skraup and Beng, Ber. **60**, 942 (1927).

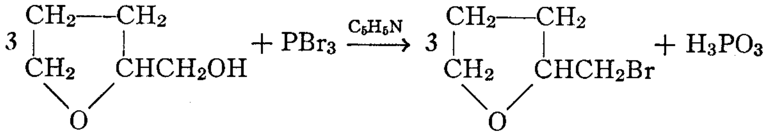
[6] (*a*) Meisenheimer and Heim, Ann. **355**, 249 (1907); (*b*) Tschitschibabin, J. Russ. Phys. Chem. Soc. **34**, 130 (1902); Loeb, Ber. **36**, 3059 (1903); Acree, Am. Chem. J. **29**, 593 (1907).

[7] (*a*) Liebermann and Homeyer, Ber. **12**, 1971 (1879); (*b*) Limpricht, Ann. **139**, 303 (1866); Lippmann and Hawliczek, Jahresb. **1877**, 405.

[8] Meerwein, Büchner, and van Emster, J. prakt. Chem. (2) **152**, 237 (1939).

TETRAHYDROFURFURYL BROMIDE

[Furan, 2-(bromomethyl)tetrahydro-]



Submitted by L. H. Smith.
Checked by John R. Johnson and R. L. Sawyer.

1. Procedure

In a 500-cc. three-necked flask, fitted with a mechanical stirrer, thermometer, separatory funnel, and calcium chloride tube, are placed 96 g. (56.5 cc., 0.36 mole) of redistilled phosphorus tribromide (b.p. 174–175°/740 mm.) and 50 cc. of dry benzene. From the separatory funnel, 15 g. of dry pyridine is added with stirring over a period of fifteen minutes. The flask is then surrounded by an ice-salt mixture, and the contents are cooled to −5°. A mixture of 102 g. (1 mole) of redistilled tetrahydrofurfuryl alcohol (b.p. 79–80°/20 mm.) and 5 g. of dry pyridine (total pyridine, 20 g., 0.25 mole) is added slowly from the dropping funnel with stirring over a period of four hours. During this time the internal temperature is kept at −5° to −3°. Stirring is continued for one hour longer, and the cooling bath is then allowed to warm up to room temperature.

The mixture is allowed to stand for twenty-four to forty-eight hours (Note 1) and is then transferred to a 500-cc. Claisen flask.

---

[9] (*a*) Limpricht and Schwanert, Ann. **155**, 59 (1870); Hell, Ber. **37**, 453 (1904); (*b*) Szperl, Chemik Polski **15**, 23 (1917) [C. A. **13**, 2865 (1919)]; (*c*) Guerbet, Compt. rend. **146**, 298 (1908); Bull. soc. chim. (4) **3**, 500 (1908).

Two small portions of benzene are used for rinsing the flask. The benzene is distilled by reducing the pressure gradually to about 60 mm. and heating the flask gently in an oil bath (not above 90°). After the benzene has been removed, the pressure is reduced to 5–10 mm. and the bath is heated slowly to 150–155° until no more material distils (Note 2). The crude distillate (110–126 g.) is redistilled through an efficient column, and the purified tetrahydrofurfuryl bromide is collected at 69–70°/22 mm. (61–62°/13 mm., 49–50°/4 mm.) (Note 3). The yield is 90–102 g. (53–61 per cent of the theoretical amount).

2. Notes

1. The yields were slightly higher when the mixture was allowed to stand for forty-eight hours.
2. Most of the material distils while the bath is at 100–120°. When the bath reaches 155–160° the mixture begins to decompose and white fumes are copiously evolved.
3. Unless a good fractionation is obtained, the material will contain some pyridine and will discolor in a few days. Carefully fractionated material will remain colorless for two months or more. A considerable amount of dark, viscous residue remains in the distilling flask.

3. Methods of Preparation

Tetrahydrofurfuryl bromide has been obtained in low yields by the action of hydrobromic acid, or of phosphorus tribromide, on the corresponding alcohol.[1] The yield is improved markedly by use of phosphorus tribromide and pyridine.[2, 3] The bromide has also been prepared by the action of potassium hydroxide on 4,5-dibromopentanol-1.[4]

---

[1] Dox and Jones, J. Am. Chem. Soc. **50**, 2033 (1928).

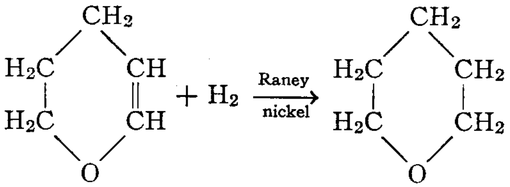
[2] Paul, Bull. soc. chim. (4) **53**, 417 (1933).

[3] Robinson and Smith, J. Chem. Soc. **1936**, 195.

[4] Paul, Ann. chim. (10) **18**, 303 (1932).

TETRAHYDROPYRANE

(Pyran, tetrahydro-)



Submitted by D. W. ANDRUS and JOHN R. JOHNSON.
Checked by NATHAN L. DRAKE and CHARLES M. EAKER.

1. Procedure

THE hydrogenation is carried out in a catalytic hydrogenation apparatus similar to that described by Adams and Voorhees (Org. Syn. Coll. Vol. **1**, **1941**, 61). Raney nickel catalyst (Org. Syn. **21**, 15) is washed with ether three times on a Büchner funnel, then 8 g. of it is transferred under ether to the hydrogenation bottle. The bottle is fitted with a rubber stopper bearing a small dropping funnel and a glass tube that leads to one arm of a three-way stopcock. The other arms of the stopcock are connected respectively to a water pump and a source of inert gas (Note 1) in such a way that the ether can be pumped off and the bottle can then be filled with the inert gas. When this has been done, 50.5 g. (0.6 mole) of dihydropyrane (p. 25) is introduced through the dropping funnel.

The bottle is connected to the hydrogenation apparatus and alternately evacuated and filled with hydrogen twice. Hydrogen is then admitted to the system until the pressure gauge reads 40 lb. The shaker is started, and the pressure drops to the theoretical value for absorption of 0.6 mole in 15–20 minutes; beyond this point shaking causes no further absorption of hydrogen (Note 2). The bottle is removed and the nickel catalyst is allowed to settle. The tetrahydropyrane is decanted, but enough is left in the bottle to cover the catalyst (Note 3). The product boils at 85–86°, but it need not be distilled for many purposes. The yield is practically quantitative.

2. Notes

1. Purified nitrogen is a convenient inert gas, but natural gas containing no oxygen, or sulfur compounds, is equally suitable; the checkers used hydrogen.

2. As the catalyst becomes older, it loses its activity somewhat and a longer time is required for the pressure to drop to the theoretical value.

3. The same catalyst may be used many times. For the next run the dihydropyrane is merely poured into the bottle containing the catalyst which is wet with the product of the previous run.

3. Methods of Preparation

Tetrahydropyrane has been prepared by hydrogenation of dihydropyrane using a platinum black catalyst;[1] by heating pentamethylene bromide with water;[2,3] or with water and zinc oxide in a sealed tube;[4] or by heating pentamethylene glycol with three volumes of 60 per cent sulfuric acid in a pressure tube.[5]

[1] Paul, Bull. soc. chim. (4) **53**, 1489 (1933).

[2] Hochstetter, Monatsh. **23**, 1073 (1902).

[3] Demjanow, J. Russ. Phys. Chem. Soc. **45**, 169 (1913) [C. A. **7**, 2226 (1913)].

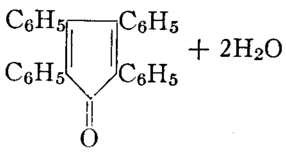
[4] Clarke, J. Chem. Soc. **101**, 1802 (1912); Allen and Hibbert, J. Am. Chem. Soc. **56**, 1398 (1934).

[5] Demjanow, J. Russ. Phys. Chem. Soc. **22**, 389 (1890) [J. Chem. Soc. **62**, 1292 (1892)].

TETRAPHENYLCYCLOPENTADIENONE

(Cyclopentadienone, tetraphenyl-)

$$C_6H_5COCOC_6H_5 + (C_6H_5CH_2)_2CO \xrightarrow[\text{Alcohol}]{\text{KOH}}$$



Submitted by John R. Johnson and Oliver Grummitt.
Checked by Nathan L. Drake and Stuart Haywood.

1. Procedure

In a 500-cc. round-bottomed flask, 21 g. (0.1 mole) of benzil (Org. Syn. Coll. Vol. 1, **1941**, 87) and 21 g. (0.1 mole) of dibenzyl ketone (Note 1) are dissolved in 150 cc. of hot alcohol. The flask is fitted with a reflux condenser, the temperature of the solution is raised nearly to the boiling point, and a solution of 3 g. of potassium hydroxide in 15 cc. of alcohol is added slowly in two portions through the condenser. When the frothing has subsided the mixture is refluxed for fifteen minutes and then cooled to 0°. The dark crystalline product is filtered with suction and washed with three 10-cc. portions of 95 per cent alcohol. The product melts at 218–220° and weighs 35–37 g. (91–96 per cent of the theoretical amount) (Note 2).

2. Notes

1. The dibenzyl ketone should melt at 34–35°.
2. This product is sufficiently pure for most purposes. It may be crystallized from a mixture of alcohol and benzene using 155–160 cc. solvent for 5 g. of tetraphenylcyclopentadienone; the melting point of the recrystallized material is 219–220°.

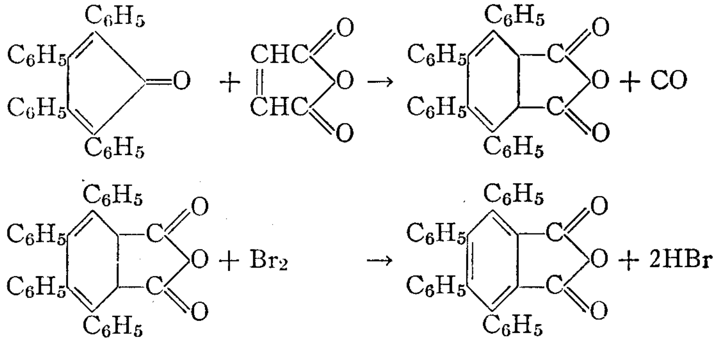
---

3. Methods of Preparation

Tetraphenylcyclopentadienone has been prepared by the action of phenylmagnesium bromide on benzaldiphenylmaleide,[1] and by reduction, dehydration, and oxidation of the methylenedesoxybenzoin obtained by condensing formaldehyde with desoxybenzoin.[2] The present procedure is essentially that of Dilthey.[3]

TETRAPHENYLPHTHALIC ANHYDRIDE

(Phthalic anhydride, tetraphenyl-)



Submitted by Oliver Grummitt.
Checked by Nathan L. Drake and Charles M. Eaker.

1. Procedure

An intimate mixture of 35 g. (0.094 mole) of tetraphenylcyclopentadienone (p. 92) and 9.3 g. (0.095 mole) of maleic anhydride is placed in a 200-cc. round-bottomed flask (Note 1), and to it is added 25 cc. of bromobenzene. After the mixture has been refluxed gently for three and one-half hours (Note 2), it is cooled

---

[1] Lowenbein and Uhlich, Ber. **58**, 2662 (1925).

[2] Ziegler and Schnell, Ann. **445**, 266 (1925).

[3] Dilthey and Quint, J. prakt. Chem. (2) **128**, 146 (1930); Ger. pat. 575,857 [Frdl. **20**, 503 (1933); C. A. **28**, 1356 (1934)].

(Note 3), a solution of 7 cc. of bromine in 10 cc. of bromobenzene is added through the condenser, and the flask is shaken until the reagents are thoroughly mixed. After the first exothermic reaction has subsided, the mixture is refluxed gently for three hours (Note 4). The flask is then immersed in a cooling bath and the temperature of the mixture is held at 0–10° for two or three hours. The mixture is filtered with suction, and the crystalline product is washed three times with 10-cc. portions of petroleum ether (b.p. 60–68°). After the product has been dried in the air, it weighs 37–38 g. (87–89 per cent of the theoretical amount) and melts at 289–290°. It is light brown in color, but when pulverized it is almost colorless. The filtrate, when diluted with an equal volume of petroleum ether and cooled to 0–10°, yields an additional 2–3 g. of a less pure product which melts at 285–288°. The impure material may be purified by recrystallization from benzene, using 8–9 cc. of benzene per gram of solid (Note 5).

2. Notes

1. Ground-glass equipment is preferred; corks are attacked by the bromine used later.
2. The operation should be carried out in a hood because of the carbon monoxide evolved.
3. The tetraphenyldihydrophthalic anhydride may be isolated at this point in practically quantitative yields by cooling the mixture, filtering with suction, and washing the solid with three 10-cc. portions of petroleum ether (b.p. 60–68°). The yield is 41–42 g.; the product melts at 235–240°.
4. This operation should also be performed in a hood, or the top of the condenser should be connected to a suitable trap (Org. Syn. Coll. Vol. **1, 1941,** 97; Coll. Vol. **2, 1943,** 4).
5. The crystallized product must be dried at 110° for one to one and a half hours; otherwise benzene, possibly benzene of crystallization, will be retained by the solid indefinitely.

