NOMENCLATURE

Preparations appear in the alphabetical order of common names of the compounds. For convenience in surveying the literature concerning any preparation through *Chemical Abstracts* subject indexes, the *Chemical Abstracts* indexing name for each compound is given as a subtitle if it differs from the common name used as the title.

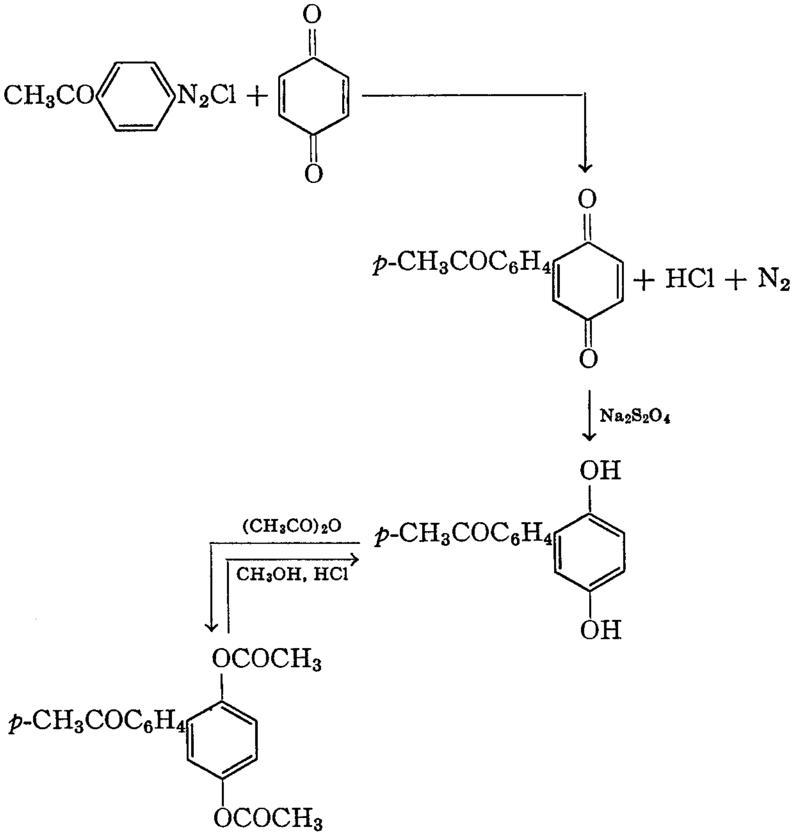
SUBMISSION OF PREPARATIONS

Chemists are invited to submit for publication in *Organic Syntheses* procedures for the preparation of compounds which are of general interest or which illustrate useful synthetic methods. The procedures submitted should represent, as nearly as possible, optimum conditions for the preparations, and should have been checked carefully by the submitter. Full details of all steps in the procedure should be included, and the range of yields should be reported rather than the maximum yield obtainable. The melting point of each solid product should be given, and the boiling-point range and refractive index (at 25°) of each liquid product. The method of preparation or source of the reactants and the criteria for the purity of the products should be stated.

Procedures submitted should be written in the style employed in the latest volume of *Organic Syntheses*. Copies of the current style sheet may be obtained upon request from the Secretary of the Editorial Board. Two copies of procedures which are submitted should be sent to the Secretary. Additions, corrections, and improvements to preparations previously published are welcomed and should be sent to the Secretary.

2-*p*-ACETYLPHENYLHYDROQUINONE

(Acetophenone, *p*-(2,5-dihydroxyphenyl)-)



Submitted by George A. Reynolds and J. A. VanAllan.[1]
Checked by R. S. Schreiber and A. H. Nathan.

1. Procedure

In a 500-ml. beaker equipped with a mechanical stirrer are placed 27 g. (0.2 mole) of *p*-aminoacetophenone (Note 1), 100 g. of chopped ice, and 53 ml. of concentrated hydrochloric acid (sp. gr. 1.19). To the stirred mixture is added, over a period of 5 minutes, a solution of 13.8 g. (0.2 mole) of sodium nitrite dissolved in 75 ml. of water. The stirring is continued for 15 minutes, during which all the insoluble amine hydrochloride reacts to form the soluble diazonium compound (Note 2).

In a 4-l. beaker, equipped with a high-speed stirrer (Note 3), are placed 20 g. (0.185 mole) of quinone (Note 4), 34 g. (0.4 mole) of sodium bicarbonate, 50 g. of chopped ice, and 500 ml. of water. About 10 ml. of the above diazonium salt solution is added (Note 5). After the frothing has subsided (Note 6), the diazonium salt solution is added in 10- to 20-ml. portions over a period of about an hour (Note 7). The temperature of the reaction mixture is kept below 15° during this period by the addition of ice. After the diazonium salt solution has been added, the mixture is allowed to warm up to room temperature, and the stirring is continued for an additional hour. The precipitate of 2-*p*-acetylphenylquinone is collected on a Büchner funnel and washed thoroughly with approximately 1 l. of water. The yield of crude yellow-brown solid is 40–41 g. (96–98%). The melting point ranges from 125–135° to 134–136° (Note 8).

The crude quinone is dissolved in 250 ml. of chloroform (Note 9) and added to a solution of 40 g. of sodium hydrosulfite in 300 ml. of water. The mixture is shaken for 10 minutes, and the light-tan 2-*p*-acetylphenylhydroquinone which precipitates from solution is collected on a Büchner funnel and dried. The yield of crude hydroquinone is 32–37 g. (78–92%). The melting point ranges from 175–180° to 184–194° (Note 10).

A suspension of 35 g. (0.153 mole) of 2-*p*-acetylphenylhydroquinone in 77 ml. of acetic anhydride is treated with 0.5 ml. of concentrated sulfuric acid (sp. gr. 1.84). The hydroquinone goes into solution immediately with the evolution of much heat. The dark-colored solution is allowed to stand at room temperature overnight; then it is poured into 400 ml. of water. The acetylated material is collected by suction filtration and dried. The crude 2-*p*-acetylphenylhydroquinone diacetate is distilled at reduced pressure (b.p. 236–241°/1 mm. or 182–190°/0.1 mm.), and the hot distillate is poured into 20 ml. of *n*-butyl alcohol (Note 11). The product immediately separates as a colorless, crystalline

mass, which is collected by suction filtration and dried. The yield is 32–35 g. (67–73%), m.p. 104–105°.

To a 300-ml. three-necked round-bottomed flask, equipped with a sealed stirrer, a condenser, and a gas inlet tube, is added a solution of 34 g. (0.11 mole) of 2-*p*-acetylphenylhydroquinone diacetate in 140 ml. of hot methanol. The solution is cooled to room temperature, causing some of the hydroquinone diacetate to crystallize. A slow stream of nitrogen is passed through the suspension, and 70 ml. of methanol containing 6.1 g. of anhydrous hydrogen chloride is added. The reaction mixture is stirred at room temperature for 2 hours under nitrogen, during which period the hydroquinone diacetate gradually dissolves. The pale yellow solution is poured onto 500 g. of chopped ice, and the colorless or faintly yellowish solid is collected by suction filtration and dried. The yield of *p*-acetylphenylhydroquinone melting at 193–194° is 24.8 g. (quantitative). The over-all yield of product based on quinone is 50–66%.

2. Notes

1. The purest grade of *p*-aminoacetophenone supplied by the Eastman Kodak Company was used without further purification.

2. This reaction has been successfully carried out on a 3-mole scale.

3. A "Lightnin" mixer (manufactured by the Mixing Equipment Company, Rochester, N. Y.) equipped with a propeller stirrer was used. If rapid stirring is not maintained, the reaction does not go to completion.

4. The checkers used a practical grade of quinone obtainable from the Eastman Kodak Company.

5. If nitrogen is not evolved immediately, the reaction may be initiated by the addition of a small amount of hydroquinone.

6. If the foaming becomes too violent, a few drops of octyl alcohol are added.

7. The checkers found it convenient to add the diazonium salt solution slowly from a dropping funnel. The time of addition was 25–45 minutes.

8. Recrystallization from butanol gives material melting at 139–140°. The pure substance is reported to melt at 152–153°.[2]

9. Ethanol can also be used as a solvent but has the disadvantage of more readily dissolving the hydroquinone, thus making it necessary to evaporate the solution nearly to dryness.

10. It is difficult to purify the crude hydroquinone by recrystallization; therefore the remainder of the procedure is recommended in order to obtain a highly purified product.

11. The checkers found it convenient to crystallize the viscous distillate from 125 ml. of methanol by chilling a hot solution in the refrigerator overnight. A small second crop amounting to about 2 g. may also be obtained by concentration of the mother liquors.

3. Methods of Preparation

This procedure is a modification of the method described for the preparation of 2-chlorophenylhydroquinone.[3] 2-*p*-Acetylphenylquinone has been prepared by carrying out the coupling in alcohol solution in the presence of sodium acetate instead of sodium bicarbonate.[2] Reduction by zinc, acetic acid, and a small amount of concentrated hydrochloric acid yielded 2-*p*-acetylphenylhydroquinone.[2]

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[1] Eastman Kodak Company, Rochester, New York.

[2] Kvalnes, *J. Am. Chem. Soc.*, **56**, 2478 (1934).

[3] B.I.O.S., Report 1146 (1946). [Reports obtainable from British Intelligence Objectives Subcommittee, 32 Bryanston Sq., London, W. 1.]

AZELANITRILE

$$HO_2C(CH_2)_7CO_2H + 2NH_3 \xrightarrow[\text{gel}]{\text{Silica}} NC(CH_2)_7CN + 4H_2O$$

Submitted by ARTHUR C. COPE, ROBERT J. COTTER, and LELAND L. ESTES.[1]
Checked by N. J. LEONARD and R. W. FULMER.

1. Procedure

Caution! This preparation should be conducted in a hood to avoid exposure to ammonia.

The reaction is carried out in the apparatus shown in Fig. 1. *A* is a Pyrex combustion tube, 54 cm. long and 3.5 cm. in diameter, having a glass star seal or indentations 14 cm. from the lower end to support the catalyst, and fitted with ground-glass joints. *B* is a Pyrex tube, 21 cm. long and 3.5 cm. in diameter, which has a 6-cm. length of 6-mm. capillary tubing attached at the lower end. The capillary tube is attached to a ground-glass joint and an inlet tube, *C*, is inserted above the end of the capillary

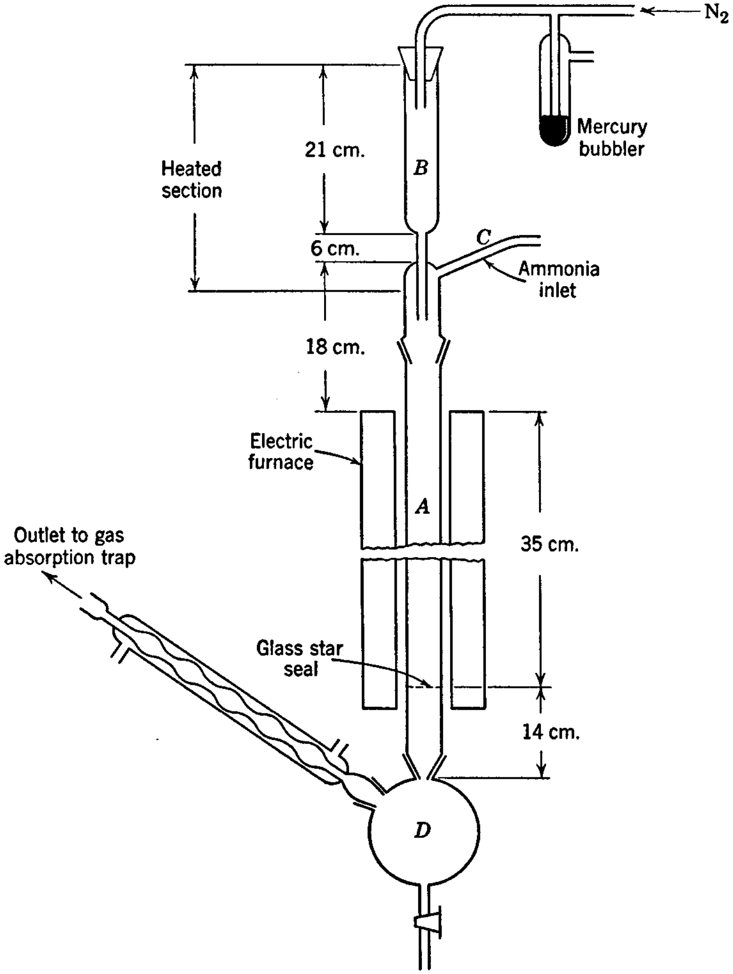

FIG. 1.

tube. The top section of the apparatus (above the first ground-glass joint) is covered with asbestos and wound with 14 ft. of No. 22 Chromel A resistance wire. *D* is a 500-ml. round-bottomed two-necked flask with ground-glass joints and a 4-mm. stopcock sealed to the bottom. An efficient condenser is attached to the flask and connected to a gas absorption trap.[2] The hot junction of a pyrometer is placed in contact with the glass combustion tube *A* at its center, and the tube is wrapped with a thin layer of asbestos paper. An electric furnace with a 33-cm. heated section which is rated at 6.8 amp. (110 v.) is used to heat the combustion tube.

A piece of glass wool is placed on the star seal, and the combustion tube is filled with 74 g. (110 ml.) of 14- to 20-mesh silica gel (Note 1). The tube is heated to 500°, and nitrogen is passed through the column for 30 minutes to activate the catalyst. Anhydrous ammonia is then passed through the column at a rate of 3.9 moles per hour (Note 2). Molten azelaic acid, 100 g. (0.53 mole) (Note 3), is poured into the reservoir *B*, which is maintained at 108–112° by means of the electrically heated jacket, and allowed to drop onto the hot silica gel over a 4-hour period (Note 4). After the azelaic acid has been added, ammonia is passed through the tube for an additional period of 30 minutes, with the temperature maintained at 500°, to complete the removal of product from the combustion tube.

Water (100 ml.) and ether (350 ml.) are added to the condensate in the receiver *D*, and the mixture is shaken. The aqueous layer is removed, and the ethereal solution is washed with 75 ml. of 6 *N* sodium hydroxide solution. The ethereal solution is washed with water until the washings are neutral and is dried over anhydrous magnesium sulfate. The ether is removed under reduced pressure by warming with a water bath, and the residue is distilled through a Vigreux or packed column. The azelanitrile is collected at 120–121°/0.2 mm., 175–176°/6 mm., in a yield of 50–54 g. (63–68%), n_{D}^{25} 1.4443–1.4448 (Notes 5 and 6).

2. Notes

1. Refrigeration-grade silica gel, 14- to 20-mesh, obtained from the Davison Chemical Corporation, Baltimore, Maryland, was used.

2. A manometer-type flow meter[3] was calibrated by passing ammonia through the meter into a standard solution of 4 *N* hydrochloric acid containing a few drops of phenolphthalein solution. The time required for exact neutralization of a measured volume of acid was recorded, together with the pressure differential, in millimeters, between the manometer arms. The logarithm of the rate of flow in moles per hour plotted against the logarithm of the pressure, for various rates of flow, gave a straight-line plot which was used to determine flow rates for other pressure differentials.

3. Azelaic acid obtained from Emery Industries, Inc., Cincinnati, Ohio, was recrystallized from water to a melting point of 101–102°.

4. Comparable results have been obtained when the acid was added over a 2-hour period. It is desirable to maintain a nitrogen atmosphere over the acid at a pressure slightly above that of the ammonia flow to prevent reduction of the acid flow by salt formation in the capillary.

5. Cooling the receiver *D* may help prevent loss of product by mechanical carry-over in the gas flow.

6. This preparation illustrates a general method for producing nitriles from monocarboxylic[4] and dicarboxylic acids.[5]

3. Methods of Preparation

Azelanitrile has been prepared in 80% yield by treating 1,7-dibromoheptane with potassium cyanide;[6] by treating 1,7-diiodoheptane with potassium cyanide;[7] from azelaic acid through the intermediate acid chloride and diamide;[8] in 60–70% yield by the dehydration of the diamide of azelaic acid;[9] and by the action of sodium amide and acetonitrile on the 1,5-dihalopentanes.[10]

[1] Massachusetts Institute of Technology, Cambridge, Massachusetts.

[2] *Org. Syntheses* Coll. Vol. **2**, 4 (1943).

[3] Altieri, *Gas Analysis and Testing of Gaseous Materials,* American Gas Association, Inc., New York, N. Y., 1945, p. 57.

[4] Mitchell and Reid, *J. Am. Chem. Soc.*, **53**, 321 (1931).

[5] Lazier, U. S. pat. 2,144,340 [*C. A.*, **33**, 3398 (1939)].

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[7] Dionneau, *Ann. chim.*, [9], **3**, 248 (1915).

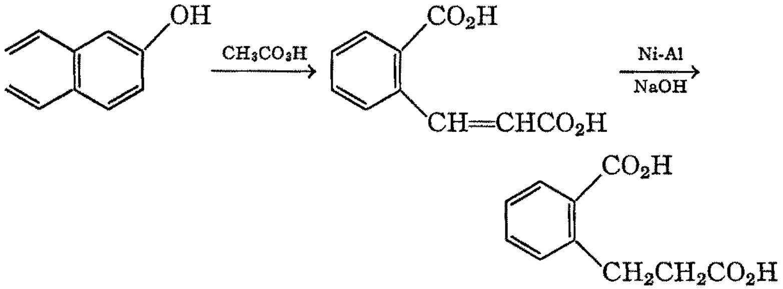
[8] Trunel, *Ann. chim.*, [11], **12**, 112 (1939).

[9] Solonia, *J. Russ. Phys. Chem. Soc.*, **29**, 410 (1897) [*Chem. Zentr.*, [2], **68**, 848 (1897)].

[10] Paul and Tchelitcheff, *Bull. soc. chim. France*, **1949**, 470.

β-(o-CARBOXYPHENYL)PROPIONIC ACID

(Hydrocinnamic acid, 2-carboxy-)



Submitted by G. A. Page and D. S. Tarbell.[1]
Checked by William S. Johnson, Shirley Rosenberg, and
Robert D. Eberhardt.

1. Procedure

A. *o-Carboxycinnamic acid.* Eighty-eight grams (78 ml., 0.46 mole of peracid) of 40% peracetic acid (Note 1) is placed in a 250-ml. Erlenmeyer flask which is immersed in a water bath maintained at 25–30°. A 150-ml. dropping funnel is mounted so that the stem enters the flask to within about 4 cm. of the liquid surface. With mechanical stirring (Note 2), a cold solution of

20 g. (0.14 mole) of β-naphthol (Note 3) in 100 ml. of glacial acetic acid is added dropwise over a period of 4 hours to the peracid. With the appropriate rate of addition, the temperature of the reaction mixture slowly rises to 30–35° and should not exceed 40°. Solid material begins to separate from the orange solution when one-third or more of the naphthol solution is introduced. When the addition is complete, the mixture is stirred for 1 hour and the flask is allowed to stand in the water bath until the exothermic reaction ceases (usually 6–8 hours), then at room temperature for 4 days (Note 4). The solid material is collected by suction filtration and washed on the filter with sufficient (10–20 ml.) acetic acid to remove colored impurities. Drying in the air gives 19.6–20.1 g. of crude *o*-carboxycinnamic acid as a pale yellow crystalline solid (Notes 4 and 5).

The crude acid is purified by dissolving in 360–400 ml. of cold 5% sodium bicarbonate solution, filtering, and acidifying the filtrate with sufficient excess of mineral acid to turn Congo red paper blue. The product is separated by suction filtration, washed with water to remove mineral acid, and air-dried. Material thus obtained weighs 17.9–18.7 g. (67–70% yield). It melts generally (Note 6) between 202° and 205°, and is sufficiently pure (Note 7) for most practical purposes.

B. *β-(o-Carboxyphenyl)propionic acid.* In an open 1-l. wide-mouthed round-bottomed flask are placed 18 g. (0.094 mole) of *o*-carboxycinnamic acid and 550 ml. of 10% sodium hydroxide solution. The mixture is warmed to 90° (Note 8) on a steam bath and stirred mechanically. The steam bath is then removed while 54 g. (Note 9) of nickel-aluminum alloy (Raney catalyst) powder is added through the open neck of the flask in small portions (from the end of a spatula) at frequent intervals (Note 10). When addition of the alloy is complete (about 50 minutes), the mixture is stirred and maintained at 90–95° for 1 hour by warming on a steam bath. Distilled water is added as needed to maintain the total volume at approximately 550 ml. The hot mixture is filtered with suction, and the metallic residue is washed with 50 ml. of hot 10% sodium hydroxide solution and two 50-ml. portions of hot water in such a manner that the solid is always covered with liquid (Note 11). The cooled filtrate and washings are added dropwise with mechanical stirring to 300 ml. of concentrated hydrochloric acid (sp. gr. 1.19) in an open 2-l. beaker at such a rate that the temperature does not exceed 80–85° (Note 12). Separation of crystalline material begins almost immediately and is complete when the beaker contents have cooled to room temperature. The β-(*o*-carboxyphenyl)propionic acid is separated by suction filtration, washed with water, and air-dried (Note 13). The yield is 16.8–17.3 g. (92–95%), m.p. 165.5–167° (Note 14).

2. Notes

1. Commercial 40% (w/w) peracetic acid is available from the Becco Sales Corporation, Buffalo 7, New York. The use of a 3.3 molecular proportion of the peracid results in slightly higher and more consistent yields of product than when the theoretical 3.0 proportion is employed. The procedure gives the same yield (percentage) of product when using proportionately smaller quantities of reactants.

2. The operator should be protected by means of a safety shield. A glass (propeller-blade) stirrer passing through the open neck of the Erlenmeyer flask is convenient; rapid stirring is not essential.

3. β-Naphthol of C.P., U.S.P., or N.F. grade has been used with equal success.

4. After 15 hours' standing, 15.0–16.8 g. of crude *o*-carboxycinnamic acid may be recovered by filtration, washing, and drying.

5. The filtrate, either on concentration under reduced pressure or upon dilution with water, fails to yield more *o*-carboxycinnamic acid, but a crystalline by-product, presumably 4-(*o*-carboxyphenyl)-5,6-benzocoumarin,[2] may be encountered in small yield.

6. On melting, *o*-carboxycinnamic acid cyclizes to give the lactone of β-hydroxy-β-(*o*-carboxyphenyl)propionic acid (phthalideacetic acid), m.p. 153°. If the melting point is taken too slowly, or if the diacid is not washed completely free of mineral acid, it may therefore melt considerably below 200°. The reduction step (part *B*), however, proceeds normally with such material.

7. The acid may be recrystallized from aqueous ethanol to give small, white, felted prisms, m.p. 205°.

8. It is advisable to insert a thermometer only at intervals since the alkaline mixture attacks glassware to an appreciable extent on prolonged contact.

9. Using less than 50 g. of the alloy results in the same yield of final product, which, however, contains small amounts of unchanged *o*-carboxycinnamic acid. Equally good results are obtained when proportionately smaller quantities of reactants are used.