3. Methods of Preparation

Tetraphenylphthalic anhydride has been prepared by condensation of tetraphenylcyclopentadienone and maleic anhydride in nitrobenzene,[1] followed by dehydrogenation of the tetraphenyldihydrophthalic anhydride with sulfur.[2,3]

TRIBIPHENYLCARBINOL

[Carbinol, tris-(4-phenylphenyl-)]

$$3C_6H_5C_6H_4Cl(p) + (C_2H_5O)_2CO + 6Na \rightarrow (p\text{-}C_6H_5C_6H_4)_3CONa + 3NaCl + 2NaOC_2H_5$$

$$(p\text{-}C_6H_5C_6H_4)_3CONa + H_2O \rightarrow (p\text{-}C_6H_5C_6H_4)_3COH + NaOH$$

Submitted by A. A. Morton, J. R. Myles, and W. S. Emerson.
Checked by R. L. Shriner, Joseph Dec, and J. Harkema.

1. Procedure

In a 3-l. three-necked round-bottomed flask, equipped with a mercury-sealed stirrer and a 12-bulb reflux condenser, are placed 188.5 g. (1 mole) of *p*-chlorobiphenyl (Note 1), 47.2 g. (0.4 mole) of ethyl carbonate (Note 2), and 1.5 l. of anhydrous, thiophene-free benzene. The side tube is closed with a cork, stirring is begun, and the mixture is heated by means of a hot plate (Note 3). As soon as the mixture begins to boil, 2 g. of powdered sodium (Note 4) is added. The reaction starts in one or two minutes, as indicated by more vigorous refluxing and a change in color from yellow to brown (Note 5). Powdered sodium is then introduced in small portions, over a period of one hour, until an additional 28 g. has been added (total amount of sodium, 30 g.). The reaction mixture is refluxed and vigorously stirred (Note 6) for two hours.

---

[1] Dilthey, Schommer, and Trosken, Ber. **66**, 1627 (1933).

[2] Dilthey, Thewalt, and Trosken, Ber. **67**, 1959 (1934).

[3] Allen and Sheps, Can. J. Research **11**, 171 (1934).

When the mixture has cooled somewhat, 75 to 100 cc. of absolute alcohol is added. After all the particles of sodium have reacted, 500 cc. of water is added, the condenser is arranged for downward distillation, and the benzene and unchanged *p*-chlorobiphenyl are removed by distillation from a steam bath (Note 7). The crude product remaining in the flask is separated by filtration, washed with 100–200 cc. of water, and pressed as dry as possible. The solid is dissolved in 600 cc. of xylene in a 1-l. distilling flask, and the solution is subjected to distillation until 25 to 50 cc. of distillate (xylene and water) has been collected. The solution is cooled somewhat, 1 to 2 g. Norite is added, and then the mixture is boiled for five minutes. The hot solution is filtered rapidly and the filtrate is cooled. The product is collected by filtration, washed with 25 to 50 cc. of cold xylene then with 200 cc. of petroleum ether, and dried. The tribiphenylcarbinol forms small white crystals which melt at 207–208°. The product weighs 57–65 g. (35–40 per cent of the theoretical amount) (Note 8).

2. Notes

1. Technical *p*-chlorobiphenyl was purified by recrystallizing 300 g. of it from 750 cc. of petroleum ether. The recovery was 240–250 g.

2. Technical ethyl carbonate was washed successively with 10 per cent aqueous sodium carbonate and saturated calcium chloride solution. It was then dried with magnesium sulfate and distilled. The fraction boiling at 124–125° was used.

3. A hot plate should be used to reduce the fire hazard. All flames in the vicinity should be extinguished.

4. The powdered sodium is prepared by melting 30 g. of the clean metal under 1 l. of dry xylene. The mixture is then stirred vigorously with a metal stirrer until the sodium is powdered.

5. If anhydrous reagents are used and the benzene solution is boiling, the reaction starts immediately. The reaction must start before more sodium is added.

6. The stirring must be sufficiently vigorous to prevent caking on the sides of the flask.

7. Unchanged *p*-chlorobiphenyl steam-distils along with the benzene. It is essential that it be removed, since a pure product is difficult to obtain by crystallization if unchanged chloro compound is present.

8. Better yields may be obtained in small-scale preparations if sodium chips are used. A solution of 19 g. of *p*-chlorobiphenyl, 5 g. of ethyl carbonate, and 50 cc. of anhydrous thiophene-free benzene is heated on a steam bath until refluxing begins. During half an hour 5 g. of sodium, cut into particles about 0.5 mm. square and 2 mm. thick, is dropped through the condenser. After the mixture has refluxed for twelve hours, it is decomposed and the product is isolated as described above, but with one-tenth the amounts of solvents. The yields range from 7 to 9 g. (47 to 55 per cent), but the long period of refluxing required and the tedious cutting of the sodium chips make this method of value for small-scale preparations only. A large-scale run by this method gave only a 31 per cent yield.

3. Methods of Preparation

Tribiphenylcarbinol has been prepared by the action of 4-xenylmagnesium iodide upon 4,4′-diphenylbenzophenone, or upon the methyl ester of *p*-phenylbenzoic acid;[1] and by the action of *p*-chlorobiphenyl upon ethyl carbonate in the presence of powdered sodium[2] or sodium wire.[3]

[1] Schlenk, Ann. **368**, 295 (1909).

[2] Morton and Stevens, J. Am. Chem. Soc. **53**, 4028 (1931); Morton and Emerson, ibid. **59**, 1947 (1937); Morton and Wood, private communication.

[3] Bachmann and Wiselogle, J. Org. Chem. **1**, 372 (1936).

TRIPHENYLCARBINOL

(Carbinol, triphenyl-)

$$2C_6H_5MgBr + C_6H_5CO_2C_2H_5 \rightarrow (C_6H_5)_3COMgBr + MgBrOC_2H_5$$

$$(C_6H_5)_3COMgBr + H_2O \rightarrow (C_6H_5)_3COH + MgBrOH$$

Submitted by W. E. Bachmann and H. P. Hetzner.
Checked by R. L. Shriner and P. L. Southwick.

1. Procedure

In a 2-l. three-necked flask, fitted with a separatory funnel, reflux condenser, and a mercury-sealed stirrer, 27 g. (1.1 gram atoms) of magnesium, 181 g. (122 cc., 1.15 moles) of bromobenzene, and a total of 450 cc. of anhydrous ether (Note 1) are converted into phenylmagnesium bromide by the procedure described in Org. Syn. Coll. Vol. **1, 1941,** 226. Calcium chloride tubes are used to prevent the entrance of moisture through the condenser and the separatory funnel during the addition. In order to dissolve all the magnesium it may be necessary, in some instances, to continue stirring for longer than the prescribed ten minutes after the addition is complete.

To the Grignard solution, 75 g. (71.5 cc., 0.5 mole) of ethyl benzoate (Org. Syn. **10,** 51) in 200 cc. of dry benzene (Note 2) is added at such a rate that the mixture refluxes gently. The flask is cooled in a pan of cold water during the addition, which requires about an hour. After the addition is complete, the mixture is refluxed for an hour on a steam bath. The reaction mixture is cooled in an ice-salt bath and then poured slowly, with constant stirring, into a mixture of 1.5 kg. of cracked ice and 50 cc. of concentrated sulfuric acid. The mixture is stirred at intervals until all the solid which separates at the benzene-water interface has dissolved. If necessary, 50 g. of ammonium chloride is added to facilitate the decomposition of the magnesium salt, and additional benzene may be added if the amount present

is insufficient to dissolve all the product. When the solids have disappeared, the benzene layer is separated and washed, successively, with 200 cc. of water, 200 cc. of a 5 per cent solution of sodium bicarbonate, and finally with 200 cc. of water. The solvents are removed as completely as possible by distillation on a steam bath, and the remaining solution or solid mass is steam-distilled to remove biphenyl and unchanged bromobenzene. The product is filtered, washed with water, and dried. The crude triphenylcarbinol, which weighs 120–125 g., is recrystallized from carbon tetrachloride (4 cc. of solvent per gram of solid). The weight of the first crop of colorless triphenylcarbinol is 110–115 g. (Note 3). A second crop may be obtained by heating the filtrate with a gram of Norite, then concentrating to about 125 cc. and cooling the solution. The total yield of triphenylcarbinol melting at 161–162° is 116–121 g. (89–93 per cent of the theoretical amount) (Note 4).

2. Notes

1. Commercial anhydrous ether, before it is used, should be dried over slices of sodium, and the bromobenzene should be dried by distillation.

2. The benzene may be dried over anhydrous magnesium sulfate.

3. Triphenylcarbinol separates from carbon tetrachloride with solvent of crystallization. The solvent is readily lost on exposure of the crystals to air. The weight mentioned is that of the solvent-free product.

4. Practically the same yield of triphenylcarbinol was obtained from benzophenone and phenylmagnesium bromide; in this reaction only one-half as much Grignard reagent is required as that needed for the reaction with ethyl benzoate. To the cooled Grignard reagent prepared from 13.5 g. (0.55 gram atom) of magnesium, was added a solution of 91 g. (0.5 mole) of benzophenone (Org. Syn. Coll. Vol. **1, 1941,** 95) in 200 cc. of dry benzene at such a rate that the mixture refluxed gently. After the mixture had been refluxed for one hour, the isolation of the triphenylcarbinol was carried out in the manner described above.

3. Methods of Preparation

Triphenylcarbinol has been obtained by the reaction between phenylmagnesium bromide and benzophenone,[1] methyl benzoate,[2] or phosgene;[3] by action of phenylsodium upon benzophenone, benzoyl chloride, ethyl chlorocarbonate, or ethyl benzoate;[4] by hydrolysis of triphenylchloromethane;[5] and by oxidation of triphenylmethane.[6]

TRIPHENYLCHLOROMETHANE

(Methane, chlorotriphenyl-)

(A) From Triphenylcarbinol and Acetyl Chloride

$$(C_6H_5)_3COH + CH_3COCl \rightarrow (C_6H_5)_3CCl + CH_3COOH$$

Submitted by W. E. Bachmann.
Checked by R. L. Shriner and Eldred Welch.

1. Procedure

A mixture of 250 g. of pure triphenylcarbinol (p. 98) and 80 cc. of dry benzene is placed in a 1-l. round-bottomed flask provided with a reflux condenser. The condenser is provided with a calcium chloride tube at the top (Note 1). The mixture is heated on a steam bath; when it is hot, 50 cc. of acetyl chloride (Note 2) is added through the top of the condenser. Heating is continued while the mixture is shaken vigorously. In about five minutes all the solid triphenylcarbinol disappears and a clear solution results. In the course of ten minutes, an additional 100 cc. of acetyl chloride is added in 10-cc. portions. The solution is then refluxed for one-half hour longer.

The solution is cooled by shaking the flask under running water, and during this operation 200 cc. of petroleum ether (Note 3) is added through the top of the condenser; the triphenylchloromethane separates in sugarlike crystals. The mixture is cooled in an ice bath for an hour or two, and the product is filtered and washed with 100–150 cc. of petroleum ether (Note 4). The colorless solid, after drying in a desiccator over soda-lime and paraffin (Note 5), weighs 212–224 g. (79–83 per cent of the theoretical amount) and melts at 111–112° with slight previous softening. An additional 30–37 g. of colorless material may be obtained by concentrating the filtrate to a volume of about 75 cc. For this purpose, the petroleum ether and acetyl chloride are distilled at ordinary pressure, and the acetic acid under reduced pressure. The warm solution is treated with 2 g. of Norite, filtered, and again warmed with 2 g. of Norite. The mixture is filtered, 50 cc. of petroleum ether is added to the filtrate, and the solution is then cooled in an ice bath. The crystals of triphenylchloromethane are collected on a filter and washed with 70 cc. of cold petroleum ether. This second crop of material is pure white, like the first crop; the solid melts at 110.5–112° with previous softening (Note 6). The total yield is 249–254 g. (93–95 per cent of the theoretical amount).

2. Notes

1. It is best to carry out the reaction under a hood.

2. The acetyl chloride should be of good quality. Good results were obtained with practical acetyl chloride which was distilled just before use.

3. Petroleum ether having a boiling point of 30–60° should be used because it is easily removed from the product.

4. The filtration should be rapid. Triphenylchloromethane is hydrolyzed by moisture in the air.

5. The final product is perfectly colorless and should have no sharp odor. This product is sufficiently pure for most purposes. It may be recrystallized by dissolving it in 100 cc. of hot benzene

---

[1] Acree, Ber. **37**, 2755 (1904).

[2] Ullmann and Münzhuber, Ber. **36**, 406 (1903).

[3] Sachs and Loevy, Ber. **36**, 1588 (1903).

[4] Acree, Am. Chem. J. **29**, 594 (1903).

[5] Meissel, Ber. **32**, 2422 (1899).

[6] Law and Perkin, J. Chem. Soc. **93**, 1637 (1908); Schwarz, J. Am. Chem. Soc. **31**, 848 (1909).

and cooling the solution after diluting it with 200 cc. of petroleum ether. If the product is kept in a bottle, the stopper should be coated with paraffin in order to keep out the moisture of the air.

6. Triphenylbromomethane may be made in a similar manner by substituting acetyl bromide for the acetyl chloride.

(B) From Benzene and Carbon Tetrachloride, by the Friedel-Crafts Reaction

$$3C_6H_6 + CCl_4 + AlCl_3 \longrightarrow (C_6H_5)_3CCl\cdot AlCl_3 + 3HCl$$

$$(C_6H_5)_3CCl\cdot AlCl_3 + xH_2O \xrightarrow{HCl} (C_6H_5)_3CCl + AlCl_3\cdot xH_2O$$

Submitted by C. R. Hauser and Boyd E. Hudson, Jr.
Checked by R. L. Shriner and Flavius W. Wyman.

1. Procedure

A mixture of 2 kg. (2.28 l., 25.6 moles) of dry thiophene-free benzene (Note 1) and 800 g. (470 cc., 5.2 moles) of dry sulfur-free carbon tetrachloride (Note 2) is placed in a 5-l. three-necked flask immersed in an ice bath and equipped with a mercury-sealed mechanical stirrer and a reflux condenser which is connected to a trap for the absorption of hydrogen chloride (Note 3). The third neck of the flask is connected to a 1-l. Erlenmeyer flask by means of short pieces of large-bore (15-mm.) glass and rubber tubing (see Fig. 5, p. 59). In the Erlenmeyer flask is placed 600 g. (4.51 moles) of fresh resublimed aluminum chloride (Note 4). The Erlenmeyer flask is tilted and gently tapped, so that the aluminum chloride is added in small portions to the reaction mixture, and at such a rate that addition is completed in one and one-half to two hours. The reaction mixture is not allowed to reflux during the addition of the aluminum chloride. Fifteen minutes after all the aluminum chloride has been added, the ice bath is removed, and the reaction is allowed to proceed without further cooling. When no further heat is evolved, the mixture is refluxed until the evolution of hydrogen chloride subsides (about two hours). The mixture is then allowed to cool to room temperature.

A 10-l. copper can (22.5 cm. in diameter and 30 cm. deep) (Note 5) is equipped with a powerful mechanical stirrer and a thermometer and is immersed to a depth of 20 cm. in an ice bath. A mixture of 1 l. of thiophene-free benzene and 2 l. of 6 *N* hydrochloric acid is placed in the copper vessel. The above reaction mixture is added to the vigorously stirred contents of the copper can at such a rate that the temperature does not rise above 25° (about two hours is required). When the addition is complete, the reaction flask is rinsed with a little ice water, and the rinsings are added to the hydrolysis mixture. Stirring is continued for ten minutes longer. The benzene layer is decanted, and the aqueous layer is diluted with 1 l. of ice water. The aqueous layer is extracted with 500 cc. of benzene and is discarded. The combined benzene solutions are washed with 250 cc. of ice-cold hydrochloric acid and are dried for two hours in a stoppered flask over 250 g. of anhydrous calcium chloride.

The dried benzene solution is filtered through glass wool into a 5-l. flask fitted with a cork carrying a delivery tube and a thermometer which reaches within 5 cm. of the bottom of the flask. Several boiling chips are added, and the benzene is removed by distillation, slowly towards the last, until the temperature of the boiling residue reaches 120°. The residue is transferred to a 2-l. Erlenmeyer flask with the aid of 40–50 cc. of dry benzene and is cooled to about 40°. Twenty-five cubic centimeters of acetyl chloride (Note 6) is added, and the mixture is heated nearly to the boiling point. The solution is vigorously shaken while it is cooled rapidly to room temperature; it is then chilled in ice water for two hours. The solid triphenylchloromethane is crushed thoroughly with a porcelain spatula and is filtered with suction. The filtrate is set aside, and the crystals are washed with three 300-cc. portions of ligroin (b.p. 70–90°) (Note 7). The solvent is removed from the product by allowing it to stand in a vacuum desiccator over mineral oil or paraffin shavings for twenty-four hours. The crystals are stirred occasionally, and the desiccator is evacuated to 5–10 mm. (Note 8). The light greenish yellow crystals melt at 111–112° and weigh 870–940 g. (69–75 per cent of the theoretical amount based on the aluminum chloride).

Second crops of crystals may be obtained by distilling, separately, the filtrate and washings until the temperature reaches 110° and 100°, respectively, and cooling the residues rapidly while they are shaken. The crystals are washed with minimum quantities of ligroin (b.p. 70–90°) and are dried as described for the first crop. The second crop from the filtrate weighs 70–80 g. and melts at 111–112° with sintering at 108°; that from the washings weighs 50–135 g. and melts at 110–111° with sintering at 107°. These second crops are darker in color than the first crop, and of the two second crops, that from the washings is the darker greenish yellow. The total yield of product varies from 1060 g. to 1085 g. (84–86 per cent of the theoretical amount based on the aluminum chloride) (Note 9).

2. Notes

1. The presence of sulfur compounds, especially thiophene, in the reagents leads to low yields and a dark-colored product. A good grade of thiophene-free benzene should be used. The benzene may be dried by distillation or by allowing it to stand over calcium chloride. The benzene which is recovered in this preparation may be used in future runs after it has been extracted with alkali, washed, and dried. Small amounts of carbon tetrachloride in the benzene do not interfere, since the quantities of benzene and carbon tetrachloride used are in excess of the relative quantity of the aluminum chloride.

2. A good grade of commercial carbon tetrachloride (b.p. 75–76°) may be used without a noticeable decrease in yield. However, if a colorless product is desired, sulfur-free C.P. carbon tetrachloride is recommended. The carbon tetrachloride may be dried in the same manner as the benzene.

3. A convenient trap for the absorption of water-soluble gases is described in Org. Syn. Coll. Vol. 1, **1941**, 97.

4. The yield of triphenylchloromethane depends very much upon the quality of the aluminum chloride used. Fresh commercial resublimed aluminum chloride, in powder form, has been used in the preparation described.

5. The high thermal conductivity of copper makes possible rapid removal of heat during the hydrolysis; the presence of copper in the mixture does not appear to produce any undesirable effects. If a metal can is not available, a 3-gal. enameled bucket may be used.

6. A technical grade of acetyl chloride may be used, since the presence of small amounts of acetic acid does not interfere. The acetyl chloride serves to convert into triphenylchloromethane any triphenylcarbinol which may be present.

7. Technical ligroin (b.p. 90–120°) should be extracted several times with concentrated sulfuric acid, washed, and dried before use.

8. The vacuum desiccator shown in Fig. 7 has been in use in the research laboratories of the Eastman Kodak Company for some time, and has been found to be of great convenience when large amounts of materials must be handled. One of two similar round-bottomed flasks (B) is provided with a tube for connection to the vacuum pump. Although not necessary, a glass stopcock in this tube is a convenience, and it enables the flask to be used as a large separatory funnel. A glass sleeve C, which must not fit too loosely, serves as a guide for the union between the two flasks A and B. The sleeve carries a rubber gasket (D) which is most conveniently cut from an old inner tube. The gasket provides a tight seal for the vacuum, and the sleeve prevents the contact surfaces from slipping sidewise. *Without the guiding sleeve, the assembly is not safe.* Special guiding clamps may be used, but they offer no particular advantage. When in use, flask A contains the product and B contains the drying agent. E is a steam bath, and F is any convenient support. The apparatus, assembled from 5-l. stock flasks chosen at random, holds a vacuum

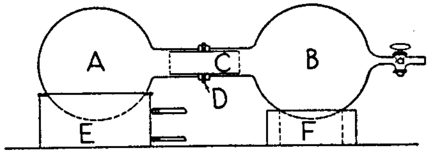


Fig. 7.

of 2 mm. for twenty-four hours with the aid of a high-grade vacuum grease. This "dumb-bell desiccator" is particularly useful for synthetic work; frequently one operation may be eliminated, for flask A may be the vessel in which a reaction, or process of concentration, was performed and the product may be dried without transferring it, or flask A may be the vessel in which a subsequent reaction is to be carried out; while the product is drying, it may be stirred by rotating the assembly; and, within limits, the desiccator may be of any size desired. It is desirable to coat the flasks on the outside with a thin film of some soluble plastic, for the hazards are thereby greatly reduced; very little shattering occurred when evacuated flasks so coated were experimentally "imploded." A comparative test, in which a highly hygroscopic syrup was used, indicated that, with this form of vacuum desiccator and with equal amounts of drying agent, operations may be performed about twice as rapidly as in the conventional model. When the flask A is warmed gently, the efficiency of the assembly is at least four times that of a conventional desiccator. (F. P. PINGERT, private communication.)

9. The product may be stored satisfactorily in ordinary screw-top bottles, provided that they are well sealed with paraffin or some similar material. Triphenylchloromethane is slowly hydrolyzed to triphenylcarbinol by the moisture of the air. Partially hydrolyzed triphenylchloromethane may be purified by recrystallization from one-third its weight of benzene containing 5–25 per cent of acetyl chloride. The product is washed with ligroin containing a little acetyl chloride.

3. Methods of Preparation

Triphenylchloromethane has been made by the action of phosphorus pentachloride,[1] hydrogen chloride,[2] or acetyl chloride [3] upon triphenylcarbinol. It has also been made by the reaction between carbon tetrachloride and benzene in the presence of aluminum chloride [4] or ferric chloride; [5] and by the action of phosphorus pentachloride,[6] or of sulfuryl chloride in the presence of peroxides,[7] upon triphenylmethane. Procedure A is based upon that of Gomberg and Davis; [3] procedure B is a modification of that originally reported by Gomberg [4] and later described by Gattermann and Wieland.[8]

---

[1] Hemilian, Ber. **7**, 1207 (1874); Fischer and Fischer, Ann. **194**, 257 (1878).

[2] Gomberg, Ber. **35**, 2401 (1902).

[3] Gomberg and Davis, Ber. **36**, 3925 (1903).

[4] Gomberg, Ber. **33**, 3147 (1900).

[5] Wertyporoch, Kowalski, and Roeske, Ber. **66**, 1237 (1933).

[6] Cone and Robinson, Ber. **40**, 2163 (1907).

[7] Kharasch and Brown, J. Am. Chem. Soc. **61**, 2148 (1939).

[8] Gattermann and Wieland, "Laboratory Methods of Organic Chemistry," p. 346, The Macmillan Company, New York, 1937.

SUBJECT INDEX

(This cumulative Index comprises material from Volumes 20 through 23 of this series; for previous volumes see Collective Volumes 1 and 2.)

Names in small capital letters refer to the titles of individual preparations. 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 substances formed either as principal products or as by-products; numbers in ordinary type indicate pages on which a compound or a subject is mentioned in connection with other preparations. For example, ACETONE CYANOHYDRIN, **20**, 42, ***43***, indicates that acetone cyanohydrin is mentioned on page 42 and that directions for its preparation are given in detail on page 43 of Volume 20.

Absorbent cotton, **20**, 8, 9
Acenaphthene, **20**, 1; **21**, 1, 2
ACENAPHTHENOL-7, **21**, ***1***
ACENAPHTHENOL ACETATE, **21**, ***1***
Acenaphthenone, **21**, 3
β-3-ACENAPHTHENYLCARBONYLPROPIONIC ACID, **20**, ***1***
β-(1-ACENAPHTHOYL)-PROPIONIC ACID, **20**, ***4***
β-(3-ACENAPHTHOYL)-PROPIONIC ACID, **20**, ***1***
Acetaldehyde, **23**, 61, 84
ACETALDEHYDE, BROMO-, DIETHYL ACETAL, **23**, ***8***
p-ACETAMINOBENZENESULFINATE, SODIUM, **22**, ***31***
α-Acetamino-3,4-methylenedioxycinnamic acid, **22**, 93
Acetic acid, **22**, 57, 87; **23**, 37
ACETIC ACID, BENZOYL-, ETHYL ESTER, **23**, ***35***
ACETIC ACID, BROMO-, ETHYL ESTER, **23**, ***37***
Acetic anhydride, **20**, 6, 55, 75, 102; **21**, 13, 105; **22**, 1, 54, 56, 91; **23**, 37, 64
ACETOACETANILIDE, **21**, ***4***
ACETOBROMOGLUCOSE, **22**, ***1***
Acetone, **20**, 6, 8, 40, 43, 62; **22**, 101; **23**, 66, 79
    drying, **20**, 7
Acetone—*Continued*
    pyrolysis to ketene, **21**, 64, 65
ACETONE CYANOHYDRIN, **20**, 42, ***43***
Acetophenone, **20**, 32; **21**, 39; **22**, 99; **23**, 30, 48, 68
ACETOPHENONE, 2,4-DIHYDROXY-, **21**, ***103***
Acetophenone oxime, **22**, 27
ACETOPHENONE PHENYLHYDRAZONE, **22**, 98, ***99***
1-ACETOXY-3-NAPHTHALDEHYDE, **21**, ***87***
ACETYLACETONE, **20**, ***6***; **21**, 68
    COPPER SALT, **20**, ***6***
Acetylation, **20**, 21, 74
    of gentiobiose, **22**, 54
    of glucose, **22**, 1
    of 6-trityl-β-*d*-glucose, **22**, 56
ACETYLBENZOYL, **23**, ***1***
Acetyl bromide, **23**, 102
Acetyl chloride, **20**, 21; **21**, 46; **23**, 100, 103, 105
Acetylene, **20**, 40; **22**, 101
ACETYLKETENE, **21**, ***64***
Acetylsalicylyl chloride, **23**, 66
Acetylsalicylyl peroxide, **23**, 66
Acetyl-*o*-toluidine, **22**, 94
    substituted, conversion to indoles, **22**, 95
Acetylxylidines, conversion to indoles, **22**, 95
ACRIDINE, 5-(9-)AMINO-, **22**, ***5***