10. If excessive foaming is encountered it may be controlled as required by the addition of a few drops of octyl alcohol.

11. The metallic residue may ignite if allowed to dry on the filter. Disposal can be carried out by dissolving the residue in dilute nitric acid. (*Caution! vigorous reaction.*)

12. With this order of addition, aluminum salts remain in solution, thus simplifying the procedure. External cooling may be applied in order to save time.

13. Extraction of the filtrate with ether gives an additional 0.4–0.5 g. of the crude acid after removal of solvent by distillation. It may be purified by conventional means to give an additional 0.25–0.35 g. of the pure product.

14. β-(*o*-Carboxyphenyl)propionic acid may be recrystallized from hot water (about 20 ml./g.), giving material m.p. 166.5–167.5°.

3. Methods of Preparation

o-Carboxycinnamic acid has been prepared by the hydrolysis of *o*-carboxycinnamonitrile,[3] by the opening of the lactone ring in phthalideacetic acid,[4,5] and by the dehydration of metallic salts of β-hydroxy-β-(*o*-carboxyphenyl)propionic acid.[4] It has also been obtained from β-naphthol by reaction with the following oxidizing agents: potassium permanganate in neutral or alkaline solutions;[6] 30% hydrogen peroxide in acetic acid;[7] and peracetic acid in acetic acid.[8] β-Naphthoquinone may be oxidized to give *o*-carboxycinnamic acid, with 30% hydrogen peroxide [9] or perbenzoic acid.[10] Naphthalene also yields this acid on oxidation with peracetic acid.[11] The procedure described here is essentially that of Böeseken and Königsfeldt and of Greenspan.[8]

β-(*o*-Carboxyphenyl)propionic acid has been prepared by the action of reagents (mostly potassium permanganate as an oxidant) upon di- and tetrahydronaphthalenes and their derivatives.[12] *o*-Carboxycinnamic acid has been reduced by means of sodium amalgam,[13] and cinnam-*o*-hydroxamic acid has been reduced catalytically,[14] to give the propionic acid. The dialdehyde of β-(*o*-carboxyphenyl)propionic acid has been oxidized to the diacid, using potassium permanganate in sodium carbonate solution.[15] The diacid has also been prepared by the action of heat upon *o*-carboxybenzylmalonic acid,[16] and from *o*-cyanohydrocinnamonitrile,[17] β-(*o*-cyanophenyl)propionic acid,[18] and ethyl *o*-cyanobenzylmalonate [19] by procedures involving hydrolysis. Hydrolytic cleavage of bis(1-keto-2-hydrindylidenemethyl)hydroxylamine and of 2-cyanohydrindone-1 [20] also gives β-(*o*-carboxyphenyl)propionic acid. The present procedure is adapted from a general method for reducing cinnamic acids.[21]

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[1] University of Rochester, Rochester, New York. The submitters wish to thank the National Institutes of Health for a grant under which this work was done.

[2] Bader, *J. Am. Chem. Soc.*, **73**, 3731 (1951); Dischendorfer and Danziger, *Monatsh.*, **48**, 325 (1927).

[3] Beckmann and Liesche, *Ber.*, **56**, 7 (1923); Edwards, *J. Chem. Soc.*, **1926**, 816.

[4] Gabriel and Michael, *Ber.*, **10**, 2203 (1877).

[5] Leupold, *Ber.*, **34**, 2834 (1901); Rowe, Haigh, and Peters, *J. Chem. Soc.*, **1936**, 1104; Titley, *J. Chem. Soc.*, **1928**, 2576.

[6] Ehrlich and Benedikt, *Monatsh.*, **9**, 528 (1888); Leman and Deremaux, *Bull. soc. chim. France*, **9**, 165 (1942).

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[8] Böeseken and Königsfeldt, *Rec. trav. chim.*, **54**, 316 (1935); Greenspan, *Ind. Eng. Chem.*, **39**, 847 (1947).

[9] Böeseken, Lichtenbelt, Milo, and van Marlen, *Rec. trav. chim.*, **30**, 146 (1911); Böeseken and Slooff, *Rec. trav. chim.*, **49**, 91 (1930).

[10] Karrer and Schneider, *Helv. Chim. Acta*, **30**, 859 (1947).

[11] Böeseken and Slooff, *Rec. trav. chim.*, **49**, 100 (1930).

[12] Bamberger and Bammann, *Ber.*, **22**, 967 (1889); Bamberger and Helwig, *Ber.*, **22**, 1915 (1889); Bamberger and Kitschelt, *Ber.*, **23**, 1562 (1890); Straus and Ekhard, *Ann.*, **444**, 158 (1925); Straus and Lemmel, *Ber.*, **46**, 239 (1913); Straus and Rohrbacher, *Ber.*, **54**, 66 (1921).

[13] Beckmann and Liesche, *Ber.*, **56**, 7 (1923); Gabriel and Michael, *Ber.*, **10**, 2204 (1877).

[14] Neunhoeffer and Kölbel, *Ber.*, **68**, 262 (1935).

[15] von Braun and Zobel, *Ber.*, **56**, 2140 (1923).

[16] Wislicenus, *Ann.*, **242**, 39 (1887).

[17] Snyder and Poos, *J. Am. Chem. Soc.*, **71**, 1395 (1949).

[18] Linstead, Rowe, and Tuey, *J. Chem. Soc.*, **1940**, 1076; Mayer, Philipps, Ruppert, and Schmitt, *Ber.*, **61**, 1971 (1928).

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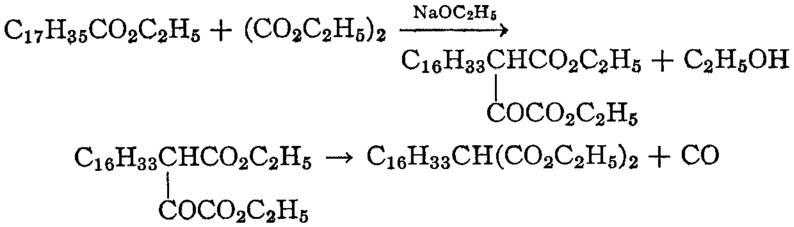
CETYLMALONIC ESTER

(Malonic acid, cetyl-, diethyl ester)



$$C_{17}H_{35}CO_2C_2H_5 + (CO_2C_2H_5)_2 \xrightarrow{NaOC_2H_5} C_{16}H_{33}\underset{\substack{|\\ COCO_2C_2H_5}}{C}HCO_2C_2H_5 + C_2H_5OH$$

$$C_{16}H_{33}\underset{\substack{|\\ COCO_2C_2H_5}}{C}HCO_2C_2H_5 \rightarrow C_{16}H_{33}CH(CO_2C_2H_5)_2 + CO$$

Submitted by DON E. FLOYD and SIDNEY E. MILLER.[1]
Checked by JAMES CASON and GEORGE A. GILLIES.

1. Procedure

A solution of sodium ethoxide in ethanol is prepared by adding 23 g. (1 gram atom) of freshly cut sodium metal, as ¼-in. cubes, in portions of 3–4 g., to 300 ml. of absolute ethanol, contained in a 1-l. three-necked flask, fitted with a thermometer and an upright, water-cooled condenser, the open end of which is capped with a drying tube filled with a mixture of Drierite and coarse lime (Note 1). The sodium is added through the third neck of the flask, which is otherwise kept stoppered.

When all the sodium has dissolved, the condenser is removed and 584 g. (4 moles) of diethyl oxalate (Note 2) and 312 g. (1 mole) of ethyl stearate (Note 3) are quickly added. The condenser is replaced by a still head connected to a condenser and receiver arranged for distillation at reduced pressure. If a water aspirator is used, a drying tube filled with Drierite should be inserted in the line between the receiver and aspirator. The receiver is cooled in a bath of ice water. The reaction mixture is heated at 50°, and the pressure in the system is reduced to about 100 mm. The temperature is gradually raised to 60°, with the system at a pressure of 100 ± 10 mm., to remove the ethanol used as solvent and formed as by-product. This distillation requires 2–3 hours (Note 4).

The receiver is changed and the excess diethyl oxalate is distilled under reduced pressure in the range of 76–82°/15 mm. (Note 5). The residue in the reaction flask, a viscous, red-brown mass, consists of the sodio derivative of ethyl α-ethoxalylstearate (Note 6). To it is gradually added, without cooling, 66 g. (1.1 mole) of glacial acetic acid. As the mixture is stirred by hand, 1 l. of water is added. Finally, the mixture is stirred mechanically for a few minutes, then allowed to separate into layers. The organic (upper) layer is taken up in 300 ml. of ether and washed well with sodium bicarbonate solution and with water; then the ether is removed by distillation from a steam bath.

The residual α-ethoxalyl ester is decarbonylated to cetylmalonic ester by heating at 160–170° under reduced pressure. A water aspirator is sufficient to facilitate removal of the carbon monoxide formed during the heating. The decarbonylation requires about 1–1.5 hours (Note 7). The cetylmalonic ester which remains as a dark liquid is fractionated under reduced pressure (Note 8).

A fore-run, consisting of ethyl stearate and an intermediate fraction, amounts to about 60 g., b.p. 185–204°/2 mm. (Note 8). The product is a colorless liquid amounting to 265–275 g. (68.5–71% yield), b.p. 204–208°/2 mm., n_D^{25} 1.4433 (Notes 9 and 10).

2. Notes

1. The evolved hydrogen should be led into a hood or out of a window to minimize the explosion hazard.

2. Diethyl oxalate can be dried satisfactorily by distilling a small portion from the bulk of the material. The water is removed with the distillate.

3. The ethyl stearate used by the checkers was prepared by esterifying commercial stearic acid (Armour Neo-Fat 1–65 or General Mills Aliphat 7) with 8 equivalents of absolute ethanol containing 10% by weight of concentrated sulfuric acid. The washed and dried product was distilled directly through a 60-cm. Vigreux column with a heated jacket and partial reflux head to give an 80% yield of material, b.p. 186.5–189°/3.5 mm., m.p. 32.2–34.2° (cor.). The purest grade of ethyl stearate as supplied by the Eastman Kodak Company is also satisfactory.

4. A column is not needed during distillation of the ethanol. When low-molecular-weight esters are substituted for ethyl stearate a suitable indented column should be used at this point to prevent loss of the ester. The reaction temperature should not be allowed to exceed 60°, because decomposition of the condensation product may result.

5. The contents of the flask should not be heated to a temperature higher than 90° during removal of the excess oxalate or some decomposition of the product may result. The recovered diethyl oxalate contains small amounts of ethanol and ethyl carbonate. It can readily be purified by fractional distillation; however, it is quite suitable for reuse in repeat preparations without purification.

6. This sodio derivative can be dissolved in a solvent such as toluene and employed as an intermediate for other reactions (alkylation, acylation, etc.).

7. The carbon monoxide evolved should be led into a hood to avoid the dangers of poisoning and explosion. No difficulties have been encountered at this stage, but precautions are advisable.

8. A 60-cm. column of the Vigreux type, with heated jacket and partial reflux head, was found satisfactory by the checkers. Ethyl stearate may solidify in the condenser if a total reflux head is used. Refractionation of the fore-run gives an additional 30–40 g. (10–13%) of pure product. Material containing a few

per cent of ethyl stearate can be obtained in 85–90% yield by simply distilling the total crude product from a Claisen flask.

9. Cetylmalonic acid, m.p. 115.5–120.5°, is obtained by saponification of the ester and one crystallization from acetone.

10. This general procedure is applicable to lower fatty acid esters.

3. Methods of Preparation

This method is based on the general procedure previously described by Floyd and Miller.[2] Cetylmalonic ester has also been prepared by condensation of ethyl stearate with ethyl carbonate[3] and by alkylation of sodiomalonic ester with cetyl iodide[4] or cetyl bromide.[5]

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[1] General Mills Laboratory, Minneapolis, Minnesota.

[2] Floyd and Miller, *J. Am. Chem. Soc.*, **69**, 2354 (1947).

[3] Wallingford, Homeyer, and Jones, *J. Am. Chem. Soc.*, **63**, 2056 (1941).

[4] Kraft, *Ber.*, **17**, 1630 (1884); Guthzeit, *Ann.*, **206**, 357 (1881).

[5] Phillips and Mumford, *J. Chem. Soc.*, **1931**, 1736.

2-CHLORO-1,1,2-TRIFLUOROETHYL ETHYL ETHER

(Ether, 2-chloro-1,1,2-trifluoroethyl ethyl)

$$CFCl{=}CF_2 + C_2H_5OH \xrightarrow{C_2H_5ONa} HCFClCF_2OC_2H_5$$

Submitted by BRUCE ENGLUND.[1]
Checked by R. S. SCHREIBER and BURRIS D. TIFFANY.

1. Procedure

The apparatus used is shown in Fig. 2 (Note 1). A solution of sodium ethoxide prepared by dissolving 2.5 g. of clean sodium metal (0.11 gram atom) in 230 g. (292 ml., 5 moles) of absolute ethanol under anhydrous conditions is added to the reaction tube *C*. The tube *C* thus charged is weighed, and placed in position with the gas inlet tube, fitted with fritted-glass dispersion cylinder *D*, extending nearly to the bottom. Several inches of ethanol is placed in the tube *G*, which serves as a flow indicator. The traps *A* and *F* are provided to protect against suck-back if the gas flow is interrupted. The seal at *B* is a sleeve of rubber tubing. Any efficient reflux condenser *E* is satisfactory.

Chlorotrifluoroethylene (Note 2) is introduced at such a rate, controlled by the needle valve, that it is essentially all absorbed in the reaction tube *C*, as indicated by the escape of little or no gas through tube *G*. At this rate, 233 g. (2 moles) (Note 3) is absorbed in 2–2.5 hours, during which the temperature rises to the point of reflux (Note 4).

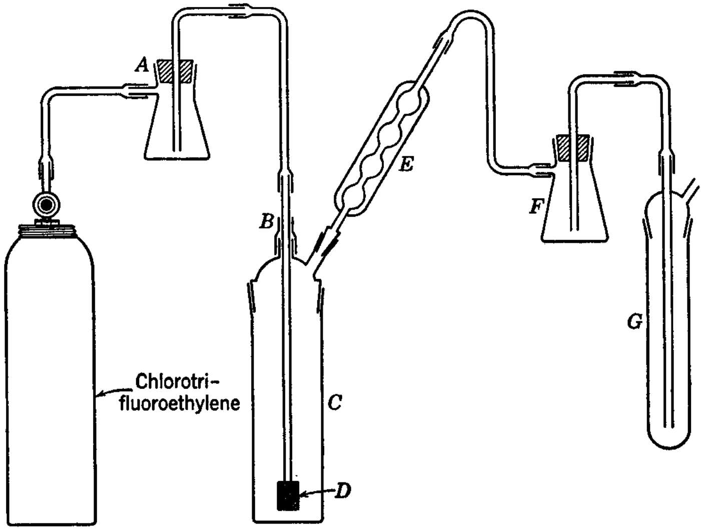

FIG. 2.

When the required amount of chlorotrifluoroethylene has been absorbed, the reaction mixture is poured into 500 ml. of water. The product separates as a light-yellow oil, which is separated, washed with 250 ml. of water, and dried over 20 g. of anhydrous calcium chloride. From 233 g. of chlorotrifluoroethylene (2 moles), the yield of crude product is 300–315 g. (92–97%). This material is suitable for use in preparation of ethyl chlorofluoroacetate.[2] It may be fractionated through an efficient column to give 285–300 g. (88–92%) of pure chlorotrifluoroethyl ethyl ether, b.p. 87–88°, n_D^{25} 1.3427.

2. Notes

1. The reaction tube *C* may be of any convenient size. The tube used by the submitter was 300 by 55 mm., fitted with a 55/35 standard taper ground-glass joint. The checkers used a 500-ml. calibrated dropping funnel which was convenient for following the increase in volume during the absorption of the chlorotrifluoroethylene. For safety, a heavy grease such as Cello-Grease was used in the stopcock.

2. The chlorotrifluoroethylene used was inhibited polymerization grade, supplied by the Kinetic Chemicals Division, Organic Chemicals Department, E. I. du Pont de Nemours and Company, Wilmington, Delaware.

3. The amount of chlorotrifluoroethylene absorbed is determined by weighing the reaction tube *C* and contents. A convenient alternative is to note the increase in volume of the reaction mixture, which in this case amounts to 165 ml.

4. The rate of absorption is slow at first but increases as the temperature rises.

3. Methods of Preparation

2-Chloro-1,1,2-trifluoroethyl ethyl ether has been prepared by the base-catalyzed addition of ethanol to 1-chloro-1,2,2-trifluoroethylene.[3,4]

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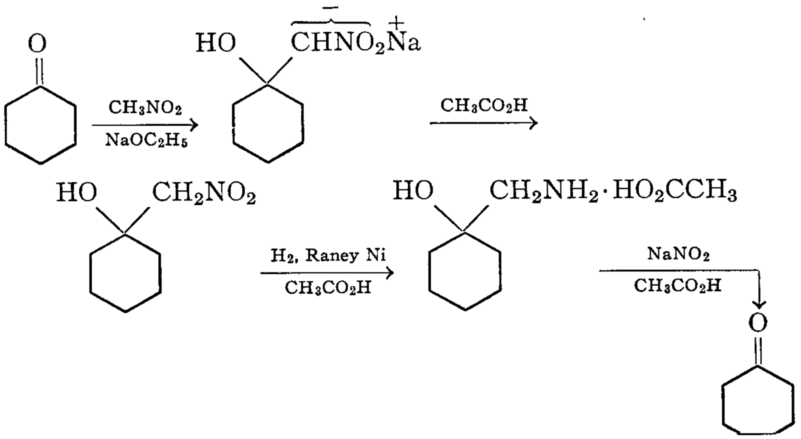
[1] Chemical Department, Experimental Station, E. I. du Pont de Nemours and Company, Wilmington, Delaware.

[2] *Org. Syntheses*, **34**, 49 (1954).

[3] Hanford and Rigby, U. S. pat. 2,409,274 [*C. A.*, **41**, 982 (1947)].

[4] Park, Vail, Lea, and Lacher, *J. Am. Chem. Soc.*, **70**, 1550 (1948).

CYCLOHEPTANONE



Submitted by **Hyp J. Dauben, Jr.**, **Howard J. Ringold**, **Robert H. Wade**, **David L. Pearson**, and **Arthur G. Anderson, Jr.**[1]
Checked by **Arthur C. Cope**, **Warren N. Baxter**, and **Robert J. Cotter**.

1. Procedure

A solution of sodium ethoxide is prepared by adding 57.5 g. (2.5 gram atoms) of clean sodium to 1.2 l. of absolute ethanol (Note 1) in a 3-l. three-necked flask equipped with an Allihn reflux condenser fitted with a drying tube, a large sturdy sealed Hershberg stirrer, and a dropping funnel. After the sodium has dissolved, the solution is cooled to 40° and the condenser is replaced by a thermometer extending into the liquid. A mixture of 245.5 g. (258.5 ml., 2.5 moles) of redistilled cyclohexanone and 198 g. (175 ml., 3.25 moles) of redistilled nitromethane (Note 2) is added dropwise with vigorous stirring over the course of about 3 hours at a rate that maintains an internal temperature of 45 ± 3° (Note 3). After addition is complete, the white, pasty mass is stirred for an additional 3 hours without cooling or heating and then is allowed to stand overnight. The resulting suspension is cooled with an ice bath, and the white sodium salt of 1-(nitromethyl)cyclohexanol is collected on a 25-cm. Büchner funnel and dried by suction for about 1 hour. The sodium salt cake is broken up and transferred to a 4-l. beaker equipped with a Hershberg stirrer and immersed in an ice bath. A cold solution of 184 g. (175 ml., 2.9 moles) of glacial acetic acid in 1250 ml. of water is added in a single portion, and the mixture is stirred for 10–30 minutes to complete dissolution. The oily layer of 1-(nitromethyl)cyclohexanol is separated, and the aqueous layer is extracted with three 100-ml. portions of ether. The ether extracts and the 1-(nitromethyl)cyclohexanol are combined, dried briefly over magnesium sulfate, and concentrated by distillation from a steam bath with a water aspirator at 20–35 mm. to remove ether and excess nitromethane. The crude, undistilled 1-(nitromethyl)cyclohexanol (Note 4) is dissolved in 450 ml. of glacial acetic acid in a 2-l. externally cooled stainless-steel hydrogenation bottle (Note 5). Three heaping teaspoonfuls of W-4 Raney nickel catalyst[2] are added, and the mixture is shaken with hydrogen at 40–45 p.s.i., with cooling to maintain the temperature below 35°, until about 90% of the theoretical amount (7.5 moles) is taken up and absorption ceases (Note 6). The catalyst is separated by filtration with suction through Filter-Cel, and the filtrate (sometimes green or tan) containing the 1-(aminomethyl)cyclohexanol is used directly in the next step (Note 7).

The filtrate is transferred to a 5-l. round-bottomed flask, immersed in an ice-salt mixture and equipped with a Hershberg stirrer, a thermometer, and a dropping funnel. The solution is diluted with 2.3 l. of ice water; then an ice-cold solution of 290 g. (4.2 moles) of sodium nitrite in 750 ml. of water is added dropwise during a period of about 1 hour with stirring and cooling (ice-salt bath) to maintain the temperature at $-5°$. The mixture is stirred for an additional period of 1 hour and then allowed to come to room temperature overnight as the ice in the cooling bath melts. The acetic acid in the reaction mixture is neutralized by the addition of small portions of solid sodium bicarbonate, and the neutral (to litmus paper) solution is then steam-distilled until about 2 l. of distillate is collected. The oily cycloheptanone layer is separated, the aqueous layer is extracted with three 100-ml. portions of ether, and the combined organic layers are dried briefly over magnesium sulfate. Most of the ether is removed by distillation through a 17 by 2.5 cm. glass helix-packed column at atmospheric pressure (Note 8). The residue is then distilled through the same column, and the fraction boiling at 80–85°/30 mm. is collected. The yield of cycloheptanone is 112–118 g. (40–42%), n_D^{25} 1.4600 (Notes 9 and 10).

2. Notes

1. Commercial absolute ethanol is used without additional drying. The submitters state that the use of absolute ethanol may be avoided by employment of the alternative condensation procedure of Wood and Cadorin[3] using 5 mole per cent of sodium hydroxide in aqueous methanol at 15–20° for 6 hours, but the yield of 1-(nitromethyl)cyclohexanol is appreciably lower (51%).

2. Cyclohexanone is dried over magnesium sulfate or calcium sulfate (Drierite) for 1 day and distilled; the fraction boiling at 152.5–154° (uncor.) is used. Nitromethane is dried in the same manner and distilled; small quantities of acidic impurities are removed in the fore-run, and the fraction boiling at 101.5–102.5° (uncor.) is used. Drying is frequently unnecessary when good grades of cyclohexanone and nitromethane are used.