Acridone, **22**, 5
Acylation by an ester, **23**, 35
Acylchlororesorcinols, **20**, 58
Acylresorcinols, **20**, 58
Adapter for steam distillation, **22**, *11*
Addition, of bromine to a double bond, **22**, 50; **23**, 9
  of bromine to an unsaturated acid, **22**, 76, 82
  of chlorine to aromatic iodo compounds, **22**, 69, 70
  of a cyanide to a lactone, **22**, 30
  of hydrogen bromide to ethyl acrylate, **20**, 65
  of hydrogen bromide to methyl acrylate, **20**, 64
  of hydroxylamine to cinnamic acid, **22**, 26
  of a lithium aryl to an aldehyde, **23**, 84
  of a lithium aryl to ethylene oxide, **23**, 85
  of methylamine to ethyl acrylate, **20**, 36
  of methylamine to methyl acrylate, **20**, *37*
Addition tube, **20**, 21
Air trap, **23**, 42
Alanine, **23**, 15
ALANINE, β-(3,4-DIHYDROXYPHENYL)-*N*-METHYL-, **22**, *89*, *91*
Alcoholic-hydrochloric acid, **22**, 77, 83
  standardization, **22**, 80
Alcoholysis, **20**, 67
  of dibromoethyl acetate, **23**, 8
Aldehyde synthesis, **20**, 14
  from acid chlorides by Rosenmund reaction, **21**, 84, 87, 88, 110
  Gattermann, **23**, 57
ALDEHYDOACID, **23**, *76*
Alkylation of thiourea, **22**, 59
Alkylchlororesorcinols, **20**, 59
Alkylene bromide, **20**, 24
S-ALKYLTHIURONIUM HALIDES, **22**, *60*
dl-ALLOTHREONINE, **20**, *104*
ALLOXAN, **23**, *3*
  DIHYDRATE, **23**, 3, *6*
  MONOHYDRATE, **21**, *5*
  TETRAHYDRATE, **23**, *3*
Alumina, activated, **23**, 25
  regeneration of, **23**, 25
Aluminum, commercially pure (2S), **21**, 9
Aluminum alloy (17ST), **21**, 9
ALUMINUM *tert.*-BUTOXIDE, **21**, *8*, 18, 39
Aluminum chloride, **20**, 1, 29
  anhydrous, **21**, 25; **23**, 57, 102
Aluminum ethoxide, **21**, 9
Aluminum isopropoxide, **21**, 9
AMALGAMATED ZINC, **20**, 57; **23**, *86*
Amide, **20**, 37, 62, 66
  preparation by ammonolysis, **20**, 62
Amination, by reduction of a ketone in the presence of ammonia, **23**, 68
  of α-bromoisocaproic acid, **21**, 75
  of α-bromo-β-methylvaleric acid, **21**, 62
  of α-bromo-β-phenylpropionic acid, **21**, 101
  of 3-hydroxy-2-naphthoic acid, **22**, 19
Aminoacetic acid, **22**, 59
Amino acid, **20**, 81, 101; **22**, 13, 23, 26, 59, 90, 93
9-AMINOACRIDINE, **22**, *5*
  basic strength of, **22**, 8
9-Aminoacridine hydrochloride, fluorescence of, **22**, 7
9-AMINOACRIDINES, SUBSTITUTED, **22**, *7*
2-Aminobenzothiazole, **22**, 18
o-AMINOBENZYL ALCOHOL, **21**, *10*
α-AMINOBENZYL CYANIDE, **22**, *23*, 25
2-AMINO-*p*-CYMENE, **22**, *9*
α-AMINODIETHYLACETIC ACID, **22**, *13*
α-AMINO-α-ETHYLBUTYRIC ACID, **22**, *13*
2-AMINOHEPTANE, **23**, *70*
dl-β-AMINOHYDROCINNAMIC ACID, **22**, *26*
α-AMINOISOVALERIC ACID, **20**, *106*
2-AMINO-6-METHYLBENZOTHIAZOLE, **22**, *16*
α-AMINO-β-METHYLVALERIC ACID, **21**, *60*
3-AMINO-2-NAPHTHOIC ACID, **22**, *19*
1-Amino-2-naphthol-4-sulfonic acid, **21**, 91, 94
2-Amino-5-nitrotoluene, **20**, 73; **22**, 44
dl-α-AMINOPHENYLACETIC ACID, **22**, *23*
dl-α-AMINO-β-PHENYLPROPIONIC ACID, **21**, *99*

dl-β-AMINO-β-PHENYLPROPIONIC ACID, **22**, *26*
Ammonia, **20**, 87; **22**, 19; **23**, 14
  alcoholic, **23**, 23
  chloroform solution of, **22**, 6
  liquid, **20**, 62; **21**, 70, 71; **23**, 20, 68, 71
    action on a copper safety disk, **23**, 70
    introduction into a bomb, **23**, *69*, 71
  methanolic, **23**, 72
Ammonium carbonate, **20**, 42; **22**, 6
Ammonium chloride, **22**, 13, 23
Ammonolysis, **20**, 62
n-Amyl cyanide, **23**, 72
Amylene, **22**, 82
Analysis of iodoso and iodoxy compounds, **22**, *71*, 72, 73, 74
Aniline, **21**, 4
ANILINE, *p,p'*-SULFONYLBIS-, **22**, *31*
Anisoyl chloride, **23**, 66
ANISOYL PEROXIDE, **23**, *66*
Anthracene, **20**, 11
9-ANTHRALDEHYDE, **20**, *11*
Anthranilic acid, **21**, 10
ANTHRAQUINONE, 2,3-DIMETHYL-, **22**, *37*
Antioxidant, **20**, 65
Apparatus, adapter for steam distillations, **22**, 10, *11*
  automatic water trap for azeotropic distillation, **23**, *38*
  Claisen flask modified with column, **22**, *11*
  continuous extractor, **23**, *49*
  for absorption of gases, **23**, 48
  for adding a solid without exposure to air, **23**, *59*, 102
  for catalytic dehydration, **22**, *40*
  for distillation of solids, **20**, 20
  for fractional distillation, **20**, 26, *52*, 96
  for generating dry methyl amine, **20**, 35
  for heating under pressure, **20**, 85
  for introduction of bromine in a current of air, **23**, *9*, *75*
  for manipulation of liquid ammonia, **23**, *21*
  for partial condensation during distillation, **20**, 26, 27
Apparatus—*Continued*
  for preparation of sodamide, **20**, 87
  for steam distillation, **20**, 2
  shaking extractor, **23**, *78*
  spray trap, **23**, 1
d-ARABINOSE, **20**, *14*
d-ARABINOSE DIPHENYLHYDRAZONE, **20**, *15*
Autoclave, **20**, 82, 85, 102; **21**, 72
  stirring, **22**, 20
  use of hydrogenation bomb as, **21**, 68; **22**, 20
    cleaning, **22**, 21
Autooxidation, **22**, 81, 85
Azeotropic distillation, **20**, 66, 106; **23**, 38
Azide, formation from a hydrazine, **22**, 96
AZOBENZENE, **22**, *28*

Barbituric acid, **21**, 5
Barium carbonate, **22**, 86
Barium chloride, **23**, 17
Barium hydroxide, **22**, 87, 91
Barium malonate, **23**, 17
Barostat, **23**, 46, 47
Bayberry wax, **20**, 67
BENZALBARBITURIC ACID, **21**, *5*
Benzaldehyde, **21**, 5, 51, 108; **22**, 24
Benzene, dry, thiophene-free, **23**, 95, 97, 102, 103
  use in azeotropic esterification, **23**, 38
BENZENE, IODO-, DICHLORIDE, **22**, *69*
BENZENE, IODOSO-, **22**, *70*
BENZENE, IODOXY-, **22**, *72*, *73*
BENZENE, TRIAZO-, **22**, *96*
Benzil, **20**, 48; **23**, 92
BENZIL MONOHYDRAZONE, **20**, 47, *48*
Benzoic acid, **21**, 27; **22**, 48, 49
BENZOIC ACID, 2,5-DINITRO-, **22**, *44*
BENZOIC ACID, 3,5-DINITRO-, **22**, *48*, *49*
Benzoin, **23**, 86
BENZONITRILE, 2,6-DIMETHOXY-, **22**, *35*
Benzophenone, **23**, 99
BENZOPYRROLE, **23**, *42*
BENZOTHIAZOLE, 1-AMINO-5-METHYL-, **22**, *16*
BENZOTHIAZOLE, 2-AMINO-6-METHYL-, **22**, *16*

1,2,3-BENZOTRIAZOLE, **20**, *16*
BENZOYLACETIC ESTER, **23**, *35*
Benzoylation of acetoacetic ester by ethyl benzoate, **23**, 35
Benzoyl-*o*-toluidines, conversion to indoles, **22**, 95
Benzoylxylidines, conversion to indoles, **22**, 95
Benzyl alcohol, **23**, 14
BENZYLAMINE, *α*-METHYL-, **23**, *68*
BENZYL CARBAMATE, **23**, *14*
Benzyl chloride, **21**, 99
BENZYL CHLOROFORMATE, **23**, *13*
Benzyl cyanide, **23**, 71
Bisulfite compound, use for purification of an aldehyde, **23**, 78
  use for purification of a ketone, **23**, 79
Blood, defibrinated, **21**, 53
Booster pump, use of, for hydrogenation, **23**, 69
Boron trifluoride, **20**, 6
Bromination, **20**, 18, 81, 92, 101
  of acetic acid, **23**, 37
  of a lactone, phthalide, **23**, 74
Bromine, **20**, 18, 23, 81, 92, 101; **21**, 61, 93; **22**, 50, 76, 82
  dry, **20**, 93, 106, *108;* **21**, 74, 101; **23**, 9, 37, 74, 94
BROMOACETAL, **23**, *8*, 45
BROMOACETIC ACID, **23**, *37*
3-Bromo-4-aminotoluene, **23**, 11
m-BROMOANILINE, **23**, *12*
Bromobenzene, **21**, 79; **23**, 83, 93, 98
p-Bromobenzoyl chloride, **23**, 66
p-BROMOBENZOYL PEROXIDE, **23**, *66*
γ-Bromobutyronitrile, **23**, 22
o-BROMO-*p*-CRESOL, **23**, *11*
1-BROMO-2-ETHOXYETHANE, **23**, *32*
3-BROMO-4-HYDROXYTOLUENE, **23**, *11*
α-BROMOISOCAPROIC ACID, **21**, *74*
α-BROMOISOVALERIC ACID, **20**, *106*
Bromomesitylene, **21**, 77
α-BROMO-*β*-METHOXY-*n*-BUTYRIC ACID, **20**, *101*
α-BROMO-*β*-METHOXYPROPIONIC ACID, **20**, *82*
o-Bromo-*p*-methylanisole, **23**, 12
α-BROMO-*β*-METHYLVALERIC ACID, **21**, *61*
α-Bromonaphthalene, **21**, 89
6-BROMO-2-NAPHTHOL, **20**, *18*
m-Bromophenol, **23**, 12
α-BROMO-*β*-PHENYLPROPIONIC ACID, **21**, *100*
2-BROMOPHTHALIDE, **23**, *74*
β-Bromopropionic acid, **20**, 65
1,3-BUTADIENE, 2,3-DIMETHYL-, **22**, *39*, *40*
2-BUTENE-1,4-DIONE, 1,4-DIPHENYL-, **20**, *29*
tert.-BUTYL ACETATE, **20**, *21*
n-Butyl alcohol, **23**, 43
tert.-Butyl alcohol, **20**, 21; **21**, 8, 39; **23**, 42
  ANHYDROUS, **23**, *46*
sec.-Butyl bromide, **21**, 60
sec.-BUTYLMALONIC ACID, **21**, *61*
n-BUTYL *p*-TOLUENESULFONATE, **20**, *51*
3-BUTYN-2-OL, 2-METHYL-, **20**, *40*
n-Butyric anhydride, **21**, 14
Butyrylchlororesorcinol, **20**, 58
o-Butyrylphenol, **20**, 58
p-Butyrylphenol, **20**, 58

Calcium carbonate, **22**, 54
Calcium chloride, **23**, 103
n-Caproic acid, **21**, 13
n-CAPROIC ANHYDRIDE, **21**, *13*
Caproylchlororesorcinol, **20**, 58
o-Caproylphenol, **20**, 58
p-Caproylphenol, **20**, 58
Caproylresorcinol, **20**, 58
CARBINOL, TRIPHENYL-, **23**, *98*
CARBINOL, TRIS-(4-PHENYLPHENYL)-, **23**, *95*, *97*
Carbitol, **22**, 32
CARBOBENZOXYALANINE, **23**, *15*
CARBOBENZOXY CHLORIDE, **23**, *13*
CARBOBENZOXYGLYCINE, **23**, *14*
Carbon dioxide, **23**, 74
  solid (Dry Ice), **21**, 71, 77; **22**, 101
Carbon dioxide atmosphere, **22**, 78, 84, **91**
Carbon disulfide, **21**, 81
Carbon tetrachloride, **23**, 102
Carborundum crystals, **20**, 96
  as column filling, **22**, 39; **23**, 22