3. Efficient stirring of the pasty reaction mixture is necessary to obtain maximum yield.

4. Removal of residual amounts of acetic acid in the crude product is unnecessary; their presence is actually preferable to the presence of traces of bases, such as any sodium bicarbonate remaining from neutralization, which reverse the condensation on attempted distillation of 1-(nitromethyl)cyclohexanol.[3] The submitters state that, in preparations conducted on twice the scale specified, fractional distillation of the residue yielded 620–670 g. (78–84%) of 1-(nitromethyl)cyclohexanol, b.p. 129–132°/19 mm., n_D^{25} 1.4835.

5. A Pyrex bottle can be used; it must be enclosed to prevent possible injury by fragments of glass in case of explosion.

6. Catalytic hydrogenation of 1-(nitromethyl)cyclohexanol in acetic acid solvent is a markedly exothermic reaction, and, unless the temperature is moderated to about 35°, low yields of 1-(aminomethyl)cyclohexanol result owing to hydrogenolysis and deactivation of the catalyst. Cooling can be accomplished by running cold water through a copper coil surrounding the hydrogenation bottle or by periodically adding ice to the container in which the bottle is placed. Considerable cooling is necessary during initial stages of the hydrogenation, but cooling below 25° greatly retards the reduction. Absorption of hydrogen is usually complete in 15–18 hours under these conditions, but longer times may be required, depending on the temperature and pressure and on the amount and activity of the catalyst.

7. 1-(Aminomethyl)cyclohexanol can be isolated as its acetic acid salt by the addition of 2 volumes of ether to the acetic acid solution or to the residue after removal of the acetic acid under reduced pressure, followed by trituration and refrigeration overnight. After filtration of the first crop of crystals, m.p. 118–121°, a second crop of the salt, m.p. 113–116°, is obtained on removal of the dissolved nickel from an aqueous solution of the concentrated filtrate by saturation with hydrogen sulfide, concentration, and treatment with ether. Total yields of the air-dried crude acetic acid salt of 1-(aminomethyl)cyclohexanol obtained from 100–350 g. lots of 1-(nitromethyl)cyclohexanol in this manner ranged from 69% to 94%.

8. Distillation of the product from a modified Claisen flask and collection of the fraction boiling at 67–77°/20 mm. (largely 69–72°) gave 140–149 g. of impure cycloheptanone, n_D^{25} 1.4570–1.4590, containing about equal amounts (10–15 g.) of lower-boiling and higher-boiling (mainly 1-(nitromethyl)cyclohexanol) contaminants, which were separated by distillation through the glass helix-packed column.

9. The submitters state that the yields of cycloheptanone obtained from 60- to 700-g. quantities of the crude acetic acid salt of

1-(aminomethyl)cyclohexanol (isolated by the procedure of Note 7) were 57–65%.

10. Small quantities of cycloheptanone are prepared more conveniently by the diazomethane method [4] or by dry distillation of suberic acid salts [5–7] or suberic acid admixed with iron filings and barium hydroxide.[8]

3. Methods of Preparation

Cycloheptanone has been prepared by variations of two general routes, ring closure and ring enlargement. Ring-closure methods that have been employed are: (*a*) dry distillation of calcium [5] (35–50% yield), thorium [6] (45% yield), cerium [6] (45% yield), and zinc or magnesium [7] (55–60% yield) salts of suberic acid; (*b*) pyrolysis of a mixture of suberic acid, iron filings, and barium hydroxide [8] (40% yield); (*c*) Dieckmann condensation of diethyl suberate with sodium ethoxide in ether; [9] (*d*) Thorpe-Ziegler condensation of suberonitrile using preferably sodium methylanilide in ether by a high-dilution technique followed by hydrolysis and decarboxylation (80-85% yield); [10] and (*e*) dehydrohalogenation of suberyl chloride using triethylamine by a high-dilution technique (33% yield).[11] Ring-enlargement methods that have been used are: (*a*) diazomethane on cyclohexanone (33–36% yield) [4] and (*b*) reduction of cyclohexanone cyanohydrin and treatment of the resulting 1-(aminomethyl)cyclohexanol with nitrous acid (23–29% yield).[12] The present method represents an improved modification of the method of Dauben, Ringold, Wade, and Anderson.[13]

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[1] Department of Chemistry, University of Washington, Seattle, Washington.

[2] Pavlic and Adkins, *J. Am. Chem. Soc.*, **68**, 1471 (1946).

[3] Wood and Cadorin, *J. Am. Chem. Soc.*, **73**, 5504 (1951).

[4] *Org. Syntheses*, **34**, 24 (1954); Kohler, Tishler, Potter, and Thompson, *J. Am. Chem. Soc.*, **61**, 1059 (1939); Mosettig and Burger, *J. Am. Chem. Soc.*, **52**, 3460 (1930); Meerwein, Ger. pat. 579,309 [*C. A.*, **27**, 4546 (1933)].

[5] Day, Kon, and Stevenson, *J. Chem. Soc.*, **1920**, 642.

[6] Ruzicka, Brugger, Pfeiffer, Schinz, and Stoll, *Helv. Chim. Acta*, **9**, 515 (1926).

[7] Böeseken and Derx, *Rec. trav. chim.*, **40**, 530 (1921); Derx, *Rec. trav. chim.*, **41**, 338 (1922).

[8] Vogel, *J. Chem. Soc.*, **1928**, 2032.

[9] Dieckmann, *Ann.*, **317**, 49 (1901).

[10] Ziegler, Eberle, and Ohlinger, *Ann.*, **504**, 120 (1933); Ziegler and Aurnhammer, *Ann.*, **513**, 57 (1934).

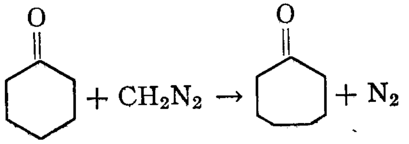
[11] Blomquist and Spencer, *J. Am. Chem. Soc.*, **70**, 30 (1948).

[12] Tchoubar, *Bull. soc. chim. France*, **1949**, 160, 164, 169.

[13] Dauben, Ringold, Wade, and Anderson, *J. Am. Chem. Soc.*, **73**, 2359 (1951).

CYCLOHEPTANONE

$$p\text{-}CH_3C_6H_4SO_2N(NO)CH_3 + C_2H_5OH \xrightarrow{\text{aq. KOH}} p\text{-}CH_3C_6H_4SO_2OC_2H_5 + CH_2N_2 + H_2O$$



Submitted by Th. J. de Boer and H. J. Backer.[1]
Checked by James Cason, John B. Rogan, and Wm. G. Dauben.

1. Procedure

Caution! Diazomethane is very toxic; therefore the operations must be carried out in a well-ventilated hood.

In a 500-ml. round-bottomed flask, provided with a mechanical stirrer (Note 1), a thermometer, and a dropping funnel, are placed 49 g. (0.5 mole) of cyclohexanone (Note 2), 125 g. (0.58 mole) of *p*-tolylsulfonylmethylnitrosamide,[2] 150 ml. of 95% ethanol, and 10 ml. of water (Note 3). The nitroso compound is largely undissolved. The stirrer is adjusted so that only the upper portion of solution is stirred and the precipitate moves slightly. The thermometer bulb is placed in the liquid.

The reaction mixture is cooled to about 0° with an ice-salt bath; then with gentle stirring a solution of 15 g. of potassium hydroxide in 50 ml. of 50% aqueous ethanol is added dropwise very slowly from the dropping funnel. After the addition of 0.5–1 ml. of the alkaline solution a brisk evolution of nitrogen commences and the temperature rises. The rate of addition is adjusted so that the temperature is maintained at 10–20° (Note 4). The addition of

the alkali requires about 2 hours, during which the nitroso compound gradually disappears. The orange-yellow solution is stirred for an additional 30 minutes, then 2 *N* hydrochloric acid (about 50 ml.) is added until the solution is acidic to litmus paper.

A solution of 100 g. of sodium bisulfite (Note 5) in 200 ml. of water is added as stirring is continued. After a few minutes a thick precipitate separates. The mixture is stirred or preferably shaken mechanically at room temperature with exclusion of air for 10 hours. The bisulfite addition product is separated by suction filtration, washed with ether until colorless, and decomposed in a flask with a lukewarm solution of 125 g. of sodium carbonate in 150 ml. of water. The ketone layer is separated, the aqueous layer is extracted with four 25-ml. portions of ether, and the combined organic layers are dried over anhydrous sodium sulfate. Most of the ether is removed by distillation at atmospheric pressure, and the residual oil is distilled at reduced pressure (Note 6).

After a few drops of fore-run, practically all the liquid distils at 64–65°/12 mm. The yield of cycloheptanone is 18.5–20.2 g. (33–36%) (Note 6).

2. Notes

1. If it is desired to determine the amount of nitrogen evolved, then it is necessary to use a sealed stirrer and a discharge tube for the nitrogen; however, observing the amount of nitrogen evolved affords no particular advantage. The temperature exerts a sufficient control on the reaction rate, and dissolution of the nitroso compound indicates the progress of the reaction.
2. Cyclohexanone was distilled before use, b.p. 154–155°.
3. The water keeps in solution the potassium *p*-toluenesulfonate, which is formed by partial saponification of the ester.
4. In some experiments, the temperature was allowed to rise temporarily to 35° without mishap, but the lower temperature is preferred for reasons of safety.
5. Cyclooctanone, which is a by-product, is removed at this stage since it does not form an adduct with bisulfite.

6. The checkers found it desirable to distil the product through a fractionating column in order to effectively remove the small fore-run and a smaller after-run. The pattern obtained in a 50-cm. column of the simple Podbielniak type follows: fraction 1, 1.13 g., b.p. up to 63°/12 mm., n_D^{25} 1.4549; fraction 2, 19.44 g., b.p. 63–64°/12 mm., n_D^{25} 1.4592; fraction 3, 0.55 g., b.p. > 64°/12 mm., n_D^{25} 1.4604. A center cut of fraction 2 had n_D^{25} 1.4590.

3. Methods of Preparation

The methods of preparing cycloheptanone are summarized in the preceding preparation.[3]

The present procedure is a modification of earlier diazomethane methods and employs the relatively stable *p*-tolylsulfonylmethylnitrosamide.

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[1] De Rijks-Universiteit, Groningen, the Netherlands.

[2] *Org. Syntheses*, **34**, 96 (1954).

[3] *Org. Syntheses*, **34**, 19 (1954).

DI-*tert*-BUTYL MALONATE

(Malonic acid, di-*t*-butyl ester)

$$CH_2(CO_2H)_2 + 2(CH_3)_2C{=}CH_2 \overset{H_2SO_4}{\rightleftarrows} CH_2[CO_2C(CH_3)_3]_2$$

Submitted by Allen L. McCloskey, Gunther S. Fonken,
Rudolph W. Kluiber, and William S. Johnson.[1]
Checked by James Cason, Gerhard J. Fonken, and William G. Dauben.

1. Procedure

A 500-ml. Pyrex heavy-walled narrow-mouthed pressure bottle is charged with 100 ml. of ether (Note 1), 5 ml. of concentrated sulfuric acid, 50.0 g. (0.48 mole) of malonic acid, and approximately 120 ml. (about 1.5 moles) of isobutylene (Note 2), which is liquefied by passage into a large test tube immersed in a Dry

Ice-acetone bath. The bottle is closed with a rubber stopper which is clamped or wired securely in place (Note 3) and is shaken mechanically at room temperature until the suspended malonic acid dissolves (Note 4). The bottle is chilled in an ice-salt bath and opened; then the contents are poured into a separatory funnel containing 250 ml. of water, 70 g. of sodium hydroxide, and 250 g. of ice. The mixture is shaken (carefully at first), the layers are separated, and the aqueous portion is extracted with two 75-ml. portions of ether. The organic layers are combined, dried over anhydrous potassium carbonate, and filtered into a dropping funnel attached to the neck of a 125-ml. modified Claisen flask (Note 5). The flask is immersed in an oil bath at about 100°, and the excess isobutylene and ether are removed by flash distillation effected by allowing the solution to run in slowly from the dropping funnel. The dropping funnel is then removed, and the residue is distilled at reduced pressure. The fraction boiling at 112–115°/31 mm. is collected. The yield of colorless di-*tert*-butyl malonate is 60.0–62.0 g. (58–60%), n_D^{25} 1.4158–1.4161, freezing point −5.9 to −6.1° (Notes 6 and 7).

2. Notes

1. Increase in the concentrations of reactants and product by elimination of the solvent shifts the equilibrium to the right and thus increases the yield of ester. In several runs by the checkers in which the described procedure was followed except that ether was omitted, isobutylene was increased to 240 ml. (3 moles), and shaking was continued for 12–15 hours to effect solution, yields of 88–91% were obtained. When ether was used as solvent, the larger amount of isobutylene raised the yield to only 73%. The submitters, however, have found that in the procedure without solvent the yield is more variable (in the range 69–92%), complete solution of the acid sometimes fails to occur, and in runs requiring long shaking for complete solution there is formed a lower-boiling substance, the separation of which requires fractional distillation. Without solvent, there is usually an exothermic reaction as the mixture warms up. In the size run described

this is no disadvantage, but in larger runs the heat evolved might be sufficient to cause the reaction to get out of control.

2. Technical grade isobutylene supplied by the Matheson Company was used.

3. The pressure during reaction on this scale does not exceed 40 p.s.i.

4. Solution is usually complete within 6 hours, but sometimes as much as 12 hours may be required.

5. The flask should be carefully washed with alkali before rinsing and drying, to ensure the removal of traces of acid which will catalyze the decomposition of the ester on warming to give isobutylene, carbon dioxide, and acetic acid. Once this decomposition begins, as evidenced by severe foaming, it is autocatalyzed (by the acetic acid formed) and cannot be prevented from continuing at an accelerated rate except by rewashing the product and apparatus with alkali. The addition of some solid potassium carbonate or magnesium oxide before distillation has been used with some *tert*-butyl esters to aid in inhibiting incipient decomposition. This treatment, however, does not appear to be necessary in the present preparation.

6. This preparation has been carried out by H. C. Dehm on a larger scale. From 150 g. of malonic acid, 200 ml. of ether, 10 ml. of concentrated sulfuric acid, and 375 ml. of isobutylene, there was obtained after shaking for 22 hours in a 1-l. bottle 201.3 g. (64% yield) of ester, $n_D^{24.2}$ 1.4161.

7. Other esters that have been prepared by this general procedure are: *tert*-butyl acetate, 50% yield, b.p. 94–97°/738 mm., n_D^{25} 1.3820; *tert*-butyl chloroacetate, 63% yield, b.p. 56–57°/16–17 mm., n_D^{25} 1.4204–1.4210 (carried out by R. C. Hunt); *tert*-butyl bromoacetate, 65% yield, b.p. 74–76°/25 mm., n_D^{25} 1.4162; *tert*-butyl α-chloropropionate, yield 63%, b.p. 52–53°/12 mm., n_D^{25} 1.4163 (carried out by J. S. Belew); *tert*-butyl *o*-benzoylbenzoate, 70% yield, m.p. 65–69°; di-*tert*-butyl succinate (dioxane was used instead of ether as solvent), 52% yield, b.p. 105-107°/7 mm., m.p. 31.5–35°; di-*tert*-butyl glutarate, 60% yield, b.p. 113–119°/9 mm., n_D^{25} 1.4215; di-*tert*-butyl β,β-dimethylglutarate, 67% yield, b.p. 72–75°/1 mm., n_D^{25} 1.4246.

3. Methods of Preparation

This procedure is a modification [2] of the method of Altschul [3] for preparing *tert*-butyl esters. Di-*tert*-butyl malonate has been prepared by the reaction of malonyl chloride with *tert*-butyl alcohol in the presence of a tertiary amine.[4]

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[1] Department of Chemistry, University of Wisconsin, Madison, Wisconsin.

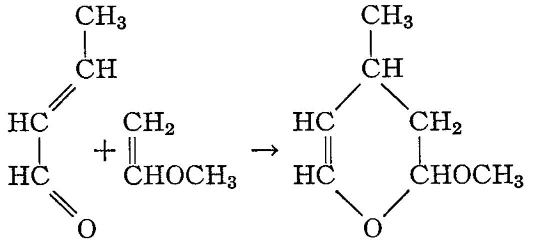
[2] Fonken and Johnson, *J. Am. Chem. Soc.*, **74**, 831 (1952).

[3] Altschul, *J. Am. Chem. Soc.*, **68**, 2605 (1946).

[4] Backer and Lolkema, *Rec. trav. chim.*, **57**, 1234 (1938); Backer and Homan, *Rec. trav. chim.*, **58**, 1048 (1939); *Org. Syntheses*, **33**, 20 (1953).

3,4-DIHYDRO-2-METHOXY-4-METHYL-2H-PYRAN

(2H-Pyran, 3,4-dihydro-2-methoxy-4-methyl-)



Submitted by Raymond I. Longley, Jr., William S. Emerson, and Albert J. Blardinelli.[1]
Checked by T. L. Cairns and T. E. Young.

1. Procedure

In a high-pressure autoclave, arranged for agitation by shaking or rocking, are placed 286 g. (336 ml., 4.08 moles) of crotonaldehyde, 294 g. (5.06 moles) of methyl vinyl ether, and 1.1 g. of hydroquinone (Notes 1 and 2). The autoclave is heated to 200° (Note 3) and held there for 12 hours. The autoclave is cooled and vented, and the black product is distilled through a 1 by 60 cm. helix-packed column. The yield of 3,4-dihydro-2-methoxy-

4-methyl-2H-pyran is 270–297 g. (52–57%), b.p. 42–50°/19 mm., n_D^{25} 1.4349–1.4374 (Notes 4, 5, and 6).

2. Notes

1. The purer grade of crotonaldehyde supplied by the Eastman Kodak Company was used. Methyl vinyl ether was obtained from the Matheson Chemical Company.

2. The submitters condensed the methyl vinyl ether in the aldehyde cooled to 0° and then charged this mixture to a precooled autoclave. The checkers cooled the autoclave containing the crotonaldehyde to −70°, evacuated, and condensed the required amount of methyl vinyl ether directly into the autoclave.

3. The autoclave should be capable of withstanding a pressure of 3000 p.s.i. This provides a margin of safety, since at 220° the pressure is about 2600 p.s.i.

4. Pure 3,4-dihydro-2-methoxy-4-methyl-2H-pyran boils at 135–138°/760 mm. and at 79–80°/100 mm. and has n_D^{25} 1.4370.

5. The submitters used approximately three times the quantities reported here and obtained yields of 82–83%.

6. Under comparable conditions the submitters found that the corresponding dihydropyran derivatives were similarly obtained by the condensation of acrolein with methyl vinyl ether in 80–81% yield, with ethyl vinyl ether (77–85% yield), with *n*-butyl vinyl ether (82% yield), with ethyl isopropenyl ether (50% yield), and with *n*-butyl cyclohexenyl ether (40% yield). Other α,β-unsaturated carbonyl compounds that have thus been condensed with ethyl vinyl ether are crotonaldehyde (87% yield), methacrolein (40% yield), α-ethyl-β-*n*-propylacrolein (54% yield), cinnamaldehyde (60% yield), β-furylacrolein (85% yield), methyl vinyl ketone (50% yield), benzalacetone (75% yield), and benzalacetophenone (74% yield).

3. Methods of Preparation

3,4-Dihydro-2-methoxy-4-methyl-2H-pyran has been prepared only by the addition of methyl vinyl ether to crotonaldehyde.[2-4]

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[1] Central Research Department, Monsanto Chemical Company, Dayton 7, Ohio.

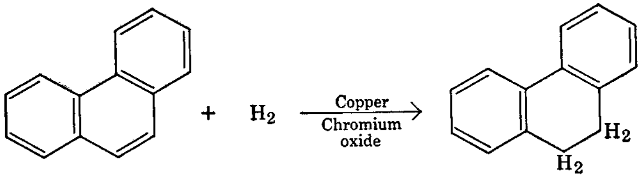
[2] Longley and Emerson, *J. Am. Chem. Soc.*, **72**, 3079 (1950).

[3] Smith, Norton, and Ballard, *J. Am. Chem. Soc.*, **73**, 5267 (1951).

[4] Smith, Norton, and Ballard, U. S. pat. 2,514,168.

9,10-DIHYDROPHENANTHRENE

(Phenanthrene, 9,10-dihydro-)



Submitted by Donald D. Phillips.[1]
Checked by William S. Johnson and David C. Remy.

1. Procedure

A. *Purification of phenanthrene.* 1. By azeotropic distillation.[2] A mixture of 300 g. of commercial phenanthrene (Note 1), 90 g. of maleic anhydride, and 600 ml. of xylene, contained in a 2-l. round-bottomed flask, is heated under reflux for 20 hours (Note 2). The initially yellow solution rapidly turns to a dark brown on heating. This solution is cooled to room temperature and filtered by suction to remove any insoluble adduct. The filtrate is then extracted with two 100-ml. portions of dilute sodium hydroxide, and the basic extracts are discarded. The organic phase is next washed with water and saturated sodium chloride solution, and finally is filtered through a layer of anhydrous magnesium sulfate. The excess xylene is removed by distillation, first at atmospheric pressure; then the final portions are removed at reduced pressure. The residue, while still hot, is poured into a large mortar and, after solidification, is powdered to a convenient size. The yield of crude phenanthrene is 230–240 g.

A solution of 52 g. of the crude phenanthrene in 400 ml. of diethylene glycol (Note 3) is azeotropically distilled through a small column (Note 4). A fore-run of approximately 50 g. is collected at 155–165°/100 mm., followed by the main fraction of 390–400 g., b.p. 140–141°/21 mm. (Note 5). The fore-run contains considerable fluorene and should be discarded. The main fraction is added to five times its volume of water, and the precipitated hydrocarbon is collected by suction filtration and washed well with water to remove the last traces of diethylene glycol. The colorless product (41–43 g.) is heated under reflux for 3 hours with about 450 ml. of 95% ethanol containing approximately 9 g. of Raney nickel catalyst. The hot solution is filtered with slight suction through a sintered-glass funnel. On being concentrated to about 250 ml. and cooled, the filtrate deposits 33–35 g. (63-67%) of colorless phenanthrene, m.p. 97.5–98°.

2. By sodium treatment.[3] Commercial phenanthrene (Note 1) is treated with maleic anhydride as described above (part 1), and 170 g. of the residue is added to a 1-l. three-necked flask equipped with a Hershberg mercury-sealed Nichrome stirrer,[4] an air condenser, and a thermometer. Ten grams of sodium is added, and the mixture is vigorously stirred at 190–200° for 6 hours. The dark residue is cooled to about 80°, and 300 ml. of benzene is added. The mixture is brought to reflux with stirring and, while still hot, is *cautiously* filtered through a coarse sintered-glass funnel with *gentle* suction (Note 6). The benzene is removed by distillation at atmospheric pressure, and the residual phenanthrene is distilled through a small column (Note 4) adapted to the distillation of solids to give 125–130 g. (74–76%) of colorless phenanthrene, b.p. 183–183.5°/15 mm. This product is heated under reflux for 3 hours with about 1.2 l. of 95% ethanol containing approximately 9 g. of Raney nickel catalyst, and the hot solution is filtered as described under paragraph 1. The filtrate on cooling deposits 115–120 g. (68–71%) of colorless phenanthrene, m.p. 97–98°.

B. *Catalytic reduction.* A hydrogenation bomb of approximately 300 ml. total capacity is charged with 29.5 g. (0.17 mole) of purified phenanthrene (Note 7); then 70 ml. of cyclohexane (Note 8) and 1.5 g. of copper chromium oxide catalyst (Note 9) are added. The bomb is filled with hydrogen to an initial pressure of 2000 p.s.i. at 20° and heated with shaking to 150° (maximum pressure about 2900 p.s.i.). The hydrogenation proceeds rapidly under these conditions, and about 85% of the theoretical uptake is complete within 1.75–2 hours. The reaction is interrupted at this point (Note 10), and the catalyst is removed by centrifugation or filtration. The cyclohexane is evaporated, and the residue is distilled through a small column (Note 4). After a small fore-run (0.2–0.3 g.) distilling below 182°, there is collected 21–23 g.(70–77% yield) of 9,10-dihydrophenanthrene, b.p. 183–184°/25 mm., n_D^{25} 1.6401–1.6416. The residue consists of 4.5–5.0 g. (15–17%) of phenanthrene, m.p. 96.5–98°, which may be recycled.

2. Notes

1. Technical grade phenanthrene (80–90%) is satisfactory for this preparation.

2. An electric heating mantle is convenient for this operation.

3. Technical diethylene glycol may be used with satisfactory results.

4. The submitter used a 65-cm. Podbielniak type column equipped with partial reflux head.[5] For distillation of the sodium-treated phenanthrene the checkers employed a 6-in. Vigreux column. For the fractionation of the dihydrophenanthrene, the checkers employed a 15-cm. spinning-band column obtainable from Nester and Faust, Exton, Pennsylvania.

5. At these concentrations, the azeotrope is solid and adequate heating of the condenser and receivers must be provided by an infrared lamp or similar device. The use of twice this amount of diethylene glycol is reported [2] to give a liquid azeotrope but requires the distillation of proportionately larger amounts, for the azeotrope has nearly the same boiling point as diethylene glycol.

6. The finely divided sodium presents a serious fire hazard, and as much of it as possible should be retained in the flask. This may be accomplished by careful decantation. The material that

is collected on the funnel should always be covered with a layer of solvent and should not be allowed to become dry. The residues may be safely destroyed by placing the funnel and flask in a large pail and adding about 1 l. of isopropyl alcohol. This operation is best conducted out-of-doors.

7. Phenanthrene purified by the sodium treatment was found superior to that from the azeotropic distillation, but both products gave satisfactory results. A good grade of commercially available phenanthrene ("white label" grade supplied by the Eastman Kodak Company), although recrystallized and treated with Raney nickel, resisted hydrogenation under the described conditions.

8. Cyclohexane as supplied by Matheson Company was used without further purification. The use of ethanol as solvent [6] gave inconsistent results, and the yield of 9,10-dihydrophenanthrene never exceeded 50%. Erratic results were also obtained when the solvent was omitted.

9. Copper-chromium oxide (HJS2) was prepared as reported by Adkins and coworkers.[7]

10. If the hydrogenation is allowed to proceed to completion, the product is contaminated with considerable polyhydrogenated material, as indicated by its low refractive index. The optimum time for obtaining about 85% hydrogenation may vary with the purity of the phenanthrene and activity of the catalyst. The purest 9,10-dihydrophenanthrene is obtained when the lower limits of hydrogen uptake are realized, although the yield is correspondingly lower.

3. Methods of Preparation

9,10-Dihydrophenanthrene has been prepared from 2,2′-bis(bromomethyl)biphenyl and sodium; [8] from the reduction of 2,2′-diiodobibenzyl in the presence of 1% palladium on barium carbonate catalyst; [9] by the hydrogenation of phenanthrene in the presence of nickel [8] or copper-chromium oxide catalyst; [3, 6, 10] and by the coupling of 2,2′-bis(bromomethyl)biphenyl with lithium phenyl.[11]

[1] Department of Chemistry, Cornell University, Ithaca, New York.

[2] Feldman, Pantages, and Orchin, *J. Am. Chem. Soc.*, **73**, 4341 (1951).

[3] Fieser and Johnson, *J. Am. Chem. Soc.*, **61**, 168 (1939).

[4] *Org. Syntheses* Coll. Vol. **2**, 117 (1943).

[5] Cason and Rapoport, *Laboratory Text in Organic Chemistry*, Prentice-Hall, New York, 1950, p. 237.

[6] Durland and Adkins, *J. Am. Chem. Soc.*, **59**, 135 (1937).

[7] Adkins, Burgoyne, and Schneider, *J. Am. Chem. Soc.*, **72**, 2626 (1950).

[8] Schroeter, Müller, and Huang, *Ber.*, **62**, 645 (1929).

[9] Busch and Weber, *J. prakt. Chem.*, **146**, 1 (1936).

[10] Burger and Mosettig, *J. Am. Chem. Soc.*, **58**, 1857 (1936).

[11] Hall, Lesslie, and Turner, *J. Chem. Soc.*, **1950**, 711.

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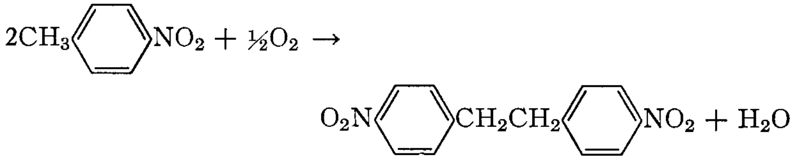
p,p′-DINITROBIBENZYL

(Bibenzyl, 4,4′-dinitro-)



Submitted by Herbert O. House.[1]
Checked by John C. Sheehan and J. Iannicelli.

1. Procedure

In a 3-l. three-necked flask equipped with a mechanical stirrer and an inlet tube extending to the bottom of the flask is placed 2 l. of 30% methanolic potassium hydroxide (Note 1). The flask is immersed in an ice bath, and, when the solution has cooled to 10°, 100 g. (0.729 mole) of solid *p*-nitrotoluene (Note 2) is added to the flask. Vigorous stirring is begun, and a rapid stream of air from a compressed-air source is passed through the inlet tube. After 3 hours the ice bath is removed and the passage of air through the mixture is continued with uninterrupted, vigorous stirring for an additional 5 hours. The reaction mixture is immediately filtered with suction (Note 3), and the solid, while still on the filter, is washed with 2 l. of boiling water followed by 300 ml. of 95% ethanol at room temperature. The product is allowed to dry thoroughly in air and then is dissolved in a minimum quantity of boiling benzene (Note 4). The hot solution is filtered to remove a small amount of insoluble red-orange material and is allowed to cool. The *p,p'*-dinitrobibenzyl crystallizes as orange needles, m.p. 178–180°. The yield is 73–75 g. (74–76%). A second recrystallization from benzene gives yellow needles, m.p. 179–180°.

2. Notes

1. Thirty per cent methanolic potassium hydroxide may be prepared by dissolving 680 g. of C.P. (minimum 85%) potassium hydroxide pellets in 2 l. of methanol.
2. A good grade of *p*-nitrotoluene, m.p. 51–52°, such as supplied by the Eastman Kodak Company, was used.
3. A double layer of ordinary filter paper is satisfactory for this filtration.
4. Two to three liters of benzene is required. The checkers found the use of a heated funnel to be advantageous.

3. Methods of Preparation

p,p'-Dinitrobibenzyl has been prepared by the nitration of bibenzyl;[2] by the action of alkaline zinc chloride on *p*-nitrobenzyl chloride;[3] by the action of alkali on *p*-nitrotoluene;[4] by the oxidation of α,α-bis(*p*-nitrobenzyl)hydrazine with mercuric oxide;[5] and by the present method.[6]

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[1] Department of Chemistry, University of Illinois, Urbana, Illinois.

[2] Rinkenbach and Aaronson, *J. Am. Chem. Soc.*, **52**, 5040 (1930).

[3] Roser, *Ann.*, **238**, 363 (1887).

[4] Green, Davies, and Horsfall, *J. Chem. Soc.*, **1907**, 2076.

[5] Busch and Weiss, *Ber.*, **33**, 2701 (1900).

[6] Fuson and House, *J. Am. Chem. Soc.*, **75**, 1325 (1953).

1,4-DINITROBUTANE

(Butane, 1,4-dinitro-)

$$ICH_2CH_2CH_2CH_2I + 2AgNO_2 \rightarrow O_2NCH_2CH_2CH_2CH_2NO_2 + 2AgI$$

Submitted by HENRY FEUER and GERD LESTON.[1]
Checked by JOHN C. SHEEHAN and J. IANNICELLI.

1. Procedure

The reaction is carried out in a 1-l. three-necked round-bottomed flask fitted with a ball-sealed mechanical stirrer, a reflux condenser, and a dropping funnel. The openings of the condenser and dropping funnel are protected from moisture by drying tubes. In the flask, which is protected from light (Note 1), are placed 170 g. (1.1 mole) of silver nitrite and 300 ml. of absolute ether. The silver nitrite is suspended by vigorous stirring, and the mixture is cooled to 0° by an ice bath. Then 155 g. (0.5 mole) of 1,4-diiodobutane[2] is added dropwise over a period of 3 hours. The temperature is maintained at 0° for an additional 2 hours, and then the reaction mixture is allowed to come slowly to room temperature (25°) by permitting the ice in the cooling bath to melt (Note 2). Twenty-four hours after the addition of the diiodobutane has been completed, the solution is tested for unreacted iodide (Note 3). If the test is negative, the mixture is filtered and the silver iodide washed with a total of 200 ml. of benzene (Note 4). The ethereal solution and the benzene washings are combined, and the solvents are distilled on a steam bath, the pressure being reduced (water aspirator) toward the end of the distillation.

In a 500-ml. three-necked flask equipped with a mechanical stirrer, a dropping funnel, and a thermometer is placed 200 ml. of concentrated sulfuric acid. The flask is immersed in an ice-salt bath, and the acid is cooled to 0–5°. The crude dinitrobutane is added dropwise with vigorous stirring at such a rate that the temperature does not exceed 8°. Stirring is continued for an additional 10 minutes after completion of the addition. The solution is poured cautiously onto 1 kg. of crushed ice with manual stirring. The ice is allowed to melt, and the product is separated by suction filtration, washed with water, and air-dried. Recrystallization from methanol at −70°, using a Dry Ice-methylene chloride cooling bath, yields 30–34 g. (41–46%) of 1,4-dinitrobutane, m.p. 33–34° (Notes 5, 6, 7, and 8).

2. Notes

1. All light should be excluded. It is most convenient to run the reaction in a dark room.

2. The cooling bath should not be removed, or the temperature of the mixture will rise above room temperature.

3. The Beilstein test is carried out in the following manner: A copper wire is cleaned in the flame of a Bunsen burner and allowed to cool. The stirring is stopped, and the wire is inserted carefully into the clear ether solution so as not to touch the silver iodide at the opening and at the bottom of the flask. The wire is withdrawn and held in the reducing part of the flame. A green color constitutes a positive test, and stirring is resumed until the test is negative.

4. An alternative method of purification is to wash the silver iodide with 250 ml. of methanol instead of benzene. The ether is evaporated, and the residue is combined with the methanol solution. The product is crystallized at −70°. Recrystallization of this crude product from methanol at −70° gives the same yields as the other method of purification.

5. The methanol solution may be treated with charcoal if a colorless product is not obtained.

6. Starting with 169 g. of 1,6-diiodohexane,[3] 1,6-dinitrohexane may similarly be obtained in 46–48% yield, m.p. 36.5–37.5°. The alternative procedure of isolation described in Note 4 may also be used.

7. 1,3-Dinitropropane may be prepared in a similar manner starting with 148 g. of 1,3-diiodopropane (supplied by the Eastman Kodak Company and by the Eastern Chemical Corporation). However, the dinitro compound is a liquid and has to be purified in the following manner: The crude 1,3-dinitropropane is extracted from the aqueous acid layer with four 150-ml. portions of benzene. The benzene is removed by distillation at atmospheric pressure, and the residue is distilled from a 50-ml. Claisen flask, b.p. 108–110°/1 mm., n_D^{20} 1.465. The yield is 24–25 g. (36–37%). It is colorless during the distillation but rapidly turns yellow on storage. If the aqueous layer is extracted continuously with benzene or ether for 24 hours an additional 3 g. of product may be obtained.

8. 1,4-Dinitropentane may be prepared in a similar manner starting with 162 g. of 1,5-diiodopentane prepared from tetrahydropyran according to the directions for 1,4-diiodobutane.[2] The dinitro compound is a liquid and is obtained by extracting the aqueous acid layer with three 125-ml. portions of benzene. The benzene is removed by distillation at atmospheric pressure, and the residue is distilled from a 50-ml. Claisen flask. The fraction, b.p. 134°/1.2 mm., amounts to 36.6 g. (45% yield), n_D^{20} 1.461. The distillate is colorless but rapidly turns yellow.

3. Methods of Preparation

1,3-Dinitropropane,[4,5] 1,4-dinitrobutane,[6,7] 1,5-dinitropentane,[6,7] and 1,6-dinitrohexane [7] have been prepared only by the method described here, which is that of Victor Meyer.

---

[1] Purdue University, Lafayette, Indiana.

[2] *Org. Syntheses*, **30**, 33 (1950).

[3] *Org. Syntheses*, **31**, 31 (1951).

[4] Keppler and Meyer, *Ber.*, **25**, 1710 (1892).

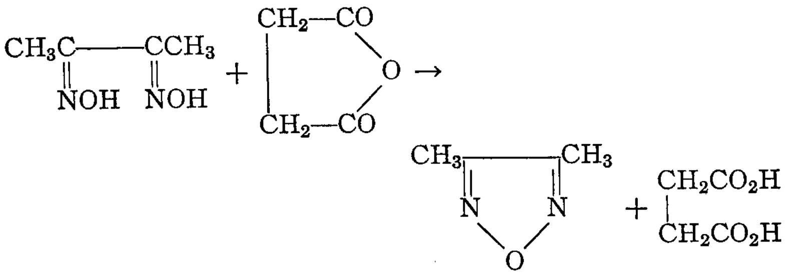
[5] Kispersky, Hass, and Holcomb, *J. Am. Chem. Soc.*, **71**, 516 (1949).

[6] von Braun and Sobecki, *Ber.*, **44**, 2528 (1911).

[7] McElroy, Ph.D. Thesis, Purdue University, 1943.

DIMETHYLFURAZAN

(Furazan, 3,4-dimethyl-)



Submitted by LYELL C. BEHR and JOHN T. BRENT.[1]
Checked by T. L. CAIRNS and J. E. CARNAHAN.

1. Procedure

One hundred grams (1 mole) of succinic anhydride and 116 g. (1 mole) of dimethylglyoxime (Note 1), both finely ground, are intimately mixed and introduced into a 1-l. three-necked flask which is equipped with a sealed mechanical stirrer, a thermometer reaching nearly to the bottom of the flask, and an outlet tube connected to a water-cooled condenser arranged for distillation. The mixture is heated slowly with an electric mantle or oil bath, and stirring is commenced as soon as practicable (Note 2). The mixture liquefies at about 100°, and a rapid reaction begins at 150–170° accompanied by a sudden rise in temperature. This initial rapid reaction can be controlled readily by removing the heater when the temperature reaches 170° and applying a cooling bath until the inside temperature is 150° (Note 3). Heat is then applied again, and distillation of the product begins at a flask temperature of 160° and continues until the temperature reaches 200°. The stirrer is stopped, the receiver is changed, and, after the flask and contents have cooled to about 120°, 50 ml. of water is added. The thermometer is replaced by an inlet tube, and steam is passed in until no more insoluble material passes over.

Usually collection of about 200–300 ml. of distillate is sufficient. The distillate is extracted with two 100-ml. portions of ether, and the extracts are combined with the dimethylfurazan obtained by direct distillation (Note 4). The ether solution is dried for a short time over anhydrous magnesium sulfate. The drying agent is removed by filtration, and the ether is evaporated on a steam bath. The residue is distilled at atmospheric pressure through a short column, and after a fore-run, consisting chiefly of biacetyl, the dimethylfurazan distils at 154–159° as a colorless liquid, n_D^{25} 1.4234–1.4243, m.p. -7.2 to $-6.6°$. The yield is 59–63 g. (60–64%).

2. Notes

1. A good grade of both reagents should be used. The better-quality products supplied by the Eastman Kodak Company are satisfactory.
2. The mixture may be difficult to stir mechanically below its melting point unless a powerful motor is used.
3. The temperature usually climbs to about 190° during this interval, and some dimethylfurazan distils rapidly.
4. The product obtained by direct distillation contains some water, but the dimethylfurazan can be readily separated.

3. Methods of Preparation

Dimethylfurazan has been obtained from dimethylglyoxime by heating with water, aqueous ammonia, or aqueous sodium hydroxide.[2,3] The usual acid dehydrating agents fail.

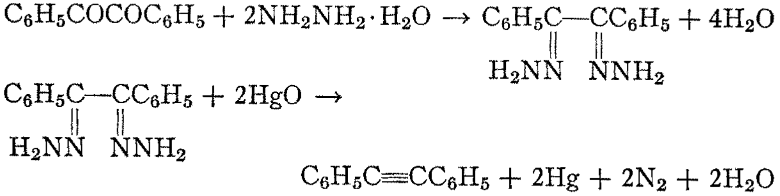
[1] Mississippi State College, State College, Mississippi. Work supported in part by a gift from the Research Corporation.

[2] Wolff, *Ber.*, **28**, 69 (1895).

[3] Rimini, *Gazz. chim. ital.*, **25**, II, 266 (1895).

DIPHENYLACETYLENE

(Acetylene, diphenyl-)



$$C_6H_5COCOC_6H_5 + 2NH_2NH_2\cdot H_2O \rightarrow C_6H_5\underset{\substack{\|\\ H_2NN}}{C}\text{—}\underset{\substack{\|\\ NNH_2}}{C}C_6H_5 + 4H_2O$$

$$C_6H_5\underset{\substack{\|\\ H_2NN}}{C}\text{—}\underset{\substack{\|\\ NNH_2}}{C}C_6H_5 + 2HgO \rightarrow C_6H_5C{\equiv}CC_6H_5 + 2Hg + 2N_2 + 2H_2O$$

Submitted by Arthur C. Cope, Douglas S. Smith, and Robert J. Cotter.[1]
Checked by Charles C. Price and Thomas F. McKeon, Jr.

1. Procedure

A solution of 105.1 g. (0.5 mole) of benzil (Note 1) in 325 ml. of *n*-propyl alcohol is prepared in a 1-l. round-bottomed flask which is fitted with an efficient reflux condenser. To this solution 76 g. (1.30 moles) of 85% hydrazine hydrate (Note 2) is added, and the mixture (Note 2) is heated under reflux for 60 hours. The solution is cooled with an ice bath, and the benzil dihydrazone is separated by suction filtration. The crystals are washed with 200 ml. of cold, absolute ethanol and dried (Note 3) on the suction filter for 1 hour. The yield of benzil dihydrazone is 99–106 g. (83–89%), m.p. 150–151.5°.

The benzil dihydrazone is added to 480 ml. of reagent grade benzene in a 1-l. three-necked flask fitted with a reflux condenser and a sealed stirrer. A small amount of yellow mercuric oxide (2–4 g.) is added to the mixture with stirring to keep the benzil dihydrazone suspended, and the mixture is warmed slightly on a steam bath. Nitrogen is evolved, and the mixture turns gray. Additional yellow mercuric oxide is then introduced in small portions so as to keep the reaction mixture gently refluxing until a total of 240 g. (1.11 moles) has been added. The mixture is stirred for 1 hour and allowed to stand overnight. It is then filtered, and the residue (mercury and mercuric oxide) is washed with 100 ml. of benzene, which is combined with the original red benzene filtrate. After drying over anhydrous sodium sulfate, the benzene is removed by distillation under reduced pressure by heating with a water bath. The residue is distilled from a flask connected to a short distillation head at 95–105°/0.2–0.3 mm. and yields 60–65 g. (67–73% from benzil) of diphenylacetylene, m.p. 59–60°. The product can be recrystallized from 100 ml. of 95% ethanol, m.p. 60–61° (Note 4).

2. Notes

1. Eastman Kodak Company "white label" grade benzil or material prepared by the procedure described in *Organic Syntheses* [2] is satisfactory.
2. Hydrazine hydrate (85%) as supplied by the Edwal Laboratories was used. On addition of this reagent to the benzil solution, the monohydrazone of benzil precipitates, but it redissolves readily on heating.
3. Benzil dihydrazone should not be dried in a vacuum desiccator, for it sublimes easily.
4. Diphenylacetylene prepared by this method has the advantage of being uncontaminated with stilbene, with which it forms a solid solution not readily separable.[3] Di-*p*-tolylacetylene [4] and α-naphthylphenylacetylene [5] have been prepared by the same method in high yields.

3. Methods of Preparation

In addition to the methods mentioned in a previous preparation,[6] diphenylacetylene has been prepared by the action of potassium hydroxide on 5,5-diphenyl-3-nitroso-2-oxazolidone (100%).[7] The present procedure is a modification of that of Schlenk and Bergmann.[8]

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[1] Massachusetts Institute of Technology, Cambridge, Massachusetts.

[2] *Org. Syntheses* Coll. Vol. **1**, 87 (1941).

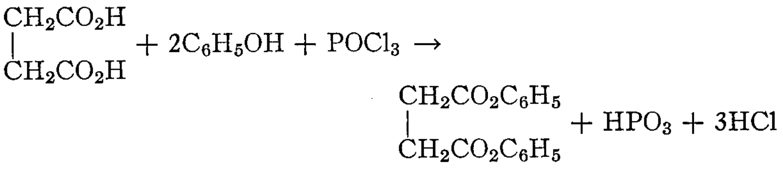
[3] Pascal and Normand, *Bull. soc. chim. France*, [4], **13**, 151 (1913).

[4] Kastner and Curtius, *J. prakt. Chem.*, [2], **83**, 225 (1911).

[5] Ruggli and Reinert, *Helv. Chim. Acta*, **9**, 67 (1926).
[6] *Org. Syntheses*, **22**, 50 (1942).
[7] Newman and Kutner, *J. Am. Chem. Soc.*, **73**, 4199 (1951).
[8] Schlenk and Bergmann, *Ann.*, **463**, 76 (1928).