CARBOXYALDEHYDE, preparation of, **23**, *76*
o-CARBOXYBENZYL CYANIDE, **22**, *30*
o-CARBOXYPHENYLACETONITRILE, **22**, *30*, 61
CARO'S ACID, **22**, *44*, 74
CARVACRYLAMINE, **22**, *9*
Catalyst, alumina, **22**, 40
  boron trifluoride, **20**, 6
  copper bronze, **20**, 45
  copper-chromium oxide for decarboxylation, **22**, 67
  copper oxide for decarboxylation, **22**, 67
  hydrobromic acid, **22**, 39
  palladium-barium sulfate, **21**, 85, 110
  poison, for use in Rosenmund reduction, **21**, 85, *87*
  sodium bicarbonate, **20**, 26
  sulfuric acid, **22**, 1
CATALYST, RANEY NICKEL, **21**, *15*, 108; **22**, 9, 12; **23**, 68, 71, 90
  estimation of quantity of, **21**, 17
  storage under alcohol, dioxane, and methylcyclohexane, **21**, 16
Cellosolve, **23**, 32
Centrifuge, **22**, 77, 83
Cerelose, **22**, 2
Chloral hydrate, **20**, 37
Chlorination of a ketone, **23**, 48
Chlorine, **22**, 69; **23**, 48
Chloroacetic acid, **23**, 53
  drying, **23**, 54
9-CHLOROACRIDINE, **22**, *6*, *7*
Chlorobenzene as a solvent, **22**, 16
4-Chlorobiphenyl, **23**, 95, 97
γ-Chlorobutyronitrile, **23**, 20
Chloroform, **22**, 35, 57, 63, 71
  anhydrous, **22**, 69
Chloromethylation, **20**, 59
α-Chloronaphthalene, **21**, 90
o-Chloronitrobenzene, **20**, 45
p-Chloronitrobenzene, **22**, 32
CHOLESTENONE, **21**, *18*
Cholesterol, **21**, 18
Chromium trioxide, **21**, 6
Cinnamic acid, **20**, 77; **22**, 26
CINNAMOYL CHLORIDE, **20**, *77*
CITRAL, BISULFITE COMPOUND, **23**, *78*
Citral, purification of, **23**, *78*
Claisen reaction, **20**, 7, 32
Clayton yellow paper, **22**, 20, *22*
Cleavage, of a disulfide, **20**, 23
  of 6-trityl group in 6-trityl-*β*-*d*-glucosetetraacetate, **22**, 57
Clemmensen reduction, **20**, 57
Clintose, **22**, 2
Cocoanut oil, **20**, 69
Condensation, of an acid and an amine, **20**, 66
  of an aldehyde and an acid, **20**, 55
  of an aldehyde and creatinine, **22**, 90
  of benzil with dibenzyl ketone, **23**, 92
  of citral and acetone, **23**, 79
  of an ester, **20**, 26
  of a ketone and an anhydride, **20**, 6
  of a ketone and an ester, **20**, 7, 32
  of a ketone and a hydroxy acid, **20**, 62
  of a sodium sulfinate and *p*-nitrochlorobenzene, **22**, 31
Condenser, partial, **20**, 26
Congo red, **22**, 20, 63, 66, 92, 93
Copper acetate, **20**, 6; **21**, 46, 47
COPPER ACETYLACETONE, **20**, *6*
COPPER BRONZE, **20**, *45*
Copper-chromium oxide, **22**, 67
COPPER ETHYL DIACETYLACETATE, **21**, *46*
Copper helices, **20**, 96
Copper oxide, **22**, 67
Copper reaction vessel, **23**, 102
Cotton, absorbent, for drying, **20**, 8, 9
Cottonseed oil, **22**, 78, 85
Coupling of two aryl residues, **20**, 45
Creatinine, **22**, 90
p-CRESOL, 2-BROMO-, **23**, *11*
Crotonic acid, **20**, 101
Cuprous cyanide, **21**, 89
Cyanoacetamide, **23**, 60
Cyanohydrins, **20**, 44; **22**, 15, 16
α-CYANO-*o*-TOLUIC ACID, **22**, *30*, 61
Cyclization, **20**, 16, 26, 42, 73
  acet-*o*-toluidide to 2-methylindole, **22**, 94
  arylthiourea to aminobenzothiazole, **22**, 17

Cyclization—*Continued*
  α-diketone and ketone to a cyclopentadienone, **23**, 92
  indole synthesis, **23**, 42
  ketone phenylhydrazone to indole, **22**, 98
  malonic ester synthesis of cyclobutane acids, **23**, 16
  phenylanthranilic acid to chloroacridine, **22**, 5
  tartaric acid dinitrate to imidazole-4,5-dicarboxylic acid, **22**, 66
CYCLOBUTANECARBOXYLIC ACID, **23**, *18*
1,1-CYCLOBUTANEDICARBOXYLIC ACID, **23**, *16*
Cyclohexanone, **20**, 42
Cyclohexene, **20**, 28
CYCLOPENTADIENONE, TETRAPHENYL, **23**, *92*
CYCLOPROPANE, CYANO-, **23**, *20*
CYCLOPROPYL CYANIDE, **23**, *20*
p-Cymene, **21**, 96
CYSTEIC ACID MONOHYDRATE, **20**, *23*
Cystine, **20**, 23

Deacetylation, **22**, 34
Debromination, of hexabromostearic acid, **22**, 83
  of tetrabromostearic acid, **22**, 77, 81
DECAMETHYLENE BROMIDE, **20**, *24*
Decamethylene glycol, **20**, 25
DECANE, 1,10-DIBROMO-, **20**, *24*
Decarboxylation, **23**, 18
  of imidazole-4,5-dicarboxylic acid, **22**, 67
  of an oximino acid to an oxime, **22**, 27
Decomposition, diazonium salt to phenol, **23**, 11
n-DECYL *p*-BROMOBENZENESULFONATE, **20**, *51*
n-Decyl mercaptan, **21**, 38
Degradation, **20**, 14
Dehydration, **20**, 48, 74
  catalytic, **22**, 39, 40
DEHYDROACETIC ACID, **20**, *26;* **21**, 66
Dehydrogenation, by air and alkali, **22**, 37
  by bromine, **23**, 94
Demethylation of a phenolic ether by hydriodic acid, **22**, 91
Desiccator, vacuum, "dumb-bell" type, **23**, *105*
4,4′-Diacetylaminodiphenylsulfone, **22**, 34
DIACETYLMETHANE, **20**, *6*
4,4′-DIAMINODIPHENYLSULFONE, **22**, *31*
1,2-DIAMINO-4-NITROBENZENE, **21**, *20*
o-Dianisidine, **21**, 31
1,3-DIAZOLE, **22**, *65*
Diazonium salt, reduction of, **21**, 30
Diazotization, **20**, 16, 73; **21**, 31, 32, 34; **23**, 11
trans-DIBENZOYLETHYLENE, **20**, *29*
DIBENZOYLMETHANE, **20**, *32*
Dibenzyl ketone, **23**, 92
1,10-DIBROMODECANE, **20**, *24*
1,5-DIBROMOPENTANE, **23**, *67*
Di-*n*-butylaminoethanol, **23**, 24
β-DI-*n*-BUTYLAMINOETHYLAMINE, **23**, *23*
Di-*n*-butylaminoethyl bromide hydrobromide, **23**, 23
DI-β-CARBETHOXYETHYLMETHYLAMINE, **20**, *35*
DI-β-CARBOMETHYOXYETHYLMETHYLAMINE, **20**, *37*
α,α-DICHLOROACETAMIDE, **20**, *37*
ω,ω-DICHLOROACETOPHENONE, **23**, *48*
o-Dichlorobenzene, **20**, 11
α,α′-DICYANO-β-METHYLGLUTARAMIDE, **23**, *60*
Diels-Alder reaction, **22**, 37; **23**, 93
Diene synthesis, **22**, 37, 40; **23**, 93
Diethylamine hydrochloride, **23**, 31
DIETHYLAMINOETHYLAMINE, **23**, *24*
β-DIETHYLAMINOPROPIOPHENONE HYDROCHLORIDE, **23**, *31*
DIETHYL BENZYLMALONATE, **21**, *99*
DIETHYL *sec.*-BUTYLMALONATE, **21**, *60*
Diethyl ketone, **22**, 13
Diethyl malonate, **21**, 60, 99
1,4-DIHYDRO-2,3-DIMETHYLANTHRAQUINONE, **22**, *37*
2,3-DIHYDROPYRANE, **23**, *25*
2,6-DIHYDROXYACETOPHENONE, **21**, *22*
3,5-DIHYDROXYBENZOIC ACID, **21**, *27*
DIKETENE, **21**, *64*

α-Diketone synthesis, **23**, *1*
1,3-Diketone, **20**, 6, 32
2,6-DIMETHOXYBENZONITRILE, **22**, *35*
3,3′-DIMETHOXYBIPHENYL, **21**, *30*
β-(3,4-DIMETHOXYPHENYL)-ETHYLAMINE, **23**, *72*
β,β-DIMETHYLACRYLIC ACID, **23**, *27*
Dimethylamine, **21**, 84
  hydrochloride, **23**, 30
β-DIMETHYLAMINOPROPIOPHENONE HYDROCHLORIDE, **23**, *30*
2,3-DIMETHYLANTHRAQUINONE, **22**, *37*
3,3′-DIMETHYLBIPHENYL, **21**, *30*
2,3-DIMETHYLBUTADIENE-1,3, **22**, 37, *39*, *40*
2,4-DIMETHYL-3-ETHYLPYRROLE, **21**, *67*
DIMETHYLETHYNYLCARBINOL, **20**, *40;* **22**, *101*
5,5-DIMETHYLHYDANTOIN, **20**, *42*
sym-Dimethylthiourea, **21**, 84
2,4-Dinitroaniline, **21**, 21
m-Dinitrobenzene, **22**, 35
2,5-DINITROBENZOIC ACID, **22**, *44*
3,4-DINITROBENZOIC ACID, **22**, *47*
3,5-DINITROBENZOIC ACID, **22**, *48*, *49*
2,2′-DINITROBIPHENYL, **20**, *45*
2,5-Dinitrotoluene, **22**, 46
Dioxane, **20**, 72; **22**, 36, 83; **23**, 27
  use of, in hydrogenations with Raney nickel, **21**, 16
DIPHENYLACETYLENE, **22**, *50*
1,4-DIPHENYL-1-BUTENE-1,4-DIONE, **20**, *29*
Di-(α-phenylethyl)-amine, **23**, 70
Di-(β-phenylethyl)-amine, **23**, 72
1,2-Diphenylethylene, **22**, 50
Diphenylhydrazine, **20**, 15
Diphenylhydrazine hydrochloride, **20**, 15
DIPHENYLIODONIUM IODATE, **22**, *52*
DIPHENYLIODONIUM IODIDE, **22**, *52*, 71
Diphenyliodonium salts, **22**, 71
DIPHENYLKETENE, **20**, *47*
1,3-DIPHENYL-1,3-PROPANEDIONE, **20**, *32*
DI-*n*-PROPYLAMINOETHYLAMINE, **23**, *24*
Disproportionation, of an iodoso and an iodoxy compound, **22**, 52
  of iodosobenzene by steam distillation, **22**, 72
Dodecanol, **20**, 50
n-Dodecyl alcohol, **20**, 50
n-Dodecyl bromide, **21**, 36
n-DODECYL *p*-BROMOBENZENESULFONATE, **20**, *51*
S-Dodecylisothiuronium bromide, **21**, 37
n-DODECYL MERCAPTAN, **21**, *36*
n-DODECYL *p*-TOLUENESULFONATE, **20**, *50*
Dry Ice, **20**, 37, 41; **21**, 64; **22**, 101
  cooling medium for condenser, **23**, 20
  use, of, for internal cooling during nitration, **21**, 96
Drying, use of absorbent cotton, **20**, 8, 9
"Dumb-bell" vacuum desiccator, **23**, *105*
DYPNONE, **21**, *39*

Elimination of hydrobromic acid from a dibromide, **22**, 50
Emulsin, **22**, 53
Enzymatic synthesis, **22**, 53
1,5-EPOXYPENTANE, **23**, 67, *90*
1,5-EPOXYPENTENE-1, **23**, *25*
Esterification, **20**, 4, 21, 24, 50, 77
  by azeotropic distillation with benzene, **23**, 38
  of linoleic acid, **22**, 77
  of linolenic acid, **22**, 83
  by nitric acid, **22**, 65
ETHANE, 1-BROMO-2-ETHOXY-, **23**, *32*
Ether, anhydrous, **22**, 57
β-Ethoxyethyl alcohol, **23**, 32
β-ETHOXYETHYL BROMIDE, **23**, *32*, 33
β-ETHOXYETHYL CYANIDE, **23**, *33*
2-ETHOXY-1-NAPHTHALDEHYDE, **20**, *11*
β-ETHOXYPROPIONITRILE, **23**, *33*
Ethyl acetate, **20**, 8; **23**, 9
  dry, **20**, 10
Ethyl acetoacetate, **20**, 26; **21**, 23, 46, 67; **23**, 35
Ethyl acrylate, **20**, 36
Ethyl alcohol, anhydrous, **22**, 59; **23**, 9, 16, 24
Ethyl benzoate, **20**, 32; **23**, 35, 98
ETHYL BENZOYLACETATE, **23**, *35*
Ethyl bromide, **22**, 59
  as solvent, **23**, 67
ETHYL BROMOACETATE, **21**, 51; **23**, *37*