DIPHENYL SUCCINATE

(Succinic acid, diphenyl ester)



$$\begin{matrix}CH_2CO_2H\\ |\\ CH_2CO_2H\end{matrix} + 2C_6H_5OH + POCl_3 \rightarrow \begin{matrix}CH_2CO_2C_6H_5\\ |\\ CH_2CO_2C_6H_5\end{matrix} + HPO_3 + 3HCl$$

Submitted by Guido H. Daub and William S. Johnson.[1]
Checked by James Cason, Robert A. Wessman, and William G. Dauben.

1. Procedure

A mixture of 118 g. (1 mole) of succinic acid, 188 g. (2 moles) of phenol, and 138 g. (83 ml., 0.9 mole) of phosphorus oxychloride (Note 1) is placed in a 2-l. round-bottomed flask fitted with an efficient reflux condenser capped with a calcium chloride tube (Notes 2 and 3). The mixture is heated on a steam bath in a hood (Note 3) for 1.25 hours, 500 ml. of benzene is added, and the refluxing is continued for an additional hour. The hot benzene solution is decanted from the red syrupy residue of phosphoric acid and filtered by gravity into a 1-l. Erlenmeyer flask. The syrupy residue is extracted with two 100-ml. portions of hot benzene, which are also filtered into the Erlenmeyer flask. The combined benzene solutions are concentrated to a volume of about 600 ml. (Note 4), and the pale yellow solution is allowed to cool, whereupon the diphenyl succinate separates as colorless crystals. It is filtered with suction on a Büchner funnel, washed with three 50-ml. portions of ether, and dried on a porous plate at 40°. The yield of diphenyl succinate, m.p. 120–121°, is 167–181 g. (62–67%) (Note 5).

2. Notes

1. The use of a larger proportion of phosphorus oxychloride failed to improve the yield and in general gave an inferior product.
2. Ground-glass joints are preferred; however, burnt-cork stoppers may be used.
3. Provision should be made to dispose of the hydrogen chloride which is evolved during the reaction.
4. If the mother liquor is concentrated further before removal of phenol and phosphorus oxychloride a dark, impure product is obtained.
5. If desired, a second crop may be obtained by the following procedure: The mother liquor is extracted in a 1-l. separatory funnel with eight 50-ml. portions of 5% potassium hydroxide solution. Each extract is extracted in turn with a 50-ml. portion of benzene. The two benzene solutions are washed in turn with a 50-ml. portion of water and two 50-ml. portions of saturated sodium chloride solution. All the benzene solutions are combined, dried over anhydrous sodium sulfate, filtered, and concentrated to a volume of 150 ml. Cooling yields a second crop of diphenyl succinate, which is collected, washed, and dried as described for the first crop. The yield is 13–27 g. (5–10%), m.p. 118–120°.

3. Methods of Preparation

The above procedure is a modification of that described by Rasinski.[2] Diphenyl succinate has also been prepared by the reaction of phenol and succinic acid in the presence of phosphorus pentoxide in toluene[3] and by the treatment of phenol with succinyl chloride.[4]

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[1] Department of Chemistry, University of Wisconsin, Madison, Wisconsin.
[2] Rasinski, *J. prakt. Chem.*, **26**, 63 (1882). See also Bischoff and Hedenstrom, *Ber.*, **35**, 4073 (1902).
[3] Bakunin, *Gazz. chim. ital.*, **30**, 358 (1900).
[4] Weselsky, *Ber.*, **2**, 519 (1869).

ETHOXYACETYLENE

(Ether, ethyl ethynyl)

$$ClCH_2CH(OC_2H_5)_2 + 3NaNH_2 \xrightarrow{\text{liq. } NH_3} NaCl + C_2H_5ONa + NaC{\equiv}COC_2H_5 + 3NH_3$$

$$NaC{\equiv}COC_2H_5 + H_2O \rightarrow NaOH + HC{\equiv}COC_2H_5$$

Submitted by E. R. H. Jones, Geoffrey Eglinton, M. C. Whiting, and B. L. Shaw.[1]
Checked by Arthur C. Cope and Ronald M. Pike.

1. Procedure

Caution! This preparation should be conducted in a hood to avoid exposure to ammonia.

A solution of sodium amide in liquid ammonia is prepared according to a procedure previously described (Note 1) in a 1-l. three-necked flask (Note 2) equipped with a cold-finger condenser (cooled with Dry Ice) attached through a soda-lime tower to a gas absorption trap [2] and an inlet tube. Anhydrous liquid ammonia (500 ml.) is introduced from a commercial cylinder through the inlet tube, and 0.5 g. of hydrated ferric nitrate is added, followed by 38 g. (1.65 gram atoms) of clean, freshly cut sodium (Note 3). The inlet tube is replaced with a 100-ml. dropping funnel, and the mixture is agitated manually (Note 2) until all the sodium is converted into sodium amide, after which 76.5 g. (0.502 mole) of diethylchloroacetal (Note 4) is added over a period of 15–20 minutes. The mixture is swirled for an additional period of 15 minutes, after which the ammonia is evaporated in a stream of pure nitrogen. The flask is cooled to −70° in a Dry Ice-trichloroethylene bath (Note 5), and 325 ml. of a saturated solution of sodium chloride which has been cooled to −20° is added all at once and as rapidly as possible with vigorous agitation (Note 6). The flask is then fitted with a still head connected to a trap cooled to −70° with Dry Ice, and the contents of the flask are slowly heated to 100° on a steam bath (Note 7). The condensate is allowed to warm to 0°, after which the trap is again cooled to −70° and the mixture is neutralized by the dropwise addition of a saturated aqueous solution of sodium dihydrogen phosphate. The aqueous layer is frozen by cooling with Dry Ice, and the supernatant liquid is decanted and dried over about 4 g. of anhydrous calcium chloride. The drying agent is removed by filtration, and the filtrate is distilled (Note 8) through a column containing a 20-cm. section packed with glass helices at partial reflux, yielding 20–21.2 g. (58–61%) of ethoxyacetylene, b.p. 49–51°/749 mm., n_D^{25} 1.3790 (Notes 9, 10, and 11).

2. Notes

1. One of the procedures for converting sodium to sodium amide described in *Organic Syntheses* is used.[3,4]

2. The flask is clamped to the free end of a long (30-in.) Duraluminum rod which is fixed at the other (top) end to a rigid frame. The rod is clamped in a vertical position, and by moving the free end the contents of the flask can be swirled very conveniently.

The submitters used a 1-l. round-bottomed flask mounted in the same way, without provision for cooling or a condenser cooled with Dry Ice, and were successful in preparing sodium amide and adding diethylchloroacetal before excessive loss of liquid ammonia occurred. Conversion of sodium to sodium amide sometimes requires a considerable period of time, in which case use of the apparatus specified avoids difficulty and the necessity of adding more liquid ammonia.

3. More liquid ammonia should be added through the inlet tube if vaporization reduces the liquid volume to less than 300 ml.

4. Diethylchloroacetal (chloroacetaldehyde diethylacetal) supplied by The Eastman Kodak Company is satisfactory.

5. *Important! This sodium derivative is extremely pyrophoric, and at this point and during the addition of the saturated sodium chloride solution it is essential that the contents of the flask be kept out of contact with air.* When the flask is immersed in the Dry Ice bath

the nitrogen stream is increased to counteract the diminution in pressure due to rapid cooling.

6. The checkers found that a dropping funnel equipped with a pressure-equalizing tube provided the most satisfactory mode of addition.

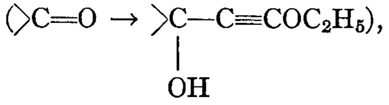
7. It is advisable to allow the mixture to warm to room temperature gradually before applying heat.

8. The distillation should be conducted in a hood since the product has lachrymatory properties.

9. Others have reported b.p. 28°/300 mm., n_D^{20} 1.3812,[5] and b.p. 48–50°/760 mm.[6]

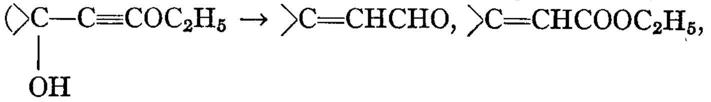
10. The submitters have used a similar procedure for the preparation of methoxyacetylene, b.p. 22.5–23.5°, n_D^{16} 1.3693, from commercial dimethylchloroacetal in 60% yield.

11. Ethoxyacetylene has proved to be a useful reagent for the conversion of ketones to acetylenic carbinols



$$(\rangle C{=}O \rightarrow \rangle \underset{\textstyle OH}{\underset{|}{C}}{-}C{\equiv}COC_2H_5),$$

which can be converted into α,β-unsaturated aldehydes, esters, and acids $(\rangle \underset{\textstyle OH}{\underset{|}{C}}{-}C{\equiv}COC_2H_5 \rightarrow \rangle C{=}CHCHO,\ \rangle C{=}CHCOOC_2H_5,\ \rangle C{=}CHCO_2H)$.[7] It has been used in the synthesis of vitamin A aldehyde [8] and in the preparation of an intermediate in one of the total syntheses of cortisone.[9]



3. Methods of Preparation

Ethoxyacetylene has been prepared from β-bromovinyl ethyl ether and potassium hydroxide in 50–55% yield; [5] from α,β-dibromoethyl ethyl ether and potassium hydroxide; [6] and from diethyl chloroacetal, diethyl bromoacetal, α,β-dichloroethyl ethyl ether, or α,β-dibromoethyl ethyl ether and sodium amide.[10]

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[1] University of Manchester, Manchester, England.

[2] *Org. Syntheses* Coll. Vol. **2**, 4 (1943).

[3] *Org. Syntheses*, **25**, 25 (1945).

[4] *Org. Syntheses*, **30**, 72 (1950).

[5] Jacobs, Cramer, and Hanson, *J. Am. Chem. Soc.*, **64**, 223 (1942).

[6] Favorskii and Shostakovskii, *J. Gen. Chem. U.S.S.R.*, **13**, 1 (1943) [*C. A.*, **38**, 330 (1944)].

[7] Heilbron, Jones, Julia, and Weedon, *J. Chem. Soc.*, **1949**, 1823.

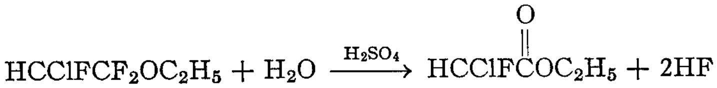
[8] Van Dorp and Arens, *Nature*, **160**, 189 (1947).

[9] Sarett, Arth, Lukes, Beyler, Poos, Johns, and Constantin, *J. Am. Chem. Soc.*, **74**, 4974 (1952).

[10] Eglinton, Jones, Shaw, and Whiting, *J. Chem. Soc.*, **1954**, 1860.

ETHYL CHLOROFLUOROACETATE

(Acetic acid, chlorofluoro-, ethyl ester)



$$HCClFCF_2OC_2H_5 + H_2O \xrightarrow{H_2SO_4} HCClF\overset{\overset{\textstyle O}{\|}}{C}OC_2H_5 + 2HF$$

Submitted by Bruce Englund.[1]
Checked by R. S. Schreiber and Burris D. Tiffany.

1. Procedure

Caution! Hydrogen fluoride vapors are highly corrosive and poisonous. An efficient hood should be used, and rubber gloves should be worn when dismantling the equipment.

A 2-l. three-necked round-bottomed flask is fitted with a mechanical stirrer and a 500-ml. dropping funnel (Note 1). The third neck is fitted with a thermometer and a length of rubber tubing to lead evolved hydrogen fluoride to the rear of the hood away from the operator. The flask is charged with 340 g. (2.09 moles) of crude 2-chloro-1,1,2-trifluoroethyl ethyl ether [2] and cooled in an ice bath until the temperature of the halo ether is below 5°. From the dropping funnel, 228 ml. of 96% sulfuric acid (420 g., 4.1 moles) is added at such a rate that the temperature can be maintained at 5–15°. The addition requires 30–45 minutes, during which evolution of hydrogen fluoride begins. The reaction mixture is stirred at 10° for 2 hours, then carefully poured onto a mixture of 1 kg. of crushed ice and 500 ml. of water.

The product, a nearly white oil, settles out as the lower layer. It is separated, washed until free of acid with three 25-ml. portions of saturated sodium bicarbonate solution (Note 2) then with four 25-ml. portions of water, and dried over 10 g. of Drierite. The weight of crude dried ester is 200–210 g. (68–71%). Fractional distillation gives 190–200 g. (65–68% yield) of pure ethyl chlorofluoroacetate, b.p. 129–130°, n_D^{25} 1.3925 (Note 3).

2. Notes

1. The hydrogen fluoride evolved etches the glass reaction vessel, but the same equipment may be used for 4–6 runs.
2. If the crude product is not washed free of acid considerable decomposition occurs during distillation with consequent reduction in yield.
3. The checkers found it necessary to use a moderately efficient (2 by 12 cm. helix-packed) column to effect satisfactory fractionation.

3. Methods of Preparation

Ethyl chlorofluoroacetate has been prepared by the action of sulfuric acid[3] or of silica[4] on 2-chloro-1,1,2-trifluoroethyl ethyl ether. The procedure given here is essentially that of Young and Tarrant.[3]

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[1] Chemical Department, Experimental Station, E. I. du Pont de Nemours and Company, Wilmington, Delaware.

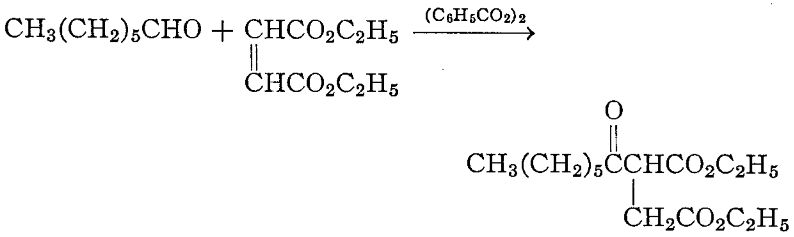
[2] *Org. Syntheses*, **34**, 16 (1954).

[3] Young and Tarrant, *J. Am. Chem. Soc.*, **71**, 2432 (1949).

[4] Hanford and Rigby, U. S. pat. 2,409,274 [*C. A.*, **41**, 982 (1947)].

ETHYL ENANTHYLSUCCINATE

(Succinic acid, heptanoyl-, diethyl ester)



$$CH_3(CH_2)_5CHO + \begin{array}{l} CHCO_2C_2H_5 \\ \| \\ CHCO_2C_2H_5 \end{array} \xrightarrow{(C_6H_5CO_2)_2} CH_3(CH_2)_5\overset{\overset{O}{\|}}{C}\begin{array}{l} CHCO_2C_2H_5 \\ | \\ CH_2CO_2C_2H_5 \end{array}$$

Submitted by TRACY M. PATRICK, JR., and FLOYD B. ERICKSON.[1]
Checked by T. L. CAIRNS and R. D. CRAMER.

1. Procedure

A mixture of 228 g. (2.0 moles) of enanthaldehyde (Note 1) and 172 g. (1.0 mole) of ethyl maleate (Note 2) is placed in a jacketed flask (Fig. 3) (Note 3) with condensers attached to the flask and the jacket openings. The jacket is charged with trichloroethylene (Note 4), which is heated to reflux, and, when the reaction mixture reaches 84–85°, 0.5 g. of benzoyl peroxide is added to the mixture through the condenser. After 3–8 hours an additional 0.5-g. portion of benzoyl peroxide is added, and heating is continued for a total of 18–24 hours (Note 5).

The reaction mixture is distilled through a short (8- to 12-in.) Vigreux column to give 108–111 g. of recovered enanthaldehyde, b.p. 64–65°/38 mm.; 6–16 g. of an intermediate fraction, b.p. 82–128°/1 mm.; and 202–216 g. (71–76% yield) of ethyl enanthylsuccinate, b.p. 119–122°/0.7 mm., n_D^{25} 1.4392–1.4398 (Notes 6, 7, and 8).

2. Notes

1. Good-quality enanthaldehyde such as the "white label" grade supplied by the Eastman Kodak Company was distilled before use. It is best stored in a brown bottle under nitrogen for protection against oxidation.

2. Ethyl maleate from Commercial Solvents Corporation, Terre Haute, Indiana, was distilled before use. Ethyl fumarate can be used also, but the yield of product is lower since a much greater proportion of high-boiling compounds is obtained. Aldehydes do not undergo free-radical addition to maleic anhydride under these conditions.

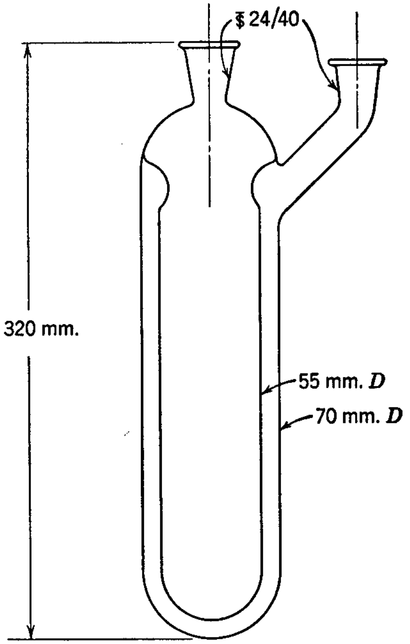


Fig. 3.

3. Although this piece of apparatus is not essential, it provides a convenient means of controlling the temperature for a mildly exothermic reaction which must be carried out overnight without close supervision. The submitters carried out one experiment in an ordinary apparatus heated by a mantle. The poorer temperature control (70–91°) resulted in a yield of only 44%.

4. Any other stable liquid having a boiling point in the neighborhood of 80–90° could be substituted for trichloroethylene.

5. The reaction time is not critical. For the sake of convenience the reaction can be started early in the day, the second portion of peroxide added before leaving in the evening, and heating discontinued upon arrival the following morning.

6. The submitters collected material boiling in the range 128–150°/1 mm. and found this product to be satisfactory for the preparation of γ-oxocapric acid (Note 7).

7. The submitters state that ethyl enanthylsuccinate can be hydrolyzed and decarboxylated to γ-oxocapric acid. The reaction is carried out by heating 57 g. of the keto ester with a solution of 140 ml. of concentrated sulfuric acid in 250 ml. of water. The mixture is stirred while the ethanol is removed gradually by distillation over a period of 3 hours. The acid is taken up in benzene, extracted from the benzene with aqueous alkali, and liberated from the alkaline solution by acidification with concentrated hydrochloric acid. After recrystallization from 50% ethanol about 29 g. (78% yield) of γ-oxocapric acid is obtained as colorless crystals, m.p. 69–70°.

The submitters also state that γ-caprilactone can be prepared by hydrogenation of 50 g. of γ-oxocapric acid in 150 ml. of ethanol over 5 g. of Raney nickel at 135° and 1000 p.s.i. Filtration and distillation gives about 38 g. (83% yield) of γ-caprilactone, b.p. 109–110°/2.5 mm., n_{D}^{25} 1.4470.

8. A number of other acylsuccinic esters can be prepared in a similar fashion from the appropriate saturated aliphatic aldehydes and maleic esters.[2,3] The procedure is equally adaptable to the preparation of α-acyltricarballylic esters from aldehydes and aconitates.[2] Good temperature control (80–90°) is most important for success in these reactions.

3. Methods of Preparation

Ethyl enanthylsuccinate has been prepared by the free-radical addition of enanthaldehyde to ethyl maleate.[2]

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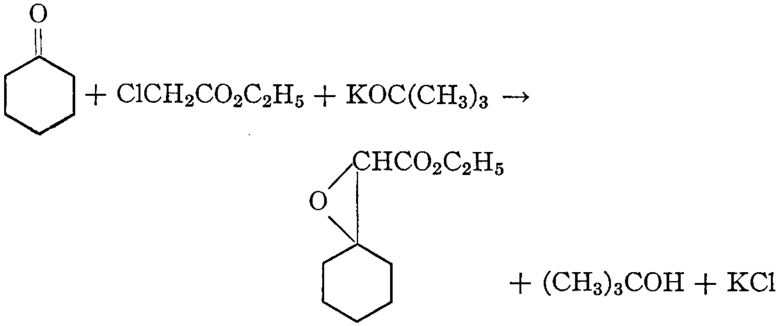
[1] Monsanto Chemical Company, Dayton, Ohio.

[2] Patrick, *J. Org. Chem.*, **17**, 1009 (1952).

[3] Ladd, U. S. pat. 2,577,133 [*C. A.*, **46**, 6147 (1952)].

ETHYL β,β-PENTAMETHYLENEGLYCIDATE

(1-Oxaspiro[2,5]octane-2-carboxylic acid, ethyl ester)



Submitted by RICHARD H. HUNT, LELAND J. CHINN, and WILLIAM S. JOHNSON.[1]
Checked by N. J. LEONARD and F. P. HAUCK, JR.

1. Procedure

The reaction is conducted in a 500-ml. round-bottomed three-necked flask to which are attached (ground-glass joints) a rubber slip-sleeve-sealed wire stirrer, a thermometer, and a pressure-equalized dropping funnel. The top of the dropping funnel is connected to a system for exhausting and filling with nitrogen.[2] The apparatus is flame-dried at reduced pressure, and the flask is charged with 14.50 g. (0.148 mole) of freshly distilled cyclohexanone and 18.15 g. (0.148 mole) of freshly distilled ethyl chloroacetate. A solution of 6.0 g. (0.153 gram atom) of potassium in 125 ml. of dry *tert*-butyl alcohol (Notes 1 and 2) is introduced into the dropping funnel, and the system is exhausted and filled with nitrogen. The flask is cooled with an ice bath, stirring is commenced, and the solution of potassium *tert*-butoxide is added from the dropping funnel over a period of about 1.5 hours, the temperature of the reaction mixture being maintained at 10–15°. After the addition is complete, the mixture is stirred for an additional 1–1.5 hours at about 10°. Most of the *tert*-butyl alcohol is removed by distillation from the reaction flask at reduced pressure (water aspirator) and a bath temperature of 100°. The oily residue is taken up in ether. The ether solution is washed with water, then with saturated aqueous sodium chloride solution, and is finally dried over anhydrous sodium sulfate. The residue obtained on evaporation of the ether is distilled through a 6-in. Vigreux column to give 22.5–26.0 g. (83–95% yield) of colorless glycidic ester, b.p. 134–137°/21 mm., 147–152°/30 mm., n_D^{25} 1.4568–1.4577 (Note 3).

2. Notes

1. The preparation of potassium *tert*-butoxide is carried out according to a procedure already described.[2] Particular attention should be paid to the precautions in handling potassium.

2. The *tert*-butyl alcohol may be dried over sodium.[2] Scrupulously dry *tert*-butyl alcohol may be prepared by distilling alcohol thus treated from calcium hydride (about 1 g./4 l.), obtainable from Metal Hydrides, Inc.

3. This material is of satisfactory quality, as shown by its conversion to solid derivatives in good yield.[3]

3. Methods of Preparation

Ethyl β,β-pentamethyleneglycidate has been prepared in 65% yield by the condensation of cyclohexanone with ethyl chloroacetate in the presence of sodium ethoxide,[4] and in 50% yield in the presence of sodium in xylene.[5] The present procedure employs potassium *tert*-butoxide as the condensing agent.[3]

[1] Department of Chemistry, University of Wisconsin, Madison, Wisconsin.