Ethyl α-bromoisobutyrate, **21**, 53
ETHYL β-BROMOPROPIONATE, **20**, ***65***
ETHYL CAPRYLATE, **20**, ***69***
Ethyl carbonate, **23**, 95, 97
Ethyl chlorocarbonate, **21**, 81
2-ETHYLCHROMONE, **21**, ***42***
ETHYL DIACETYLACETATE, **21**, ***46***
  COPPER DERIVATIVE, **21**, ***46***
ETHYL α,α-DIMETHYL-β-PHENYL-β-HYDROXYPROPIONATE, **21**, ***53***
Ethylene chloride, **20**, 28; **22**, 76
ETHYLENEDIAMINE, *N*,*N*-DIBUTYL-, **23**, ***23***
Ethylene oxide, **23**, 85
ETHYL 1,16-HEXADECANEDICARBOXYLATE, **21**, ***48***
Ethyl hydrogen sebacate, **21**, 48
  electrolysis of, **21**, 48
Ethyl isothiocyanate, **21**, 82
Ethyl lactate, **21**, 71
ETHYL LAURATE, **20**, ***69***
ETHYL LINOLEATE, **22**, ***77***
ETHYL LINOLENATE, **22**, ***83***
Ethyl malonate, **23**, 16
Ethyl mercaptan, **22**, 59
ETHYL *N*-METHYL-β-AMINOPROPIONATE, **20**, ***37***
ETHYL MYRISTATE, **20**, ***69***
ETHYL PENTANE-1,1,5,5-TETRACARBOXYLATE, **23**, ***18***
ETHYL β-PHENYL-β-HYDROXYPROPIONATE, **21**, ***51***
Ethyl propionate, **21**, 43
Ethylthiourea, **21**, 84
S-ETHYLTHIURONIUM BROMIDE, **22**, ***59***
Ethynylcarbinols, **22**, ***101***
1-ETHYNYLCYCLOHEXANOL-1, **20**, ***41***
Extraction, continuous, **20**, 99; **23**, 49
  hot, **20**, 30
Extractor, continuous, **23**, ***49***
  shaking, **23**, ***78***

Fatty acids, from natural oils, **22**, ***75***, 76, ***79***, ***82***
  linseed, distilled, **22**, 84
  saturated, separation from unsaturated, **22**, 76
  unsaturated, **22**, ***75***, ***82***
    hexabromide test for, **22**, 78
Fermentation, **22**, 53
Ferric nitrate, **23**, 20
Fieser's solution, **21**, 110
Filter fabric, Pyrex glass, **22**, 33, 65
  Vinyon, **22**, 33, 67
Filter paper, hardened, **22**, 45
Fischer indole synthesis, **22**, 98
Flash distillation, **21**, 85
Flask, modified Claisen, **22**, ***11***
Fluorescence of 9-aminoacridine hydrochloride, **22**, 7
Formaldehyde, **20**, 60
Formalin, **22**, 66
Formic acid, **20**, 66, 102; **23**, 43
FORMIC ACID, CHLORO-, BENZYL ESTER, **23**, ***13***
o-FORMOTOLUIDE, **23**, ***43***
FORMYL-*dl*-METHYLTHREONINE, **20**, ***103***, 104
Fractionating column, packed, **20**, 96
  Whitmore-Lux type, **21**, 14, 66
Friedel-Crafts reactions, **20**, 1, 29; **23**, 102
Fries rearrangement, **21**, 25
Froth dissipation, **20**, 3
FUMARYL CHLORIDE, **20**, 29, ***51***
2-FURANACRYLIC ACID, **20**, ***55***
FURAN, 2-(BROMOMETHYL)TETRAHYDRO-, **23**, ***88***
Furfural, **20**, 55; **23**, 70
FURFURYLAMINE, **23**, ***70***
Furnace, construction of, **22**, 40
  hot tube, **23**, 25
FURYLACRYLIC ACID, **20**, ***55***
Fusion, alkaline, of an aryl sulfonate, **21**, 29
Fusion pot, **20**, 86

Gas trap, **20**, 1, 12, 29, 60, 77, 92, 106; **23**, 48
Gattermann reaction, aldehyde synthesis, **23**, 57
β-GENTIOBIOSE OCTAACETATE, **22**, ***53***
Glass helices, **20**, 96
Glucose, **20**, 75; **22**, 1, 53
  anhydrous, **20**, 97
GLUCOSE OXIME, **20**, ***75***
GLUCOSE PENTAACETATE, **22**, ***1***

β-*d*-GLUCOSE-1,2,3,4-TETRAACETATE, **22**, ***56***
GLUTARIC ACID, β-METHYL-, **23**, ***60***
Glycerol, **22**, 75, 82
Glycine, **22**, 59; **23**, 14
GLYCOCYAMINE, **22**, ***59***
Glycoside, hydrolysis of, **22**, 86
GLYOXALINE, **22**, ***65***
GUANIDOACETIC ACID, **22**, ***59***

Haloform reaction, **23**, 27
Helices, **20**, 96
HEMIN, **21**, ***53***
Hempseed oil, **22**, 85
Heptabromostearic acid, **22**, 83, 85
Heptaldehyde, **23**, 70
Heptane, **20**, 41
Heptanoylchlororesorcinol, **20**, 58
o-HEPTANOYLPHENOL, **20**, 57, ***58***
p-HEPTANOYLPHENOL, **20**, ***58***
n-HEPTYLAMINE, **23**, ***70***
n-Heptyl mercaptan, **21**, 38
o-*n*-HEPTYLPHENOL, **20**, ***57***
Hershberg stirrer, **20**, 8; **22**, 74; **23**, 33
HEXABROMOSTEARIC ACID, **22**, ***82***
n-HEXADECYL *p*-BROMOBENZENESULFONATE, **20**, ***51***
n-HEXADECYL *p*-TOLUENESULFONATE, **20**, ***51***
HEXAHYDROPSEUDOIONOL, **23**, ***81***
HEXAMETHYLENE BROMIDE, **20**, ***25***
HEXAMETHYLENETETRAMINE, **22**, ***66***
n-HEXYLAMINE, **23**, ***72***
HOMOPHTHALIC ACID, **22**, ***61***
Hydrazine hydrate, **20**, 48; **21**, 68, 70
Hydrazine sulfate, **21**, 70
Hydriodic acid, **22**, 91
Hydrobromic acid, **20**, 82, 102, 103; **22**, 39
  48%, **23**, ***67***
  recovery as constant-boiling acid, **23**, 68
Hydrochloric acid, **23**, 86
Hydrocyanic acid, **22**, 25
Hydrogen, electrolytic, **21**, 85, 111
Hydrogenation, apparatus for high-pressure, **21**, 108
  dangers and precautions, **22**, 10
Hydrogenation—*Continued*
  of nitro compounds, **22**, 10
Hydrogen bromide, **20**, 25, 64; **22**, 2, 57
  bromine-free, **20**, 65; **22**, 3
Hydrogen chloride, **20**, 60, 79; **23**, 57, 63
  generator, **23**, 58
Hydrogen peroxide, **20**, 70; **23**, 66
Hydrogen sulfide, **20**, 15; **21**, 21; **22**, 14; **23**, 7
Hydrolysis, **20**, 82, 92, 98
  of an acetylamino compound, **22**, 32
  of an amide to an acid, **22**, 14; **23**, 61
  of a creatinine derivative to an amino acid, **22**, 91
  of an isonitroso ketone to an α-diketone, **23**, 1
  of a methylglycoside, **22**, 86
  of a nitrile to an acid, **22**, 23, 61
  of a nitrile to an amide, **22**, 13
Hydroquinone, **20**, 64
  as an inhibitor, **22**, 39, 41
o-Hydroxyacetophenone, **21**, 43, 45
Hydroxylamine, **20**, 74
Hydroxylamine hydrochloride, **20**, 74; **22**, 26
β-Hydroxylaminocinnamic acid, **22**, 26
2-HYDROXY-1-NAPHTHALDEHYDE, **22**, ***63***
3-Hydroxy-2-naphthoic acid, **22**, 19
2-HYDROXY-1,4-NAPHTHOQUINONE, **21**, ***56***
2-HYDROXY-5-NITROBENZYL CHLORIDE, **20**, ***59***
2-(β-HYDROXYPROPYL)-PYRIDINE, **23**, ***83***
2-(γ-HYDROXYPROPYL)-PYRIDINE, **23**, ***85***
Hypophosphorous acid, **21**, 31

IMIDAZOLE, **22**, ***65***
IMIDAZOLE-4,5-DICARBOXYLIC ACID, **22**, ***66***
INDAZOLE, **20**, ***74***
INDOLE, **23**, ***42***
INDOLE, 2-METHYL, **22**, ***94***
INDOLE, 2-PHENYL, **22**, ***98***
Inhibitor, **20**, 36, 48, 65; **22**, 39, 41
Iodine value, **22**, 79, 84
Iodobenzene, **22**, 69, 71, 72, 73
IODOBENZENE DICHLORIDE, **22**, ***69***, 70, 73
IODONIUM COMPOUND, **22**, ***52***

Iodoso and iodoxy compounds, differentiation, **22**, 71
Iodosobenzene, **22**, 52, *70*, 72
Iodotoluene dichlorides, *o*-, *m*-, *p*-, **22**, *70*
Iodoxybenzene, **22**, 52, *72*, *73*
Iron powder as reducing agent, **22**, 12
Irradiation, **20**, 81, 92, 101
Isobutyl alcohol, **23**, 43
Isocaproic acid, **21**, 74
Isocaproic acid, α-amino-, **21**, *74*
β-Isodurylaldehyde, **21**, *110;* **23**, *57*, *59*
β-Isoduryl chloride, **21**, *77*
dl-Isoleucine, **21**, *60*
Isonitrosopropiophenone, **23**, 1
Isopropyl ether, recrystallization from, **22**, 2
  removal of peroxides from, **22**, 3
Isovaleric acid, dry, **20**, 106
Isovaleric acid monohydrate, **20**, 106

Ketene, **21**, 13, 64*
Ketene diethylacetal, **23**, *45*
Ketene, diethyl ketal, **23**, *45*
Ketene dimer, **21**, 4, *64*
"Ketene lamp," **21**, 65
Keto acid, **20**, 2
Knoevenagel condensation, **23**, 60
Kolbe synthesis of an alkyl α, ω-dicarboxylate, **21**, 48
Kryptopyrrole, **21**, *67*

Lactamide, **21**, *71*
Laurel wax, **20**, 68
Lauryl alcohol, **20**, 50
Laurylisothiuronium bromide, **21**, *37*
Lauryl mercaptan, **21**, *36*
Lauryl *p*-toluenesulfonate, **20**, *50**
Lead dioxide, **21**, 1
Lead hydroxide, **22**, *15*
Lead tetraacetate, **21**, 1, 3
dl-Leucine, **21**, *74*
Linoleic acid, **22**, *75*
  tetrabromide, **22**, *76*
Linolenic acid, **22**, *82*
  hexabromide, **22**, *82*, 85
Linolic acid, **22**, *75*
Linseed oil, **22**, 82, 84, 85
Lithium, **23**, 83
  cutting, **23**, 84
  sand, **23**, 85

Magnesium, **21**, 46, 77, 79
Magnesium powder, **20**, 21
Maleic anhydride, **20**, 51; **23**, 93
Malonic acid, substituted, **21**, 61
  bromination of, **21**, 61, 100
  decarboxylation of, **21**, 61, 101
Mandelamide, **20**, *62*
Mandelic acid, **20**, 62; **23**, *48*
Mannich reaction, **23**, 30
d-Mannose, **22**, *86*
l-Menthol, **23**, 52
l-Menthoxyacetic acid, **23**, *52*, 55
l-Menthoxyacetyl chloride, **23**, *55*
Mercuric acetate, **20**, 81, 101
Mercuric chloride, **20**, 57; **21**, 8; **23**, 86
Mercuric oxide, **20**, 47, 103
Mercury, **22**, 91, 92
Mesitaldehyde, **21**, *110;* **23**, *57*, *59*
Mesitoic acid, **21**, *78*
Mesitoyl chloride, **21**, *77*, 110
Mesitylene, **23**, 57
Metalation of α-picoline by phenyl lithium, **23**, 84
Metal bath, **20**, 48
  adhering to glass, prevention of, **22**, 95
Metal reaction vessel, **23**, 102
Methane, chlorotriphenyl-, **23**, *100*, *102*
Methoxyacetonitrile, **21**, 79
ω-Methoxyacetophenone, **21**, *79*
5-(3-Methoxy-4-hydroxybenzal)-creatinine, **22**, *90*, 93
5-(3-Methoxy-4-hydroxybenzyl)-creatinine, **22**, *90*
2-Methoxy-1,4-naphthoquinone, **21**, *57*
Methyl β-(1-acenaphthoyl)-propionate, **20**, *4*
4-Methyl-7-acetoxycoumarin, **21**, *24*
Methyl acrylate, **20**, 64, 81
Methylal, **20**, *60*
Methylamine, **20**, 36
  anhydrous, **20**, 35