[2] *Org. Syntheses*, **30**, 18 (1950).

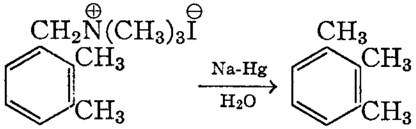
[3] Johnson, Belew, Chinn, and Hunt, *J. Am. Chem. Soc.*, **75**, 4995 (1953).

[4] Darzens and Lefebure, *Compt. rend.*, **142**, 714 (1906).

[5] Lunt and Sondheimer, *J. Chem. Soc.*, **1950**, 2957.

HEMIMELLITENE

(Benzene, 1,2,3-trimethyl-)



Submitted by W. R. Brasen and C. R. Hauser.[1]
Checked by William S. Johnson, Donald W. Stoutamire, and A. L. Wilds.

1. Procedure

A 3-l. round-bottomed three-necked flask, fitted with a reflux condenser and a sealed stirrer, is charged with 2 l. of hot water and 100 g. (0.328 mole) of 2,3-dimethylbenzyltrimethylammonium iodide (Note 1). The stirred suspension is heated on the steam bath, and 2760 g. of 5% sodium amalgam (Note 2) is added in 200- to 250-g. portions over a period of 45 minutes. Stirring and heating are continued for 24 hours; then the mixture is steam-distilled until no more oily material comes over. The distillate (1–1.5 l.) is extracted with three 50-ml. portions of ether. The combined extracts are washed with 50 ml. of 10% hydrochloric acid and 50 ml. of saturated sodium chloride solution, and dried over anhydrous calcium chloride. After removal of the ether by distillation, the residue is distilled from a Claisen flask, giving 33.5–35.5 g. (85–90% yield) of colorless hydrocarbon, b.p. 171–174°. On redistillation 85–90% of the material distils at 173–174°, n_D^{25} 1.5116–1.5120.

2. Notes

1. The methiodide is prepared from 2,3-dimethylbenzyldimethylamine according to the procedure for producing the lower homolog.[2]

2. The sodium amalgam is prepared in a 1-l. filter flask fitted with a two-hole rubber stopper carrying a dropping funnel and an outlet tube. The flask is charged with 138 g. (6 gram atom) of sodium and 300 ml. of mineral oil. With a stream of nitrogen passing through the side arm of the flask, the flask is heated on a hot plate covered with an asbestos pad until the sodium melts, and then 2622 g. of mercury is added rapidly from the dropping funnel over a 1–2 minute period with swirling. The whole operation is carried out in a large pan to catch material in case of breakage. A vigorous exothermic reaction occurs, and the hands must be adequately protected with several layers of cloth or heavy gloves as the temperature approaches 400°. If the addition is rapid enough, the amalgam will be a liquid; otherwise the material will be partially solid and must be heated vigorously to produce a homogeneous melt. The mineral oil is decanted from the molten amalgam, which is poured into a shallow metal pan while still warm and is cut or broken (with a hammer) into small pieces as it solidifies. It is finally washed with petroleum ether and stored in a tightly stoppered bottle or under petroleum ether.

3. Methods of Preparation

Hemimellitine has been prepared by the action of sodium on 2,3-dimethyliodobenzene and methyl iodide,[3] by the reduction of the chloromethylation product of *o*-xylene,[4] and by the catalytic hydrogenolysis of 2,3-dimethylbenzyl alcohol.[5] The present procedure is based on the method of Kantor and Hauser.[6]

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[1] Duke University, Durham, North Carolina. Work supported by the Office of Ordnance Research.

[2] *Org. Syntheses*, **34**, 61 (1954), Notes 5 and 8.

[3] von Auwers, *Ann.*, **419**, 116 (1919).

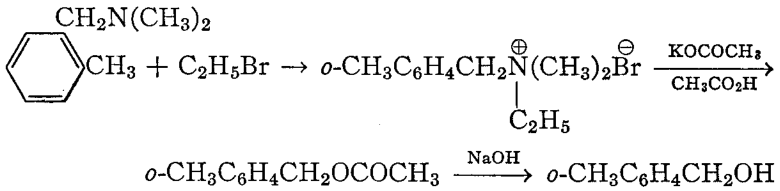
[4] von Braun and Nelles, *Ber.*, **67**, 1094 (1934).

[5] Smith and Spillane, *J. Am. Chem. Soc.*, **62**, 2639 (1940).

[6] Kantor and Hauser, *J. Am. Chem. Soc.*, **73**, 4122 (1951).

o-METHYLBENZYL ALCOHOL

(Benzyl alcohol, *o*-methyl-)



Submitted by W. R. Brasen and C. R. Hauser.[1]
Checked by William S. Johnson, Donald W. Stoutamire, and A. L. Wilds.

1. Procedure

A. *o-Methylbenzyl acetate.* A solution of 29.8 g. (0.20 mole) of 2-methylbenzyldimethylamine[2] and 32.7 g. (0.30 mole) of ethyl bromide in 40 ml. of absolute ethanol is placed in a 500-ml. round-bottomed flask fitted with a reflux condenser capped with a calcium chloride drying tube. The solution is heated under reflux on the steam bath for 1 hour; then an additional 10.8 g. (0.10 mole) of ethyl bromide is added and the heating continued for an additional 3 hours. The solvent and residual ethyl bromide are removed at reduced pressure (water aspirator) while the flask is heated in a water bath kept at about 60° (Note 1). The oily residue is treated with about 300 ml. of absolute ether, and on scratching crystallization is induced. The product is collected on a Büchner funnel, washed with two 50-ml. portions of anhydrous ether, and dried in a vacuum desiccator. The yield of colorless 2-methylbenzylethyldimethylammonium bromide is 47.5–49.0 g. (92–95%) (Note 2). It is hygroscopic and should therefore not be exposed to moist air.

In a 500-ml. round-bottomed flask, fitted with a reflux condenser capped with a calcium chloride drying tube, are placed 38.7 g. (0.15 mole) of the quaternary ammonium bromide (Note 3) described above, 24.6 g. (0.3 mole) of fused sodium acetate, and 100 ml. of glacial acetic acid. The mixture is boiled under reflux for 24 hours (Note 4) and then allowed to cool. It is transferred to a large beaker (Note 5), 250 ml. of water is added, and the acid is partially neutralized by the addition of 84 g. of solid sodium bicarbonate. The mixture is extracted with three 75-ml. portions of ether, and the combined ether solutions are washed with two or more 50-ml. portions of saturated sodium bicarbonate solution until all the acetic acid has been removed. The ether layer is then washed with 50 ml. of saturated sodium chloride solution and dried over anhydrous sodium sulfate. The ether is removed by distillation, and the residue is distilled under reduced pressure. The yield of colorless liquid acetate, b.p. 119–121°/15 mm. or 129–131°/31 mm., is 21.6–22.4 g. (88–91%), n_D^{25} 1.5041–1.5045 (Note 6).

B. *o-Methylbenzyl alcohol.* A solution of 5 g. (0.12 mole) of sodium hydroxide in 50 ml. of water is added to a solution of 16.4 g. (0.1 mole) of 2-methylbenzyl acetate (prepared as described above, part A) in 50 ml. of methanol contained in a 250-ml. round-bottomed flask fitted with a reflux condenser. The mixture is boiled under reflux for 2 hours, cooled, diluted with 50 ml. of water, and extracted with three 75-ml. portions of ether. The combined ether solutions are washed with 50 ml. of water and 50 ml. of saturated sodium chloride solution and dried over anhydrous sodium sulfate. The solvent is removed by distillation, finally at reduced pressure to remove the last traces of methyl alcohol, and the residue is dissolved in 50 ml. of boiling 30–60° petroleum ether. The colorless crystals obtained on cooling, finally in the ice bath, are collected by suction filtration, washed with a few milliliters of cold petroleum ether, and air-dried. Concentration of the mother liquors to 6–7 ml. and cooling gives an additional crop. The total yield of product melting between 33–34° and 35–36° is 11.6–11.8 g. (95–97%) (Note 7).

2. Notes

1. A capillary ebullition tube is used to prevent bumping.
2. 2,3-Dimethylbenzylethyldimethylammonium bromide can be prepared similarly in comparable yield. The salts are suitable for use in the displacement reaction without purification.
3. The ethobromides are preferable to methiodides in this reaction, because the former salts are more soluble in glacial acetic acid and do not liberate halogen as do the iodides.
4. The sodium acetate dissolves as the mixture reaches reflux temperature, but a small amount of solid (perhaps sodium bromide) remains undissolved throughout the heating.
5. Considerable foaming may occur during the neutralization, and material may be lost if the process is carried out in a small narrow-mouthed vessel.
6. The submitters have used this same procedure for the preparation of 2,3-dimethylbenzyl acetate from the corresponding quaternary salt (Note 2). The yield of material b.p. 127–129°/9 mm. was 94%.
7. Hydrolysis of 2,3-dimethylbenzyl acetate (Note 6) by this procedure gave 2,3-dimethylbenzyl alcohol, m.p. 65–66°, in 96% yield.

3. Methods of Preparation

The vicinal methylbenzyl alcohols have been prepared in general by the abnormal reaction of the appropriately substituted Grignard reagent with formaldehyde.[3] The present method is preferred because it yields purer products than the Grignard approach.

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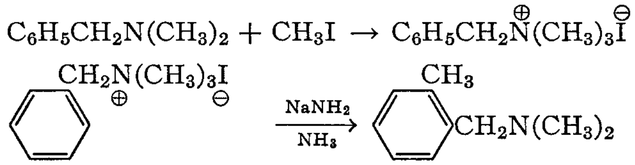
[1] Duke University, Durham, North Carolina. Work supported by the Office of Ordnance Research.

[2] *Org. Syntheses*, **34**, 61 (1954).

[3] Reichstein, Cohen, Ruth, and Meldahl, *Helv. Chim. Acta*, **19**, 412 (1936).

2-METHYLBENZYLDIMETHYLAMINE

(Benzylamine, N,N,*o*-trimethyl-)



$$C_6H_5CH_2N(CH_3)_2 + CH_3I \rightarrow C_6H_5CH_2\overset{\oplus}{N}(CH_3)_3\overset{\ominus}{I}$$

Submitted by W. R. Brasen and C. R. Hauser.[1]
Checked by William S. Johnson, Mary E. Mills, and A. L. Wilds.

1. Procedure

A. *Benzyltrimethylammonium iodide.* A solution of 135 g. (1 mole) of N,N-dimethylbenzylamine (Note 1) in 200 ml. of commercial absolute ethanol (Note 2) is placed in a three-necked flask fitted with a 125-ml. dropping funnel, a reflux condenser, and a rubber slip-sleeve-sealed stirrer. The openings of the dropping funnel and condenser are protected from atmospheric moisture with drying tubes. While the solution is stirred rapidly, 190 g. (1.34 mole) of methyl iodide contained in the dropping funnel is added slowly at first, then at such a rate as to cause gentle refluxing of the solution. After the addition is complete (30 minutes), the solution is boiled under reflux on the steam bath for 30 minutes more and transferred to a 2-l. Erlenmeyer flask with the aid of an additional 25-ml. of absolute ethanol for rinsing. On cooling to room temperature a large portion of the methiodide crystallizes, and the remaining material is then precipitated by the addition of 1 l. of anhydrous ether with stirring (Note 3). The product is separated by suction filtration, washed with two 100-ml. portions of anhydrous ether (Note 4), and dried in air at room temperature. The yield of benzyltrimethylammonium iodide, m.p. 178–179° dec., is 260–274 g. (94–99%), and is pure enough for most purposes (Note 5).

B. *2-Methylbenzyldimethylamine.* (*Caution! This preparation should be conducted in a good hood to avoid exposure to ammonia.*) To 800 ml. of liquid ammonia contained in a 2-l. three-necked flask fitted with a rubber slip-sleeve-sealed wire stirrer and an air-cooled reflux condenser, sodium is added in small pieces until the blue color persists (Note 6). At this point 0.5 g. of granulated ferric nitrate is added, and then 27.8 g. (1.2 gram atom) of sodium (cut into approximately 0.5-g. pieces), is introduced at such a rate that stirring is not hindered. After all the sodium is added (about 15 minutes), the mixture is stirred until the blue color disappears and the grayish-black suspension of sodium amide remains (15–20 minutes). Stirring is discontinued, and the mixture is swirled to wash down the mirror of sodium which forms on the upper walls of the flask (Note 7).

A 500-ml. Erlenmeyer flask is charged with 277 g. (1 mole) of benzyltrimethylammonium iodide (prepared as described above, part A) and is connected with a short section of large-diameter rubber tubing to the third neck of the flask containing the sodium amide. Stirring is started, and the salt is shaken in at a steady rate and as rapidly as possible without serious loss of material through the condenser. This operation requires about 10–15 minutes (Note 8). The greenish-violet color, which is first produced by addition of the salt, persists for about 15 minutes after all the material has been added. During this and the subsequent reaction period, more ammonia is added as necessary to maintain the original volume. The mixture is stirred for an additional 2 hours, and then 27 g. (0.5 mole) of ammonium chloride is added cautiously to destroy excess sodium amide.

The flask is fitted with a dropping funnel, and enough (about 100 ml.) water is added, dropwise at first, to bring all the solid material into solution. The mixture is stirred until it reaches room temperature, 70 ml. of ether is added, and the organic layer is separated. The water layer is extracted with two 70-ml. portions of ether, and the combined ether solutions are washed with two 50-ml. portions of saturated salt solution and dried over anhydrous potassium carbonate. After filtration and removal of the ether by distillation, the amine is distilled through a 10-cm. Vigreux column. The fraction, b.p. 72–73°/9 mm., 97–99°/13 mm., or 197–198°/atm., amounts to 134–141.5 g. (90–95% yield), n_D^{20} 1.5050–1.5060 (Note 8). On redistillation all but about 5% of the material is recovered, b.p. 78–79°/12 mm., n_D^{20} 1.5049–1.5052.

2. Notes

1. N,N-Dimethylbenzylamine supplied by the Rohm and Haas Company was used without purification.

2. Methanol may be substituted in the preparation of this as well as other quaternary salts, which, however, are generally more soluble in this medium and therefore require a larger volume of ether for complete precipitation.

3. This isolation procedure produces a granular product which is more desirable for use in the rearrangement reaction than the fluffy material obtained on rapid cooling.

4. The ether should be free of peroxides; otherwise iodine will be liberated from the salt and will color the product.

5. This procedure is suitable for the preparation of the following quaternary salts with changes only in the proportion of ethanol employed: 2-methylbenzyltrimethylammonium iodide, using 350 ml. of ethanol per mole of amine (yield 98–99%), and 2,3-dimethylbenzyltrimethylammonium iodide, using 500 ml. of ethanol per mole of amine (yield 98–99%).

6. Only about 0.05 g. of sodium is required unless the ammonia is quite wet.

7. The complete removal of sodium is indicated by the lack of formation of blue coloration when the solution is swirled over the upper walls of the flask.

8. Essentially the same procedure may be used for the preparation of 2,3-dimethylbenzyldimethylamine from 2-methylbenzyltrimethylammonium iodide except that the time of addition of the latter to the sodium amide is increased to 75 minutes. The checkers found it necessary also to use a larger volume of ammonia. Thus, on a 0.3-mole scale, 1 l. of ammonia was employed, and a total of 600 ml. more ammonia was added during the reaction to maintain the volume at 800–1000 ml.

Owing to the formation of neutral side products, the reaction mixture is extracted with excess 4 *N* hydrochloric acid, and the mixture of amines is liberated from the acid solution by neutralization with sodium hydroxide. The amine fraction is taken up in ether and dried over anhydrous sodium sulfate or solid sodium hydroxide. After removal of the ether, the 2,3-dimethylbenzyldimethylamine distils at 101–102°/15 mm., 107–109°/19 mm., n_D^{23} 1.5100–1.5102. The yield is 60–70%.

3. Methods of Preparation

This procedure is based on the method of Kantor and Hauser.[2] 2-Methylbenzyldimethylamine has also been prepared from *o*-xylyl bromide and hexamethylenetetramine.[2]

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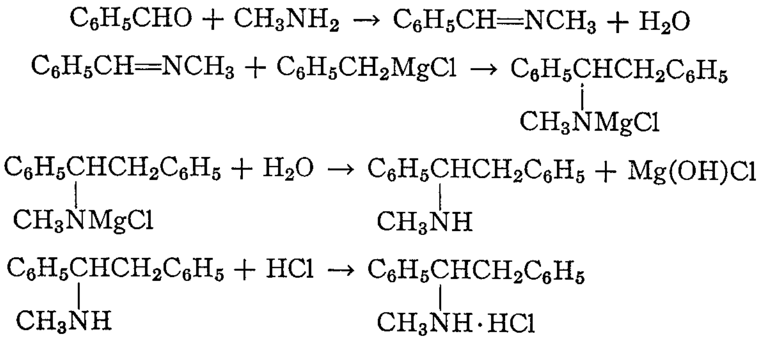
[1] Duke University, Durham, North Carolina. Work supported by the Office of Ordnance Research.

[2] Kantor and Hauser, *J. Am. Chem. Soc.*, **73**, 4122 (1951).

N-METHYL-1,2-DIPHENYLETHYLAMINE AND HYDROCHLORIDE

(Ethylamine, N-methyl-1,2-diphenyl-)



$$C_6H_5CHO + CH_3NH_2 \rightarrow C_6H_5CH{=}NCH_3 + H_2O$$

$$C_6H_5CH{=}NCH_3 + C_6H_5CH_2MgCl \rightarrow C_6H_5\underset{\substack{|\\ CH_3NMgCl}}{CH}CH_2C_6H_5$$

$$C_6H_5\underset{\substack{|\\ CH_3NMgCl}}{CH}CH_2C_6H_5 + H_2O \rightarrow C_6H_5\underset{\substack{|\\ CH_3NH}}{CH}CH_2C_6H_5 + Mg(OH)Cl$$

$$C_6H_5\underset{\substack{|\\ CH_3NH}}{CH}CH_2C_6H_5 + HCl \rightarrow C_6H_5\underset{\substack{|\\ CH_3NH\cdot HCl}}{CH}CH_2C_6H_5$$

Submitted by Robert Bruce Moffett.[1]
Checked by N. J. Leonard and L. A. Miller.

1. Procedure

A. *N-Benzylidenemethylamine.* A solution of 31.9 g. (0.3 mole) of benzaldehyde in 80 ml. of benzene contained in a 300-ml. round-bottomed flask is cooled to approximately 10°. To this is added a solution of 14 g. (0.45 mole) of anhydrous methylamine in 50 ml. of benzene (Note 1). On standing, the solution becomes warm and turns milky. After 1 hour the flask is connected to a Dean-Stark water separator[2] which is attached to a reflux condenser, and the solvent is caused to reflux until no more water separates (Note 2). The water separator is then replaced by an 8-in. Vigreux column (Note 3), and the solution is distilled under reduced pressure. After removal of the solvent, the product distils at 92–93°/34 mm. The yield is 31–34 g. (87–95%) of colorless liquid, n_D^{25} 1.5497, n_D^{20} 1.5528.

B. *N-Methyl-*1,2-*diphenylethylamine.* Benzylmagnesium chloride is prepared in a 1-l. three-necked flask as described previously,[3] using 19.5 g. (0.8 gram atom) of magnesium, 92 ml. (102 g., 0.8 mole) of benzyl chloride, and 300 ml. of anhydrous ether. From the dropping funnel a solution of 24.0 g. (0.2 mole) of N-benzylidenemethylamine in 50 ml. of anhydrous ether or benzene (Note 3) is added slowly to the Grignard reagent with stirring. After being stirred at reflux temperature for 2 hours, the mixture is cooled and poured slowly into a mixture of ice and 200 ml. of concentrated hydrochloric acid. The layers are separated, the ether layer is extracted with 100 ml. of water, and the ether solution is discarded. The aqueous layer and water extract are combined, washed with 100 ml. of ether, and made strongly basic with about 600 ml. of 20% aqueous sodium hydroxide solution. The aqueous suspension of magnesium hydroxide is extracted with 800 ml. of ether in a continuous extractor for 48 hours. The ether extract is washed with about 150 ml. of water and dried over anhydrous potassium carbonate. The solution is filtered from the drying agent, the solvent is removed by distillation on a steam bath, and the residue is distilled from a Claisen flask under reduced pressure. The product distils at 83–90°/0.04 mm., 90–93°/0.2 mm., 94–97°/0.3 mm. The yield is 38.4–40.5 g. (91–96%) of colorless liquid, n_D^{25} 1.5640, n_D^{20} 1.5667.

C. *N-Methyl*-1,2-*diphenylethylamine hydrochloride.* Hydrogen chloride gas (Note 4) is passed into a stirred solution of 30 g. (0.14 mole) of N-methyl-1,2-diphenylethylamine in 500 ml. of anhydrous ether until saturated or until a drop of the ether on moistened *p*H test paper indicates that it is strongly acid. The hydrochloride separates as a colorless crystalline precipitate. It is collected on a suction filter, washed with ether, and dried. The yield is 34.2-35.1 g. (97.5–100%), and the product is practically pure, m.p. 184–186°. If desired it can be recrystallized by dissolution in a little methanol followed by addition of absolute ether.

2. Notes

1. Methylamine is most conveniently obtained commercially in cylinders. However, it can be generated by adding 50% aqueous sodium hydroxide solution dropwise to a flask containing the hydrochloride, and allowing the amine to distil. It can also be generated by allowing an aqueous solution of methylamine to drop into a flask containing solid sodium or potassium hydroxide. The methylamine is distilled directly below the surface of a weighed quantity of benzene kept just above its freezing point. The resulting solution is reweighed to determine the concentration, or an aliquot can be titrated with standard acid.

2. The collection of the theoretical amount of water (about 5.4 ml.) requires approximately 3 hours.

3. For the preparation of N-methyl-1,2-diphenylethylamine it is not absolutely necessary to distil the N-benzylidenemethylamine. The dried benzene solution can be used directly.

4. Hydrogen chloride gas is most conveniently obtained in a cylinder which should be connected to the outlet tube through a safety trap. It can be generated if desired.[4]

3. Methods of Preparation

The only practical method for preparing N-benzylidenemethylamine is by the reaction of benzaldehyde with methylamine.[5–7]

N-Methyl-1,2-diphenylethylamine has been prepared in 8% yield by the Leuckart reaction from desoxybenzoin and methylammonium formate [8] and by the present method.[9]

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[1] The Upjohn Company, Kalamazoo, Michigan.

[2] *Org. Syntheses*, **23**, 38 (1943).

[3] *Org. Syntheses* Coll. Vol. **1**, 471 (1941).

[4] *Org. Syntheses* Coll. Vol. **1**, 293, 534 (1941).

[5] Zaunschirm, *Ann.*, **245**, 279 (1888).

[6] Kindler, *Ann.*, **431**, 187 (1923).

[7] Campbell, Helbing, Florkowski, and Campbell, *J. Am. Chem. Soc.*, **70**, 3868 (1948).

[8] Goodson, Wiegand, and Splitter, *J. Am. Chem. Soc.*, **68**, 2174 (1946).

[9] Moffett and Hoehn, *J. Am. Chem. Soc.*, **69**, 1792 (1947).

METHYLISOUREA HYDROCHLORIDE

(Pseudourea, 2-methyl-, hydrochloride)

$$CaNCN + 2CH_3CO_2H \rightarrow NH_2CN + Ca(O_2CCH_3)_2$$

$$NH_2CN + CH_3OH + HCl \rightarrow NH_2C(OCH_3)NH \cdot HCl$$

Submitted by Frederick Kurzer and Alexander Lawson.[1]
Checked by William S. Johnson and William T. Tsatsos.

1. Procedure

A. *Cyanamide.* In a large mortar are placed 57 g. (54 ml., 0.95 mole) (Note 1) of glacial acetic acid and 46 ml. of water (Note 2). To this solution, 40 g. (0.5 mole) of calcium cyanamide (Note 3) is slowly added (Note 4) with good stirring and grinding. As the introduction of the calcium cyanamide proceeds, small quantities of acetylene are evolved, while the initially thin cream gradually turns into a thick, dark gray to black paste. The mixture must remain acidic to litmus throughout the addition. After being dried at 50–55° for 4–9 hours the material forms a pale gray, perfectly dry powder. This is exhaustively extracted in a Soxhlet apparatus, for 2- to 3-hour periods, with two successive 400-ml. portions of ether (Note 5) containing a few drops of dilute acetic acid. The ethereal extracts (Note 6) are each dried over 30-g.

portions of anhydrous sodium sulfate and combined, and the solvent is removed under reduced pressure (Note 7). The colorless, viscous, oily residue of cyanamide is suitable for use in the next stage. The yield of cyanamide is 10.5–15.8 g. (50–75% calculated on the basis of formula CaNCN) (Notes 8 and 9). Cyanamide may be crystallized by dissolution in 2 parts of benzene and dilution with 1 part of ether.

B. *Methylisourea hydrochloride.* The cyanamide obtained as described above (part A) is taken up in 100 ml. of anhydrous methanol, and the clear solution is decanted from a trace of insoluble oily material if necessary. Anhydrous hydrogen chloride is passed into the clear colorless liquid until an increase in weight amounting to 1 g. of hydrogen chloride per gram of crude cyanamide (1.15 moles) is attained. During the addition of the hydrogen chloride, the cyanamide solution is maintained at room temperature by external ice-cooling. The resulting clear liquid is set aside for 3–4 days, and the methanol is removed by distillation under reduced pressure. The residual colorless crystalline solid is dried in a vacuum desiccator containing potassium hydroxide and phosphorus pentoxide; it consists of methylisourea hydrochloride. The yield is 1.8–2.1 g. per gram of cyanamide (69–80%) (Note 10).

The material may be crystallized from boiling methanol (1 ml. per gram of crude material) and forms lustrous, colorless, thick, prismatic needles, which melt with decomposition (Notes 11 and 12). They are separated by suction filtration at 0° and quickly rinsed with a very little ice-cold methanol. The product is hygroscopic and is quickly pressed between filter paper, then dried in a vacuum desiccator over phosphorus pentoxide. The filtrates yield a further crop on partial evaporation under reduced pressure, the total recovery of recrystallized material being 85–90% (Note 13).

2. Notes

1. The exact amount of acetic acid required by a particular sample of calcium cyanamide is first determined volumetrically as follows: A weighed sample of calcium cyanamide (approximately 1 g.) is suspended in about 50 ml. of distilled water and titrated with standard hydrochloric acid (preferably of approximately normal strength), using phenolphthalein as indicator. Acid is added until the pink color of the indicator does not reappear within 2–3 minutes. From the results of the titration the amount of acetic acid required is calculated by proportion, a 10% excess being allowed to ensure that the reaction mixture remains acid throughout the experiment.

2. In order to facilitate drying at a later stage, as little water is used as will produce a paste that can still be effectively mixed.

3. Commercial calcium cyanamide (nitrolime), containing carbon and small quantities of calcium carbide, is suitable for this preparation.

4. The addition of the calcium cyanamide to the acid should be slow enough to ensure thorough mixing and to prevent the reaction mixture from becoming hot.

5. The checkers found it desirable to saturate the ether (by shaking) with water before the extraction.

6. Cyanamide may be kept unchanged at 0° in ethereal solution in the presence of traces of acetic acid. The ethereal extracts from several runs of calcium cyanamide may therefore be combined and worked up collectively.

7. Distillation is best carried out from a previously weighed small flask, and the weighed residue of cyanamide is immediately dissolved in methanol for the next stage.

8. The yields of cyanamide from commercial calcium cyanamide vary from sample to sample but do not fluctuate greatly for one particular specimen.

9. This procedure was found satisfactory for preparing 15- to 30-g. batches of cyanamide.

10. This material is satisfactory for most synthetic purposes without further purification.

11. Methylisourea hydrochloride decomposes on heating with evolution of methyl chloride. The decomposition temperature depends on the rate of heating, but reproducible values are obtainable if the rate of heating is controlled. Samples of pure (98–99%) (Note 12) methylisourea hydrochloride, introduced

into the melting-point tube without undue previous exposure to atmospheric moisture, placed in the melting-point bath at 60°, and heated at the rate of 12° per minute, sinter at 118–119° and decompose at 122–124° (the mass moving rapidly up in the melting-point tube).

12. The purity of the crystallized product, determined volumetrically by Volhard's method, exceeds 98%. In this procedure, 10 ml. of a 1% solution of methylisourea hydrochloride is acidified with a few drops of nitric acid and treated with 20 ml. of 0.1 *N* silver nitrate. After removal of the silver chloride by filtration, the excess of the silver nitrate is estimated with 0.1 *N* thiocyanate solution, using ferric alum as indicator. Alternatively, 10-ml. portions of 0.1 *N* silver nitrate, acidified with nitric acid, may be titrated directly with the 1% methylisourea hydrochloride solution in the presence of tartrazine.

Owing to the presence of small quantities of free hydrochloric acid in the crude product, the above procedures are applicable to recrystallized specimens only.

13. Methylisourea hydrochloride may be safely stored over long periods if kept in small, well-stoppered, filled bottles, which are in turn placed in a desiccator.

3. Methods of Preparation

Methylisourea hydrochloride has been prepared by the action of hydrogen chloride on a suspension of silver cyanamide [2] or a solution of cyanamide [3,4] in methanol,[3] and by the action of dimethyl sulfate on urea at 112°.[5] The free base is obtained by treating the salt with powdered potassium hydroxide in a water-ether mixture [3] or with sodium methoxide in methanol.[6]

An alternative laboratory preparation of cyanamide and a selection of references to the literature have appeared in *Inorganic Syntheses*.[7] The present method is that of Werner.[8]

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[1] School of Medicine, University of London, London, England.

[2] Stieglitz and McKee, *Ber.*, **33**, 810 (1900); McKee, *Am. Chem. J.*, **26**, 244 (1901).

[3] Stieglitz and McKee, *Ber.*, **33**, 1517 (1900); McKee, *Am. Chem. J.*, **26**, 245 (1901).

[4] Basterfield and Powell, *Can. J. Research*, **1**, 261 (1929); see also Cox and Raymond, *J. Am. Chem. Soc.*, **63**, 300 (1941).

[5] Werner, *J. Chem. Soc.*, **1914**, 927.

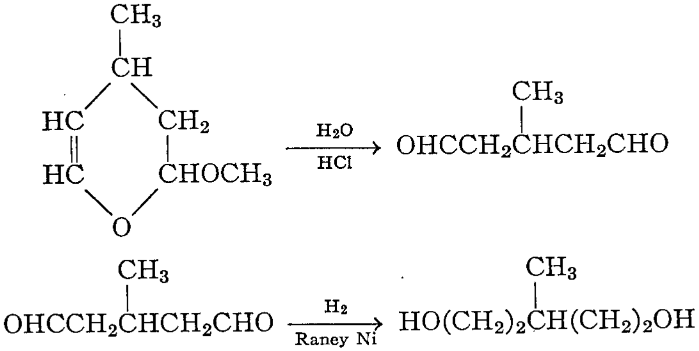
[6] Kapfhammer and Müller, *Z. physiol. Chem.*, **225**, 7 (1934); Rodionov and Urbanskaya, *Zhur. Obshcheĭ Khim.* [*J. Gen. Chem. U.S.S.R.*], 18, 2023 (1948) [*C. A.*, **43**, 3793 (1949)].

[7] Pinck and Salisbury, *Inorg. Syntheses*, **3**, 39 (1950).

[8] Werner, *J. Chem. Soc.*, **1916**, 1325; Werner, *The Chemistry of Urea*, Longmans, London, 1923, p. 184.

3-METHYL-1,5-PENTANEDIOL

(1,5-Pentanediol, 3-methyl-)



Submitted by Raymond I. Longley, Jr., and William S. Emerson.[1]
Checked by T. L. Cairns and John F. Harris, Jr.

1. Procedure

In a 2-l. three-necked flask equipped with a stirrer and thermometer are placed 336 g. (2.62 moles) of 3,4-dihydro-2-methoxy-4-methyl-2H-pyran,[2] 630 ml. of water, and 24 ml. of concentrated hydrochloric acid (sp. gr. 1.19). The mixture is stirred for 2 hours, during which the temperature may reach 50° but should not be permitted to rise higher. Solid sodium bicarbonate is then added until the solution is neutral to *p*H indicator paper (Note 1). The entire reaction mixture weighing about 1 kg. together with 39 g. of Raney nickel [3] is introduced into a 3-l.

stainless-steel rocking hydrogenation autoclave. A hydrogen pressure of at least 1625 p.s.i. (Note 2) is applied, and the autoclave is heated to 125° and held there with shaking for 4 hours. The mixture is allowed to cool overnight, and the catalyst is separated either by suction filtration through Filter-Cel or by centrifugation. The solution is distilled through a 12-in. Vigreux column. After the methanol and water are separated, the 3-methyl-1,5-pentanediol distils at 139–146°/17 mm., 149–150°/25 mm. The yield is 251–256 g. (82–87%), n_D^{25} 1.4521–1.4512.

2. Notes

1. The submitters report that β-methylglutaraldehyde may be isolated at this point from an analogous hydrolysis. The hydrolysis is carried out with 196 g. of 3,4-dihydro-2-methoxy-4-methyl-2H-pyran in 650 ml. of water and 15 ml. of concentrated hydrochloric acid for 3 hours. After neutralization with sodium bicarbonate, the solution is saturated with sodium chloride and extracted continuously with ether for 20 hours. The ether is removed by distillation, and the product is dried thoroughly by azeotropic distillation using a benzene-hexane mixture. Distillation affords β-methylglutaraldehyde, b.p. 85–86°/15 mm., n_D^{25} 1.4307–1.4351. Yields up to 90% have been secured. The aldehyde polymerizes on standing but is stable as a 50% solution in water or ether. The monomer may be recovered by careful destructive distillation of the polymer.

2. The initial hydrogen pressure should be high enough so that it does not fall below 1000 p.s.i. during the shaking period.

3. Methods of Preparation

3-Methyl-1,5-pentanediol has been prepared by the hydrogenation of ethyl β-methylglutarate,[4] by the hydrogenation of ethyl β-methyl-α,γ-dicarbethoxyglutarate,[5] by the hydrogenation of β-methylglutaraldehyde,[6] and by heating 3,4-dihydro-2-methoxy-4-methyl-2H-pyran with water, hydrogen, and copper-chromium oxide or nickel on kieselguhr.[6]

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[1] Central Research Department, Monsanto Chemical Company, Dayton 7, Ohio.

[2] *Org. Syntheses*, **34**, 29 (1954).

[3] *Org. Syntheses*, **21**, 15 (1941).

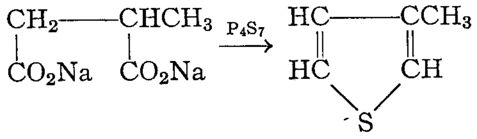
[4] Paden and Adkins, *J. Am. Chem. Soc.*, **58**, 2487 (1936).

[5] Wojcik and Adkins, *J. Am. Chem. Soc.*, **55**, 4939 (1933).

[6] Longley, Emerson, and Shafer, *J. Am. Chem. Soc.*, **74**, 2012 (1952).

3-METHYLTHIOPHENE

(Thiophene, 3-methyl-)



Submitted by R. F. Feldkamp and B. F. Tullar.[1]
Checked by Cliff S. Hamilton, Y. H. Wu, and William J. Raich.

1. Procedure

Caution! This preparation should be conducted in a well-ventilated hood to avoid exposure to hydrogen sulfide.

A 1-l. three-necked round-bottomed flask is fitted with a ground-glass-sealed stirrer, an immersed thermometer, a gas inlet tube, an addition funnel (Note 1), and a distilling head, wrapped with asbestos cloth, connected to a condenser arranged for distillation. The flask is charged with 150 ml. of mineral oil (Note 2), and the system is thoroughly swept out with a slow stream of carbon dioxide admitted through the gas inlet tube while the flask is heated with an electric heating mantle. When the temperature of the oil reaches 240–250°, a slurry of 90 g. (0.51 mole) of powdered anhydrous disodium methylsuccinate (Note 3) and 100 g. (0.287 mole) of phosphorus heptasulfide (Note 4) in 250 ml. of mineral oil is placed in the addition funnel. With efficient stirring and a slow continuous stream of carbon dioxide passing through the system, the slurry is added to the hot mineral oil at such a rate as to effect fairly rapid distillation of 3-methylthiophene accompanied by considerable gas evolution (mostly hydrogen sulfide). During the addition, which requires about 1 hour, the temperature is maintained at 240–250° (Note 5). The temperature is then raised to 275° and stirring continued in the inert atmosphere for an additional hour or until distillation ceases. The total distillate, amounting to 33–38 ml., is washed with two 50-ml. portions of 5% sodium hydroxide solution and finally with 50 ml. of water (Note 6). The crude 3-methylthiophene is then distilled (Note 7). A small fore-run is discarded, and the fraction boiling between 112° and 115° is collected. The yield is 26–30 g. (52–60%), n_D^{25} 1.5170 ± 0.0005 (Notes 8, 9, and 10).

2. Notes

1. A gravity funnel fitted with a glass rod of suitable diameter is satisfactory for regulating the addition of the slurry.

2. Dowtherm A may also be used as a solvent for this reaction. However, because the boiling point (about 265°) is close to the reaction temperature, considerable quantities of Dowtherm distil along with the 3-methylthiophene. The total distillate amounts to 60–75 ml., which after washing and fractionally distilling gives the same yield as with mineral oil. Dowtherm gives a more fluid slurry and final residue and can be easily recovered by distillation at reduced pressure.

3. Disodium methylsuccinate was made by hydrogenating a concentrated solution of itaconic acid supplied by Chas. Pfizer and Company in aqueous sodium hydroxide (*p*H 8.7) over Raney nickel catalyst at 50 p.s.i. and 80–100°. After the catalyst was removed by filtration, the product was isolated by evaporation of the water and the residue was dried in a vacuum oven at 70–80°.

4. Phosphorus heptasulfide was obtained from the Oldbury Electrochemical Company. It has been shown [2] that the "phosphorus trisulfide" used by earlier workers for such fusions was actually somewhat impure phosphorus heptasulfide.

5. The rate of addition of the slurry and the reaction temperature should be carefully controlled. About two-thirds of the crude 3-methylthiophene distillate is collected during the addition of the slurry. Further heating at 260–275° gives the remainder of the material.

6. An emulsion may be obtained on further washing with water. A small amount of sodium chloride (2–3 g.) dissolved in the wash water assists in breaking such emulsions.

7. Rather violent foaming may occur during this distillation but is easily controlled in a 250-ml. flask. The distilling head and flask may be wrapped in asbestos cloth in order to increase the speed of distillation.

8. When fresh mineral oil was used (first run), a yield of 52–54% was obtained. However, when the recovered mineral oil (Note 9) was used, the yield increased to 60%.

9. The reaction residue is allowed to cool to room temperature and is filtered by suction. The dark mineral oil filtrate may be reused in the process. The malodorous filter cake is not pyrophoric and is almost completely soluble in water or dilute alkali with liberation of hydrogen sulfide.

10. The submitters obtained comparable yields on twice the scale described. They also applied the same procedure to disodium succinate to give a 25% yield of thiophene comparable to the yield obtained by dry fusion.[3]

3. Methods of Preparation

3-Methylthiophene has been prepared by the dry fusion of a salt of methylsuccinic acid and phosphorus "trisulfide."[4] This reaction was later investigated quite completely in respect to ratio of reactants, rate of heating, carbon dioxide atmosphere, and dilution of reactants with sand.[5] An excellent technical method for preparing methylthiophenes has been described which involves a vapor-phase reaction of preheated sulfur with pentanes.[6] 3-Methylthiophene has also been prepared by adding 50% crude isoprene (amylenes) to molten sulfur at 350°.[7]

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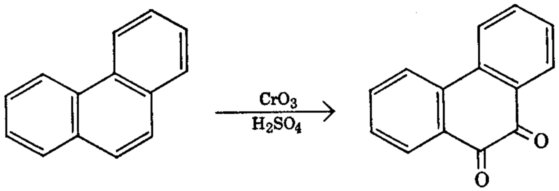
[1] Sterling-Winthrop Research Institute, Rensselaer, New York.

[2] *Chem. and Eng. News*, **27**, 2143 (1949).

[3] *Org. Syntheses* Coll. Vol. **2**, 578 (1943).

[4] Volhard and Erdmann, *Ber.*, **18**, 454 (1885).
[5] Linstead, Noble, and Wright, *J. Chem. Soc.*, **1937**, 915.
[6] Rasmussen and Hansford, U. S. pat. 2,450,686 [*C. A.*, **43**, 1067 (1949)].
[7] Shepard, Henne, and Midgley, Jr., *J. Am. Chem. Soc.*, **56**, 1355 (1934).

PHENANTHRENEQUINONE



Submitted by Ray Wendland and John LaLonde.[1]
Checked by William S. Johnson and Sol Shulman.

1. Procedure

In a 3-l. three-necked flask equipped with a reflux condenser, a sealed mechanical stirrer, and a 1-l. dropping funnel, are placed 100 g. (0.56 mole) of phenanthrene (Note 1), 210 g. (2.1 moles) of chromic acid (Note 2), and 1-l. of water. The stirrer is started, and 450 ml. of concentrated sulfuric acid is added from the dropping funnel into the suspension at such a rate that gentle boiling is induced (Note 3). After addition of the sulfuric acid is complete, a mixture of 210 g. (2.1 moles) of chromic acid and 500 ml. of water is added carefully to the reaction mixture from the dropping funnel (Note 4). The resulting mixture is boiled under reflux for 20 minutes.

After being cooled to room temperature the reaction mixture is poured into an equal volume of water and chilled to 10° in an ice bath. The crude precipitate is separated by suction filtration and thoroughly washed with cold water until the washings no longer show any chrome green color. The precipitate is triturated with three 300-ml. portions of boiling water and filtered to remove the diphenic acid formed in the reaction. The precipitate is then triturated with several (4–6) 300-ml. portions of hot 40% sodium

bisulfite solution and again filtered (Note 5). The insoluble material is a mixture of anthraquinone and some resinous products derived from anthracene and other contaminants present in the starting material (Note 6). The sodium bisulfite filtrates are combined and cooled to 5° in an ice bath. The precipitate which separates is collected by suction filtration; then it is transferred to a 1-l. beaker and finely dispersed in 300 ml. of water. To this suspension is added, with good stirring, 500 ml. of a saturated solution of sodium carbonate. The deep orange phenanthrenequinone which is liberated is separated by suction filtration (Note 7), washed well with cold water, and dried on a porcelain plate. The yield of product, melting at 205–208° cor., is 52–56 g. (44–48%). Further purification may be accomplished by crystallization from 95% ethanol (100 ml./g.). The recovery of first-crop material is over 80%, m.p. 208.5–210° cor.

2. Notes

1. Reilly Tar and Chemical Company practical grade phenanthrene is crystallized from boiling toluene using Norit. One crystallization is sufficient to produce material melting at about 99.5°. The checkers employed Eastman Kodak Company technical grade (90%) phenanthrene.
2. Technical grade chromic acid (99.5% CrO_3) in flake form was used.
3. It is safe to add 100 ml. of acid all at once to start the oxidation, but as soon as the temperature rises to 70–75° the remainder must be added slowly in order to avoid violent boiling.
4. One-half (250 ml.) of the mixture is added carefully (the reaction may become vigorous at this stage), and 20–25 minutes is allowed for the oxidation to proceed spontaneously. The remaining mixture is then added slowly.
5. A heated Büchner funnel is preferably used to prevent clogging by crystallization.
6. The anthraquinone may be purified by extracting the insoluble material with a 150-ml. solution of potassium hydroxide and sodium hydrosulfite (approximately 10% by weight of each).

The resulting red solution is quickly filtered by suction, and hydrogen peroxide is added to the filtrate until a yellow precipitate appears. Dilute hydrochloric acid is added until the mixture is acidic to litmus, and the precipitate is collected by suction filtration, washed well with water, and air-dried. Five to seven grams of anthraquinone, m.p. 280–283°, may thus be obtained.

7. The filtrate should be treated with more sodium carbonate to test for completeness of precipitation.

3. Methods of Preparation

Phenanthrenequinone has been prepared by treatment of phenanthrene with chromic acid in acetic acid;[2] potassium dichromate in sulfuric acid;[3–5] hydrogen peroxide in acetic acid;[6, 7] and selenium dioxide above 250°.[8] It can also be prepared from benzil with aluminum chloride at 120°[9] and from biphenyl-2,2′-dialdehyde with potassium cyanide.[10]

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[1] North Dakota State College, Fargo, North Dakota.

[2] Graebe, *Ann.*, **167**, 131 (1873).

[3] Anschütz and Schultz, *Ann.*, **196**, 32 (1879).

[4] Oyster and Adkins, *J. Am. Chem. Soc.*, **43**, 208 (1921).

[5] Underwood and Kochmann, *J. Am. Chem. Soc.*, **46**, 2069 (1924).

[6] Henderson and Boyd, *J. Chem. Soc.*, **1910**, 1659.

[7] Charrier and Moggi, *Gazz. chim. ital.*, **57**, 736 (1927).

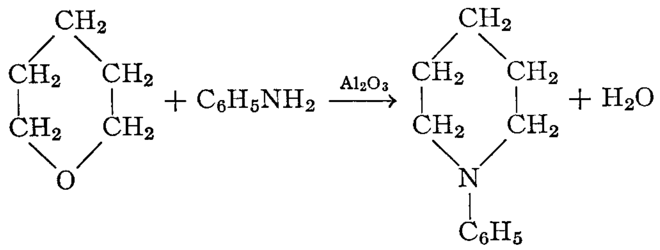
[8] Postowsky and Lugowkin, *Ber.*, **68**, 852 (1935).