Methylamine—*Continued*
  35% aqueous solution, **21**, 81
  generator, **20**, 35
  hydrochloride, **21**, 82
N-Methylaminoaromatic acids, **22**, 93
Methyl amyl ketone, **23**, 70
Methylaniline, **20**, 11, 66
Methylation, **20**, 97
Methyl α-bromo-β-methoxypropionate, **20**, *81*
Methyl β-bromopropionate, **20**, *64*
Methyl carbitol, **22**, 32
Methylcyclohexane, **21**, 16
Methyl α,β-dibromopropionate, **20**, 82
N-Methyl-3,4-dihydroxyphenylalanine, **22**, *89*, *91*, 93
β-(3,4-Methylenedioxyphenyl)-ethylamine, **23**, *72*
Methylethylethynylcarbinol, **20**, *41*
5-Methyl-5-ethylhydantoin, **20**, *44*
Methyl ethyl ketone, **20**, 41
Methyl ethyl ketone cyanohydrin, **20**, 44
N-Methylformanilide, **20**, 11, *66*
o-Methylformanilide, **23**, *43*
Methyl-β-formylpropionate, **21**, 88
α-Methylglucoside, **20**, 99
β-Methylglutaric acid, **23**, *60*
4-Methyl-7-hydroxy-8-acetylcoumarin, **21**, *25*
4-Methyl-7-hydroxycoumarin, **21**, *23*
2-Methylindole, **22**, *94*
Methyl isothiocyanate, **21**, *81*, 83
α-Methyl-*d*-mannoside, **22**, 86
N-Methyl-(3-methoxy-4-hydroxyphenyl)-alanine, **22**, *91*
Methyl myristate, **20**, *67*
Methyl palmitate, **20**, *67*
Methylphenyldiketone, **23**, *1*
β-(2-Methylphenyl)-ethylamine, **23**, *72*
β-(3-Methylphenyl)-ethylamine, **23**, *72*
β-(4-Methylphenyl)-ethylamine, **23**, *72*
Methyl sulfate, **20**, 97
  antidote, **20**, 97
Methylthiourea, **21**, *83*
Mineral oil, **23**, 103
Monel-metal stirrer, **20**, 99
Monoperphthalic acid, **20**, *70*
Myristic acid, **20**, *69*
Myrtle wax, **20**, 68

β-Naphthaldehyde, **21**, *84;* **23**, *63*
2-Naphthaldehyde, **21**, *84;* **23**, *63*
1-Naphthaldehyde, 2-hydroxy-, **22**, *63*
β-Naphthaldehydimine-stannichloride, **23**, 63
1,(2)-Naphthalenone, 3,4-dihydro-, **20**, *94*
β-Naphthoic acid, **21**, 86
2-Naphthoic acid, 3-amino-, **22**, *19*
β-Naphthol, **20**, 18; **22**, 23, 63
1-Naphthonitrile, **21**, *89*
2-Naphthonitrile, **23**, 63
1,4-Naphthoquinone, **22**, 37
1,2-Naphthoquinone-4-sulfonate, ammonium, **21**, 56
1,2-Naphthoquinone-4-sulfonate, ammonium and potassium, **21**, *91*
β-Naphthoyl chloride, **21**, *85*
β-Naphthylamine, **22**, 23
β-Naphthylethyl ether, **20**, 11
Nef reaction, **20**, 40
Nichrome helices, **20**, 96
Nickel-aluminum alloy, **21**, 15, 16
Nitrate ester preparation, **22**, 65
Nitration of benzoic acid, **22**, 48, 49
Nitric acid, anhydrous, **21**, 105, 106
  fuming, **22**, 48, 65; **23**, 3
Nitrile formation, **20**, 74; **21**, 89
4-Nitro-4′-acetaminodiphenylsulfone, **22**, *32*
3-Nitro-4-aminotoluene, **22**, 47
Nitrobenzene, **20**, 1; **22**, 28
p-Nitrobenzoic acid, **23**, 66
m-Nitrobenzoyl chloride, **23**, 66
p-Nitrobenzoyl chloride, **23**, 65
m-Nitrobenzoyl peroxide, **23**, *66*
p-Nitrobenzoyl peroxide, **23**, *65*
p-Nitrochlorobenzene, **22**, 32
2-Nitro-*p*-cymene, **21**, *96;* **22**, 9
Nitrogen atmosphere, **22**, 94; **23**, 42, 83
5-Nitroindazole, **20**, *73*

- 2-NITRO-6-METHOXYBENZONITRILE, **22**, *35*
- 3-NITRO-4-NITROSOTOLUENE, **22**, *47*
- *p*-Nitrophenol, **20**, 60
- 2-NITROSO-5-NITROTOLUENE, **22**, *44*
- *p*-Nitrotoluene, **21**, 97
- Nitrous acid, **22**, 96
- NONAMETHYLENE BROMIDE, **20**, *25*
- *n*-Nonyl mercaptan, **21**, 38

- OCTADECANEDIOIC ACID, DIETHYL ESTER, **21**, *48*
- *n*-OCTADECYL *p*-BROMOBENZENESULFONATE, **20**, *51*
- *n*-Octadecylmercaptan, **21**, 38
- *n*-OCTADECYL *p*-TOLUENESULFONATE, **20**, *51*
- Octanoylchlororesorcinol, **20**, 59
- *o*-Octanoylphenol, **20**, 58
- *p*-Octanoylphenol, **20**, 58
- Octanoylresorcinol, **20**, 58
- *n*-Octyl mercaptan, **21**, 38
- Oxidation, by air, **20**, 94
  - by air and alkali, **22**, 37
  - by bromine water, **20**, 23
  - by fuming nitric acid, **23**, 3
  - by hydrogen peroxide, **20**, 70
  - by potassium chlorate, **23**, 6
  - by potassium permanganate, **20**, 79
  - of an amine to a nitroso compound, **22**, 44, 47
  - of iodobenzenedichloride to iodoxybenzene, **22**, 73
  - of a methyl group to a carboxyl group, **22**, 45, 47
  - of a nitroso compound to a nitro compound, **22**, 45, 47
- Oxides of nitrogen, **23**, 3
- Oximation, **20**, 75

- PALMITIC ACID, **20**, *69*
- Paraffin, **23**, 103
- Paraformaldehyde, **23**, 30
- *o*-Pelargonylphenol, **20**, 58
- *p*-Pelargonylphenol, **20**, 58
- PENTAACETYL *d*-GLUCONONITRILE, **20**, 14, *74*
- PENTAMETHYLENE BROMIDE, **23**, *67*
- PENTAMETHYLENE OXIDE, **23**, 67, *90*
- PENTANE, 1,5-DIBROMO-, **23**, *67*
- 2,4-PENTANEDIONE, **20**, *6*
- Pentose synthesis, **20**, 14
- Peracid, **20**, 70; **22**, 44
- Perkin reaction, **20**, 55
- PEROXIDE, BIS(*p*-NITROBENZOYL-), **23**, *65*
- Peroxides, removal from isopropyl ether, **22**, 3
  - removal from α-tetralone, **20**, 95
- PERPHTHALIC ACID, MONO-, **20**, *70*
- Petroleum ether, **23**, 102, 104
- PHENETHYLAMINE, **23**, *71*
- Phenol, **20**, 77; **22**, 6
- Phenol red, **22**, 91
- 9-Phenoxyacridine, **22**, 7
- *dl*-PHENYLALANINE, **21**, *99*
- *N*-Phenylanthranilic acid, **22**, 5
- PHENYL AZIDE, **22**, *96*
- Phenylbenzoyldiazomethane, **20**, 48
- PHENYL CINNAMATE, **20**, *77*
- *o*-Phenylenediamine, **20**, 16
- α-PHENYLETHYLAMINE, **23**, *68*
- β-PHENYLETHYLAMINE, **23**, *71*
- *dl*-PHENYLGLYCINE, **22**, *23*
- α-PHENYLGLYCOLIC ACID, **23**, *48*
- Phenylhydrazine, **22**, 96
- PHENYLHYDRAZINE HYDROCHLORIDE, **22**, *96*
- 2-PHENYLINDOLE, **22**, *98*
- PHENYLLITHIUM, **23**, *83*
- Phenylmagnesium bromide, **21**, 79; **23**, 98
  - reaction with benzophenone, **23**, 99
  - reaction with ethyl benzoate, **23**, 98
- PHOSGENE, SOLUTION OF, IN TOLUENE, **23**, *12*
- Phosphorus, red, **22**, 91
- Phosphorus oxychloride, **20**, 11; **22**, 5
- Phosphorus pentachloride, **21**, 86
- Phosphorus tribromide, **23**, 32, 88
  - precautions and dangers in use of, **23**, 33
- Phosphorus trichloride, **20**, 106; **21**, 74
  - precautions and dangers in use of, **23**, 33
- Photoflood lamps, **20**, 84, 104

- PHTHALALDEHYDIC ACID, **23**, *74*
- Phthalic anhydride, **20**, 70
- PHTHALIC ANHYDRIDE, TETRAPHENYL-, **23**, *93*
- PHTHALIC MONOPERACID, **20**, *70*
- Phthalide, **22**, 30, 62; **23**, 75
- Phthaloyl chloride, **20**, 51
- α-Picoline, **20**, 79; **23**, 84
- PICOLINIC ACID HYDROCHLORIDE, **20**, *79*
- α-PICOLYLLITHIUM, **23**, *84*
- PINACOL, ANHYDROUS, **22**, 39, *40*, 41
- Pinacol hydrate, **22**, 39
- Pinacolone, **22**, 39, 41
- Piperidine, **23**, 61
- Poppyseed oil, **22**, 78, 85
- Potassium, **23**, 42, 45
- Potassium acetate, **20**, 55
- POTASSIUM AMIDE, **20**, *91*
- Potassium bromide, **20**, 81, 101
- POTASSIUM *tert.*-BUTOXIDE, **23**, *42*, *45*
- Potassium carbonate, **20**, 21
- Potassium chlorate, **23**, 6
- Potassium cyanide, **20**, 38, 44; **22**, 35
- Potassium dichromate, **22**, 45
- POTASSIUM ETHOXIDE, **23**, *43*
- Potassium hypochlorite, **23**, 27
- Potassium iodide, **22**, 52, 71
- POTASSIUM METHOXIDE, **23**, *43*
- Potassium permanganate, **20**, 79
- Potassium persulfate, **22**, 44
- Pressure reaction, **20**, 40, 81, 101; **22**, 9, 19; **23**, 68, 70, 71, 72, 81, 90
  - use of "booster" pump, **23**, 68
- 1,3-PROPANEDIONE, 1,3-DIPHENYL-, **20**, *32*
- 1,2-PROPANEDIONE, 1-PHENYL-, **23**, *1*
- 2-PROPANOL, 1-(2-PYRIDYL)-, **23**, *83*
- 3-PROPANOL, 1-(2-PYRIDYL)-, **23**, *85*
- PROPIONIC ACID, β-3-ACENAPHTHENYLCARBONYL-, **20**, *1*
- PROPIONIC ACID, β-3-ACENAPHTHOYL-, **20**, *1*
- PROPIONIC ACID, β,β′-METHYLIMINOBIS-, DIETHYL ESTER, **20**, *35*
- Propionic anhydride, **21**, 14
- PROPIONITRILE, β-ETHOXY-, **23**, *33*
- PROPIOPHENONE, β-DIETHYLAMINO-, **23**, *31*
- PROPIOPHENONE, β-DIMETHYLAMINO-, **23**, *30*
- Protective screen, **22**, 97
- PSEUDOIONONE, **23**, *78*
  - BISULFITE COMPOUND, **23**, *79*
- PYRAN, DIHYDRO-, **23**, *25*
- PYRAN, TETRAHYDRO, **23**, 67, *90*
- Pyridine, **20**, 50; **21**, 89; **23**, 37, 88
  - anhydrous, **22**, 56
- 1-(α-PYRIDYL)-2-PROPANOL, **23**, *83*
- 1-(α-PYRIDYL)-3-PROPANOL, **23**, *85*
- PYRROLE, 2,4-DIMETHYL-3-ACETYL-5-CARBETHOXY-, **21**, *68*
- PYRROLE, 2,4-DIMETHYL-3-ETHYL-, **21**, *67*

- Quinoline, **21**, 87
- Quinones, **22**, 37

- RANEY NICKEL CATALYST, **21**, *15*; **22**, 9, 12; **23**, 68, 71
- Rearrangement, ω,ω-dichloroacetophenone to mandelic acid, **23**, 49
  - retropinacol, **22**, 41
- Red lead, **21**, 1, 3
- Reduction, by amalgamated zinc and hydrochloric acid, benzoin to stilbene, **23**, 86
  - by hydrogen and Raney nickel, at high pressures, **22**, 9
    - at low pressures, **22**, 12
    - benzylcyanide to phenethylamine, **23**, 71
    - dihydropyrane to tetrahydropyrane, **23**, 90
    - pseudoionone to hexahydropseudoionol, **23**, 81
    - with simultaneous amination by ammonia, acetophenone to α-phenylethylamine, **23**, 68
  - by hydrogen sulfide, **23**, 7
  - by stannous chloride, Stephen reduction of β-naphthonitrile to β-naphthaldehyde, **23**, 63
  - by zinc and alkali, **22**, 28
  - by zinc and hydrochloric acid, **20**, 57
  - Clemmensen, **20**, 57
  - electrolytic, **21**, 10
  - of a double bond by sodium amalgam, **22**, 90

Reduction—*Continued*
  of a hydroxylamino acid to an amino acid by hydroxylamine, **22**, 26
  of a nitro compound to an amine, **22**, 9
  of a nitro compound to an azo compound, **22**, 28
  of a nitro compound by stannous chloride, **22**, 32
  Rosenmund (Pd-BaSO$_4$), **21**, 84, 110
Reformatsky reaction, **21**, 51
Reimer-Tiemann reaction, **22**, 63
Replacement, amino group by a hydroxyl group (diazo reaction), **23**, 11
  bromine atom by a cyano group, **21**, 89; **23**, 33
  bromine atom by a hydroxyl group, **23**, 76
  chlorine atom by an amino group, **22**, 6
  chlorine atom by a sulfone group, **22**, 31
  glycosidic hydroxyl group by a bromine atom, **22**, 2
  hydrogen atom by a cyano group, **22**, 35
  hydroxyl group by an amino group, **22**, 19
  hydroxyl group by a bromine atom, with phosphorus tribromide, **23**, 32
    with phosphorus tribromide and pyridine, **23**, 88
  hydroxyl group by a chlorine atom, **22**, 5
  hydroxyl group by chlorine or bromine with acetyl halides, **23**, 100, 102
  nitro group by a methoxyl group, **22**, 35
RESACETOPHENONE, **21**, *103*
Resorcinol, **21**, 23, 103
α-RESORCYLIC ACID, **21**, *27*
Ring opening by hydrolysis with barium hydroxide, **22**, 91
Rosenmund synthesis, aldehyde, **21**, 84, 110
  nitrile, **21**, 89

Salt bath for heating, composition of, **21**, 90
Sand as diluent to prevent caking, **22**, 98
Saponification, of ethyl linoleate, **22**, 78
  of ethyl linolenate, **22**, 84
  of natural oils, **22**, 75, 79, 82
Screen, protective, **22**, 97
Seal, rubber tube, for stirrer shaft, **21**, *40*
SENECIOIC ACID, **23**, *27*
Separatory funnel, large, construction of, **23**, *105*
dl-SERINE, **20**, *81*
Shaking extractor, **23**, *78*
Silver acetate, **20**, 15
Snyder column, **20**, 68
Sodium, **20**, 7, 74, 88; **21**, 42, 60, 68, 99; **22**, 92; **23**, 16, 18, 20, 53, 95, 97
Sodium acetate, **20**, 6, 11, 56, 75; **22**, 54
SODIUM AMALGAM, **22**, 90, *92*
Sodium amide, **20**, 40, *87;* **22**, 94; **23**, *20*
  grinding, **20**, 41, 88; **22**, 95
  handling, **20**, 41, 88
  residues, destruction of, **20**, 90
Sodium bicarbonate, **20**, 26; **23**, 78
Sodium bisulfite, **20**, 43; **23**, 78, 79
Sodium cyanide, **20**, 44; **22**, 13, 23; **23**, 33
Sodium ethoxide, **20**, 7, 9, 33; **22**, 26; **23**, 35, 79
  by "inverse" procedure, **23**, *18*
Sodium hypochlorite, **22**, 73
SODIUM *l*-MENTHOXIDE, **23**, *52*
Sodium methoxide, **20**, 14, 74
  by "inverse" procedure, **23**, *18*
Sodium nitrite, **21**, 31, 67; **22**, 96; **23**, 11; *see also* Diazotization
Sodium *p*-nitroperbenzoate, **23**, 66
Sodium peroxide, **23**, 65
SODIUM POWDER, **20**, *8;* **23**, *96*
Sodium sulfate, anhydrous, **22**, 57
Sodium sulfite, **23**, 78
Sodium thiocyanate, **22**, 17
Sodium zincate, **22**, 28
Spray trap, **23**, 1
STANNOUS CHLORIDE, ANHYDROUS, **23**, *64*
Stannous chloride dihydrate, **22**, 32; **23**, 63
Steam distillation, **20**, 2
Stephen reduction, **23**, 63
trans-STILBENE, **22**, 50; **23**, *86*

STILBENE DIBROMIDE, **22**, *50*
Stirrer, brass, **21**, 44
  glycerol-sealed, **21**, *40*
  Hershberg, **20**, 8; **22**, 23, 74; **23**, 33
  "Lightnin" mixers, **21**, 97
  Monel-metal, **20**, 99
  stainless-steel, **23**, 54
Strecker synthesis, **22**, 13, 23
Succinic anhydride, **20**, 1
SULFONE, **22**, *31*
Sulfur dioxide, **22**, 92
Sulfuric acid, **22**, 48, 49; **23**, 11
  fuming, **21**, 27
Sulfuryl chloride, **22**, 17
Sunflower seed oil, **22**, 75, 80
Superheater for steam, **23**, 64

d-Tartaric acid, **22**, 65; **23**, 79, 80
TARTARIC ACID DINITRATE, **22**, *65*
TEREPHTHALALDEHYDE, **20**, *92*
2,3,4,6-TETRAACETYL-α-*d*-GLUCOPYRANOSYL BROMIDE, **22**, *1*
Tetraacetylglucose-6-mononitrate, **22**, 58
TETRABROMOSTEARIC ACID, **22**, *76*
α,α,α′,α′-TETRABROMO-*p*-XYLENE, **20**, *92*
Tetrachloroethane, **23**, 57
  precautions in use of, **23**, 58
  -TETRADECYL *p*-BROMOBENZENESULFONATE, **20**, *51*
  -TETRADECYL *p*-TOLUENESULFONATE, **20**, *51*
Tetrahydrofurfuryl alcohol, **23**, 25, 88
TETRAHYDROFURFURYL BROMIDE, **23**, *88*
TETRAHYDROPYRANE, **23**, 67, *90*
Tetralin, **20**, 94
α-TETRALONE, **20**, *94*
2,3,4,6-TETRAMETHYL-*d*-GLUCOSE, **20**, *97*
TETRAMETHYLMETHYLGLUCOSIDE, MIXTURE OF α AND β, **20**, *100*
Tetramethyl-α-methylglucoside, **20**, 99
TETRANITROMETHANE, **21**, *105*
  as reagent for detecting double bonds, **21**, 107
TETRAPHENYLCYCLOPENTADIENONE, **23**, *92*, 93
TETRAPHENYLDIHYDROPHTHALIC ANHYDRIDE, **23**, *93*
TETRAPHENYLPHTHALIC ANHYDRIDE, **23**, *93*
Thionyl chloride, **20**, 77; **21**, 78; **23**, 55
Thiourea, **21**, 36; **22**, 59
dl-THREONINE, **20**, *101*
Tin, **20**, 19
TOLAN, **22**, *50*
o-Tolidine, **21**, 32, 34
Toluene, **20**, 66; **22**, 53; **23**, 12, 52, 65
TOLUENE, α-CHLORO-2-HYDROXY-5-NITRO-, **20**, *59*
p-Toluenesulfonyl chloride, **20**, 50
α-TOLUIC ACID, α-AMINO, *dl*, **22**, *23*
α-TOLUIC ACID, *o*-CARBOXY-, **22**, *61*
m-Toluidine, **21**, 108
m-TOLUIDINE, *N*-BENZYL, **21**, *108*
o-Toluidine, **23**, 43
p-Toluidine, **22**, 16
p-TOLUIDINE SULFATE, **22**, *17*
m-TOLYLBENZYLAMINE, **21**, *108*
o-Tolylbenzylamine, **21**, 109
p-Tolylbenzylamine, **21**, 109
p-TOLYLTHIOUREA, **22**, *17*
Toxicity, **20**, 97; **23**, 58
Trap for absorbing gases, **23**, 13, 55, 102
TRIBIPHENYLCARBINOL, **23**, *95*, *97*
3,4,5-Tribromobenzoyl chloride, **23**, 66
3,4,5-TRIBROMOBENZOYL PEROXIDE, **23**, *66*
2,4,6-TRIETHYLBENZALDEHYDE, **23**, *60*
1,3,5-Triethylbenzene, **23**, 60
2,4,6-TRIISOPROPYLBENZALDEHYDE, **23**, *60*
1,3,5-Triisopropylbenzene, **23**, 60
2,4,6-TRIMETHYLBENZALDEHYDE, **21**, *110;* **23**, *57*, *59*
TRIMETHYLENE BROMIDE, **20**, *25;* **23**, 16
Trimethylthiourea, **21**, 84
TRIPHENYLBROMOMETHANE, **22**, 57; **23**, *102*
TRIPHENYLCARBINOL, **23**, *98*, 100
TRIPHENYLCHLOROMETHANE, **22**, 56; **23**, *100*, *102*
TRIPHENYLMETHYL BROMIDE, **22**, 57; **23**, *102*
TRIPHENYLMETHYL CHLORIDE, **22**, 56; **23**, *100*, *102*
Tritylation of glucose, **22**, 56

TRITYL BROMIDE, **22**, 57; **23**, ***102***
TRITYL CHLORIDE, **22**, 56; **23**, ***100***, ***102***
6-TRITYL-*β*-*d*-GLUCOSE-1,2,3,4-TETRAACETATE, **22**, ***56***

Ullmann synthesis, **20**, 45
n-Undecyl mercaptan, **21**, 38
o-Undecylylphenol, **20**, 58
p-Undecylylphenol, **20**, 58
Urea, **23**, 11
Uric acid, **23**, 6

Vacuum desiccator, "dumb-bell" type, **23**, ***105***
Valerylchlororesorcinol, **20**, 58
o-Valerylphenol, **20**, 58
p-Valerylphenol, **20**, 58
dl-VALINE, **20**, ***106***
Vanillin, **22**, 90
Vigreux column, **20**, 22, 52
Vinyl acetate, **23**, 9

Walnut oil, **22**, 85
Wax, bayberry, **20**, 67
  myrtle, **20**, 68
Widmer column, **20**, 7, 9, 22, 41, ***52***, 68, 84
Wilson rings, **20**, 52
Wire helices, **20**, 96

Xylene, **23**, 96
  dry, **20**, 8, 9
  purified for Rosenmund reduction, **21**, 85
p-Xylene, **20**, 92

Yeast, **22**, 53

Zinc, **20**, 57; **22**, 77, 83
ZINC, AMALGAMATED, **20**, ***57***; **23**, ***86***
Zinc chloride, **20**, 52; **22**, 19
  anhydrous, **21**, 103; **22**, 98
Zinc cyanide, **23**, 57
Zinc dust, **21**, 51, 68; **22**, 28; **23**, 86
  purification of, **21**, 52

ORGANIC SYNTHESES

AN ANNUAL PUBLICATION OF SATISFACTORY METHODS FOR THE PREPARATION OF ORGANIC CHEMICALS

ADVISORY BOARD

Roger Adams
H. T. Clarke
J. B. Conant
L. F. Fieser
Reynold C. Fuson
Henry Gilman
W. W. Hartman
John R. Johnson
C. S. Marvel
C. R. Noller
F. C. Whitmore

EDITORIAL BOARD

Lee Irvin Smith, *Editor-in-Chief*

Homer Adkins
C. F. H. Allen
W. E. Bachmann
Nathan L. Drake
C. S. Hamilton
R. L. Shriner
H. R. Snyder

H. Blatt, *Secretary to the Board*
Queens College, Flushing, N. Y.

CONTRIBUTORS

Other than the members of the Board

Lawrence H. Amundsen
D. W. Andrus
J. G. Aston
Alfred Berger
A. E. Calkins
H. E. Carter
Harvey Diehl
Julian Dorsky
W. S. Emerson
R. L. Frank
Sidney Gottfried
Oliver Grummitt
George C. Harrison
C. R. Hauser
G. B. Heisig
H. P. Hetzner
E. C. Horning
Boyd E. Hudson, Jr.
D. M. Jenkins
H. W. Johnston
Robert E. Kent
R. L. Kenyon
Karl W. Krantz
Edwin Krebs
D. Kundiger
M. T. Leffler
S. M. McElvain
Charles E. Maxwell
A. A. Morton
J. R. Myles
Samuel Natelson
J. D. Newkirk
Dorothy Nightingale
E. F. Orwoll
Charles C. Price
W. W. Prichard
John C. Robinson, Jr.
L. J. Roll
S. P. Rowland
Alfred Russell
James J. Sanderson
R. L. Sawyer
M. J. Schlatter
O. E. Sheppard
L. H. Smith
Leo J. Spillane
F. H. Stodola
F. T. Tyson
H. E. Ungnade
L. A. Walter
M. L. Ward
K. H. Weber
Jonathan W. Williams
F. J. Wolf

Vol. 23

NEW YORK
JOHN WILEY & SONS, Inc.
London: CHAPMAN & HALL, Limited

Copyright, 1943
by
Organic Syntheses, Inc.

All Rights Reserved

This book or any part thereof must not be reproduced in any form without the written permission of the publisher.

Second printing, March, 1946

PRINTED IN THE UNITED STATES OF AMERICA

TABLE OF CONTENTS

PAGE
Acetylbenzoyl 1
Alloxan 3
Alloxantin Dihydrate 6
Bromoacetal 8
3-Bromo-4-hydroxytoluene 11
Carbobenzoxy Chloride and Derivatives 13
1,1-Cyclobutanedicarboxylic Acid and Cyclobutanecarboxylic Acid . . 16
Cyclopropyl Cyanide 20
β-Di-*n*-butylaminoethylamine 23
2,3-Dihydropyrane 25
β,β-Dimethylacrylic Acid 27
β-Dimethylaminopropiophenone Hydrochloride 30
β-Ethoxyethyl Bromide 32
β-Ethoxypropionitrile 33
Ethyl Benzoylacetate 35
Ethyl Bromoacetate 37
Indole 42
Ketene Diethylacetal 45
Mandelic Acid 48
l-Menthoxyacetic Acid 52
l-Menthoxyacetyl Chloride 55
Mesitaldehyde 57
β-Methylglutaric Acid 60
β-Naphthaldehyde 63
p-Nitrobenzoyl Peroxide 65
Pentamethylene Bromide 67
α-Phenylethylamine 68
β-Phenylethylamine 71
Phthalaldehydic Acid 74
Pseudoionone 78
1-(α-Pyridyl)-2-propanol 83
trans-Stilbene 86
Tetrahydrofurfuryl Bromide 88
Tetrahydropyrane 90
Tetraphenylcyclopentadienone 92
Tetraphenylphthalic Anhydride 93
Tribiphenylcarbinol 95
Triphenylcarbinol 98
Triphenylchloromethane 100

Subject Index for Volumes 20–23 109