[9] Scholl and Schwarzer, *Ber.*, **55**, 324 (1922).

[10] Mayer, *Ber.*, **45**, 1105 (1912).

1-PHENYLPIPERIDINE

(Piperidine, 1-phenyl)



Submitted by A. N. Bourns, H. W. Embleton, and Mary K. Hansuld.[1]
Checked by R. T. Arnold, William E. Parham, and Carl Serres.

1. Procedure

The apparatus (Fig. 4) consists of a reaction tube, 100 cm. long and 3 cm. in diameter, provided with an inlet tube to which a graduated dropping funnel is connected. The lower end of the reaction tube is fitted with a Friedrich condenser and receiver. A thermocouple well, concentric with the reaction tube is passed through the upper end by means of a standard ground-glass joint. The tube is packed with 200 ml. of 4- to 8-mesh alumina

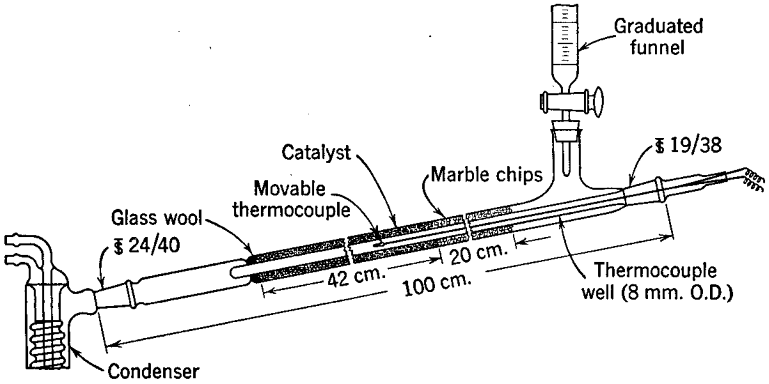


Fig. 4.

(Note 1) held in place by a plug of glass wool supported by indentations in the tube, followed by 100 ml. of marble chips which serve as a vaporizer and preheater for the reactants. The reaction tube is supported in an electrically heated furnace (Note 2) extending from the inlet tube to the joint connecting the condenser.

The reaction tube is heated to 330–340° (Note 3) and is swept out with a stream of nitrogen gas. A solution of 258 g. (3 mole) of tetrahydropyran (Note 4) and 559 g. (6 mole) of aniline is then placed in the graduated funnel and introduced into the reaction tube at a rate of 90–100 ml. per hour. The product, which is collected in a 1-l. flask containing 10 g. of sodium chloride, consists of a light-yellow oil and a lower aqueous layer. After the addition of the reactants is complete, a slow stream of nitrogen is passed through the reaction tube for 20–30 minutes to remove any product adsorbed on the catalyst. The lower aqueous layer is separated and discarded, and the upper organic layer is dried over sodium hydroxide pellets. The product is fractionated under reduced pressure using a Whitmore-Lux column [2] (Note 5) only to remove the small amount of unchanged tetrahydropyran and excess aniline. The column is permitted to drain, and the residue is distilled from an ordinary Claisen flask under reduced pressure. 1-Phenylpiperidine is obtained as a colorless or very light-yellow liquid, b.p. 123–126°/12.5 mm., 133–136°/21 mm., n_D^{25} 1.5603. The yield is 403–435 g. (83–90% based on tetrahydropyran) (Note 6).

2. Notes

1. The catalyst employed was Alcoa Activated Alumina (Grade F-1, 4- to 8-mesh) from the Aluminum Company of America. A fresh catalyst is brought to a condition of maximum activity by passing a slow stream of air through the catalyst bed for 94 hours at 390–405°. Without this pretreatment, yields are 5–10% lower than those reported here. The catalyst is reactivated after each run by passing air through it for 39 hours at 390–405°.

2. The furnace may be of the construction described in a previous volume.[3] It is desirable, although not essential, to provide separately controlled heating elements for each of the two packed zones of the reaction tube.

3. The temperature of the furnace is measured by a thermocouple which can be moved to various positions in the thermocouple well. The catalyst temperature should be maintained at 325–345°, although it may be as low as 320° at the ends of the catalyst zone, depending unon the construction of the furnace.

4. Eastman Kodak Company practical grade tetrahydropyran may be used without purification.

5. A column of equivalent efficiency may be employed.

6. 1-*m*-Tolylpiperidine (b.p. 141–143°/16 mm., n_D^{25} 1.5535) and 1-*p*-tolylpiperidine (b.p. 140–143°/15 mm., n_D^{25} 1.5509) may be prepared in 85–90% yield by a similar procedure. 1-*o*-Tolylpiperidine (b.p. 123–125°/15 mm., n_D^{25} 1.5391) is obtained in 60% yield under similar reaction conditions, but it is necessary to fractionate the product in order to obtain pure material.

3. Methods of Preparation

1-Phenylpiperidine has been prepared by warming aniline with 1,5-dibromopentane; [4,5] heating 5-anilino-1-bromopentane; [6] the dehydration of 5-anilino-1-pentanol over alumina; [7] the electrolytic reduction of N-phenylglutarimide; [8] the catalytic hydrogenation of 1-phenyl-3-hydroxypyridinium chloride; [9] the action of bromobenzene on piperidine in the presence of lithium; [10] the reaction of fluorobenzene, 1-methylpiperidine, and phenyllithium; [11] the action of diphenylsulfone on piperidine in the presence of sodamide;[12] the diazotization and deamination of 1-(2-aminophenyl)piperidine [13] and of 1-(4-aminophenyl)piperidine; [14] and the present method.[15]

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[1] Department of Chemistry, Hamilton College, Hamilton, Ontario.

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

[3] *Org. Syntheses*, **22**, 41 (1942).

[4] von Braun, *Ber.*, **37**, 3212 (1904).

[5] Paul, *Bull. soc. chim. France*, **53**, 1489 (1933).

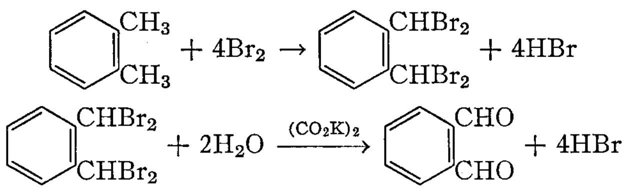
[6] von Braun, *Ber.*, **40**, 3920 (1907).

[7] Scriabine, *Bull. soc. chim. France*, **1947**, 454.

[8] Sakurai, *Bull. Chem. Soc. Japan*, **13**, 482 (1938).

[9] Koelsch and Carney, *J. Am. Chem. Soc.*, **72**, 2285 (1950).
[10] Horning and Bergstrom, *J. Am. Chem. Soc.*, **67**, 2110 (1945).
[11] Wittig and Merkle, *Ber.*, **76B**, 109 (1943).
[12] Bradley, *J. Chem. Soc.*, **1938**, 458.
[13] Le Fevre, *J. Chem. Soc.*, **1932**, 1376.
[14] Lellmann and Geller, *Ber.*, **21**, 2279 (1888).
[15] Bourns, Embleton, and Hansuld, *Can. J. Chem.*, **30**, 1 (1952).

o-PHTHALALDEHYDE



Submitted by J. C. Bill and D. S. Tarbell.[1]
Checked by Arthur C. Cope and Harris E. Petree.

1. Procedure

Caution! This preparation should be conducted in a hood, and rubber gloves should be worn, to avoid exposure to bromine as well as the by-product o-xylylene dibromide which is a lachrymator and skin irritant.

A. *α,α,α′,α′-Tetrabromo-o-xylene.* In a 2-l. three-necked flask equipped with an oil-lubricated Trubore stirrer, a dropping funnel, a thermometer extending nearly to the bottom of the flask, and a reflux condenser (Note 1) attached to a gas absorption trap [2] is placed 117 g. (1.1 moles) of dry *o*-xylene (Note 2). An ultraviolet lamp such as a General Electric R.S. Reflector Type 275-watt sun lamp is placed about 1 cm. from the flask so as to admit the maximum amount of light. The stirrer is started, and the *o*-xylene is heated to 120° with an electric heating mantle. A total of 700 g. (4.4 moles) of bromine (N.F. grade) is added in portions from the dropping funnel to the reaction flask at such a rate that the bromine color is removed as fast as it is added. After approximately one-half of the bromine has been added, the temperature is slowly increased to 175° for the remainder of the addition; the mixture becomes very dark toward the end of the reaction. The bromine can be added rapidly at first, but toward the end it must not be added at a rate exceeding 4–5 drops per minute in order to avoid loss of a visible amount of bromine with the evolved hydrogen bromide. After all the bromine has been added (10–14 hours), the mixture is illuminated and stirred at 170° for 1 hour. After removal of the stirrer, etc., the mixture is cooled and allowed to stand overnight to crystallize in the reaction flask exposed to the air.

The dark, solid tetrabromide is dissolved in 2 l. of hot chloroform (Note 3) and treated with 100 g. of 325-mesh Norit. The mixture is filtered with slight suction, the Norit is washed with hot chloroform, and the Norit treatment is repeated. The tan-colored filtrate from the second Norit treatment is concentrated to 250–300 ml. by distillation under reduced pressure and chilled to 0°. The solid product is collected on a cold Büchner funnel and washed with a small amount of cold chloroform. The filtrate is concentrated further and cooled to obtain a second crop of crystals, which is purified by recrystallization from chloroform. The yield of the tetrabromide obtained from the first crop (white) and second crop after recrystallization (light tan) is 344–370 g. (74–80%), m.p. 115–116°.

B. *o-Phthalaldehyde.* The α,α,α′,α′-tetrabromo-*o*-xylene (344–370 g.) obtained as described above, part A, is placed in a 5-l. round-bottomed flask with 4 l. of 50% (by volume) ethanol and 275 g. of potassium oxalate. The mixture is heated under reflux for 50 hours (a clear yellow solution is formed after 25–30 hours). About 1750 ml. of the ethanol is then removed by distillation (which is stopped before the product begins to steam-distil), and 700 g. of disodium monohydrogen phosphate dodecahydrate ($Na_2HPO_4 \cdot 12H_2O$) is added to the aqueous residue. The mixture is steam-distilled rapidly (Note 4), using an efficient condenser, until 10–12 l. of distillate is collected and the distillate no longer gives a black color test for *o*-phthalaldehyde [3] when a portion is treated with concentrated ammonium hydroxide followed by glacial acetic acid. The distillate is then saturated with sodium sulfate at room temperature and divided into portions of approximately 4 l.; each portion is extracted first with 200 ml. and then with six 100-ml. portions of ethyl acetate. The combined ethyl acetate extracts are dried over anhydrous sodium sulfate, filtered, and concentrated under reduced pressure. The residue is crystallized from 90–100° ligroin, and a second crop is obtained by concentration of the mother liquor. The total yield of *o*-phthalaldehyde, m.p. 55.5–56°, is 87–94 g. (74–80% based on the tetrabromide, or 59–64% based on *o*-xylene).

2. Notes

1. Best results are obtained if an all-glass apparatus with ground-glass connections is used, as noted by Wawzonek and Karll.[4]

2. Pure commercial *o*-xylene (99% or higher purity) is dried by distillation until the distillate shows no further turbidity, and the residue is used.

3. The chloroform is allowed to stand over anhydrous calcium chloride overnight to remove water and ethanol.

4. The submitters state that the steam distillation is much more efficient if superheated (175–180°) steam is used, in which case special care must be taken to condense all the distillate.

3. Methods of Preparation

o-Phthalaldehyde has been made by the action of potassium hydroxide on *o*-(dichloromethyl)benzaldehyde,[5] by the hydrolysis of $\alpha,\alpha,\alpha',\alpha'$-tetrachloro-*o*-xylene,[6] and by the hydrolysis of the $\alpha,\alpha,\alpha',\alpha'$-tetraacetate of *o*-phthalaldehyde.[3] The present method is essentially that of Thiele and Günther.[7,8] Hydrolysis of the tetrabromide may also be carried out by treatment with fuming sulfuric acid followed by water.[9] For small-scale preparations of *o*-phthalaldehyde the reduction of N,N,N′,N′-tetramethylphthalamide with lithium aluminum hydride is the method of preference.[10]

[1] University of Rochester, Rochester, New York.

[2] *Org. Syntheses* Coll. Vol. **2**, 4 (1943).

[3] Thiele and Winter, *Ann.*, **311**, 360 (1900).

[4] Wawzonek and Karll, *J. Am. Chem. Soc.*, **70**, 1666 (1948).

[5] Chaudhuri, *J. Am. Chem. Soc.*, **64**, 315 (1942).

[6] Colson and Gautier, *Ann. chim.* (*Paris*), **6**, 11, 28 (1887).

[7] Thiele and Günther, *Ann.*, **347**, 107 (1906).

[8] Cope and Fenton, *J. Am. Chem. Soc.*, **73**, 1672 (1951).

[9] Weygand, Vogelbach, and Zimmermann, *Chem. Ber.*, **80**, 396 (1947).

[10] Weygand and Tietjen, *Chem. Ber.*, **84**, 625 (1951).

SODIUM β-STYRENESULFONATE AND β-STYRENESULFONYL CHLORIDE

(Ethylenesulfonyl chloride, 2-phenyl-)

$$C_6H_5CH{=}CH_2 + \text{dioxane}\cdot SO_3 \rightarrow C_6H_5CH{=}CHSO_3H$$

$$C_6H_5CH{=}CHSO_3H + NaOH \rightarrow C_6H_5CH{=}CHSO_3Na + H_2O$$

$$C_6H_5CH{=}CHSO_3Na + PCl_5 \rightarrow C_6H_5CH{=}CHSO_2Cl + POCl_3 + NaCl$$

Submitted by Christian S. Rondestvedt, Jr., and F. G. Bordwell.[1]
Checked by T. L. Cairns and H. E. Winberg.

1. Procedure

A. *Sodium β-styrenesulfonate.* In a 3-l. three-necked flask, equipped with a drying tube, a sealed stirrer, and a ground-glass stopper, is placed 800 ml. of ethylene chloride (Note 1). The flask with fittings is weighed and then connected through the third neck to a sulfur trioxide distillation apparatus (Note 2). Sulfur trioxide is distilled into the flask until about 300 g. has been collected. During the distillation the flask is cooled with a large pan of cold water (Note 3). The distillation is stopped, the condenser is disconnected and replaced by the glass stopper, and the flask is again weighed.

The stopper is replaced by a thermometer, and the other side neck is equipped with a two-way adapter to hold a dropping funnel and a drying tube. The sulfur trioxide solution is cooled below −5° with an ice-salt bath, then an amount of dioxane (Note 4) equivalent to the sulfur trioxide is added slowly with vigorous stirring at such a rate that the temperature does not exceed 5° (Note 5).

One molar equivalent of styrene (Note 6) dissolved in 2 volumes of ethylene chloride is added with stirring to the suspension of dioxane sulfotrioxide. The temperature is maintained below 10° during the hour required for addition, during which the suspension of colorless solid changes to a milky tan solution. The cooling bath is removed, and stirring is continued for an additional hour. After standing overnight, the nearly clear yellow solution is heated under reflux for 2 hours on the steam bath. The solution, now dark brown, is allowed to cool, poured into 3 l. of ice water, and stirred or shaken to ensure transfer of the sulfonic acid to the water (Note 7). The emulsion is neutralized with sodium hydroxide solution (Note 8), the layers are separated, and the aqueous phase is extracted with two 500-ml. portions of isopropyl ether (Note 9).

Several crops of crystals are now taken by evaporating the aqueous solution to the saturation point on a hot plate with stirring, then cooling. Each crop is dried for 2 hours at 100° and analyzed for unsaturation by the bromate-bromide titration method (Note 10). The first two crops usually total about 380 g. (based on 300 g. of sulfur trioxide), 49% yield, and are about 95% pure by titration. They may be further purified by one recrystallization from water, with about 80% recovery of 99+% pure salt.

The third crop generally weighs about 100 g. and is about 80% pure; the fourth crop weighs about 75 g., and is about 60% pure (Note 11). For purification, the third crop is recrystallized from the mother liquor resulting from the recrystallization of the combined first and second crops; the fourth crop is recrystallized from the third-crop mother liquor. An additional recrystallization from water is usually required to obtain material of 95 + % purity.

The total weight of 95+% pure sodium β-styrenesulfonate from 300 g. of sulfur trioxide is 450–500 g. (58–65% yield) (Notes 12 and 13).

B. *β-Styrenesulfonyl chloride.* One hundred grams of dry sodium β-styrenesulfonate (Note 14) is placed in a 500-ml. round-bottomed flask and thoroughly mixed with 120 g. of powdered phosphorus pentachloride with vigorous shaking. The flask is attached to a reflux condenser capped with a drying tube and heated on the steam bath until the reaction mixture liquefies, then for an additional 4 hours. The phosphorus oxychloride is removed by distillation at reduced pressure (water aspirator) on the steam bath. The semisolid residue is extracted three times by boiling for 15 minutes with 100-ml. portions of chloroform. The residue in the flask is dissolved in 200 ml. of ice water and extracted with 100 ml. of chloroform. The combined chloroform solutions are washed with 200 ml. of water, two 100-ml. portions of 5% sodium bicarbonate, and finally with 100 ml. of water. After drying for 2 hours over calcium chloride, the solution is treated with 3 g. of Norit, filtered, and concentrated to 150 ml., and 200 ml. of 60–68° petroleum ether is added. On cooling, 81–86 g. (83–88% yield) of β-styrenesulfonyl chloride separates as colorless needles, m.p. 88–90°. Recrystallization raises the melting point to 89–90° (Notes 15, 16, and 17).

2. Notes

1. A good grade of ethylene chloride is dried by slowly distilling a portion and rejecting the wet fore-run. Technical grade material should be carefully fractionated before use; the fraction boiling at 82.6–82.8° gives excellent results.

2. The apparatus for distillation of sulfur trioxide is constructed from a 500-ml. round-bottomed flask, connected by a ground joint to a 6-in. section of 20-mm. glass tubing. A safety tube (8-mm. tubing) reaching to the bottom of the flask is attached at the top by means of a ground joint; it is convenient to bend the top of the tube so that any acid drip can be caught in a beaker. A side arm, sealed in near the top of the wide tube, leads through a ground joint to an air condenser consisting of a 30-in. length of 12-mm. tubing, which terminates in a ground joint (with a drip tip) to fit the reaction flask. It is imperative

that the apparatus be all glass, since sulfur trioxide rapidly attacks rubber or cork connections.

Sulfur trioxide is distilled by heating 60% fuming sulfuric acid contained in the flask. Spent acid may be fortified with "Sulfan B," stabilized liquid sulfur trioxide obtainable from the General Chemical Company, 40 Rector St., New York. Undiluted Sulfan B solidifies in the flask after a few heatings, and subsequent reheating may be dangerous.

3. Only slight cooling is needed at this stage. Stirring may be intermittent, if more convenient. If the sulfur trioxide solidifies above the level of the ethylene chloride from excessive cooling, it may easily be melted by warming the flask with a soft flame.

4. Dioxane is purified by refluxing for 12 hours with an excess of sodium, then distilling. The fraction boiling at 99.6–99.8° is collected and stored over calcium chloride or, preferably, calcium hydride.

5. If the temperature is allowed to rise much above 5°, charring results and the product is discolored. A Dry Ice bath may be used to advantage. The reagent thus prepared should be used within a few hours, since dioxane is slowly attacked by sulfur trioxide.

6. Stabilized styrene of monomeric quality is used directly. The small amount of stabilizer does not interfere with the reaction.

7. In small runs, ether may be used to break the emulsion, thus permitting the separation of the layers before neutralization. In large runs, excessively large amounts of ether are required and it is preferable to neutralize first.

8. Methyl red serves as a convenient indicator. Slightly more than 1 mole of sodium hydroxide is required per mole of sulfur trioxide. Other metal salts can be prepared, using a suitable hydroxide or carbonate for the neutralization.

9. Ethyl ether may be substituted, but its greater water solubility is a disadvantage. Evaporation of the combined organic layers at reduced pressure below 40° leaves a residue of about 5% (based on sulfur trioxide) of 2,4-diphenylbutane-1,4-sultone, which may be purified (60% recovery) by recrystallization from acetone-water; m.p. 147–149°. The yield of sultone may be increased to about 25% of pure material by using 3 moles of styrene per mole of sulfur trioxide.

10. A sample (approximately 0.2 g.) is weighed accurately and dissolved in 25 ml. of water; then 25 ml. of 0.1 *N* hydrochloric acid and 0.2 g. of potassium bromide are added. The solution is titrated with 0.017 *M* potassium bromate until a permanent yellow color is produced. Potassium iodide (0.1 g.) is added, and the solution is backtitrated to a starch end point with 0.1 *N* sodium thiosulfate. The blue color returns in about a minute since the high acidity promotes air oxidation of excess iodide. The accuracy is only slightly less if the appearance of a faint yellow bromine color is taken as the end point. One mole of potassium bromate is equivalent to 3 of sodium β-styrenesulfonate.

11. Further crops may be taken, but the recovery of pure material from them is not worth the time required. They consist mainly of sodium 2-phenyl-2-hydroxyethane-1-sulfonate along with some sodium sulfate.

12. The procedure may be modified to prepare sodium 2-phenyl-2-hydroxyethane-1-sulfonate. The temperature during the addition of styrene is maintained below 0°. After 30 minutes of additional stirring at 0°, the mixture is hydrolyzed in ice water without heating. The crops of salts are analyzed, and those that are low in unsaturation are recrystallized from 70% aqueous ethanol. The more unsaturated crops are recrystallized from the mother liquors. The yield is 45–50% of material with less than 5% unsaturation.

13. Since the sodium sulfonates have no definite melting points, they may be converted to crystalline benzylthiuronium, *p*-chlorobenzylthiuronium, aniline, or *p*-toluidine salts for characterization.[2]

14. The salt is dried at 100° for 4 hours, then powdered.

15. An additional 6–7 g. of product, m.p. 88–89°, may be obtained by evaporation of the mother liquors and distillation of the residue as rapidly as possible at 2 mm. (bath temperature 120–140°). The total yield is thus 88–92%; in smaller runs,

yields up to 96% are frequently obtained. Large batches cannot be distilled satisfactorily.

16. Carbon tetrachloride may also be used as a recrystallization solvent. The product should be stored in a tightly closed brown bottle to retard its slow decomposition.

17. The checkers used one-third quantities throughout both parts of this preparation with comparable results.

3. Methods of Preparation

Salts of β-styrenesulfonic acid have been prepared by the sulfonation of styrene with dioxane sulfotrioxide,[2] by heating styrene with ammonium sulfamate,[3] or by the reaction of styrene with sodium bisulfite in the presence of oxygen.[4]

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[1] Joint contribution from Northwestern University, Evanston, Illinois, and the University of Michigan, Ann Arbor, Michigan.

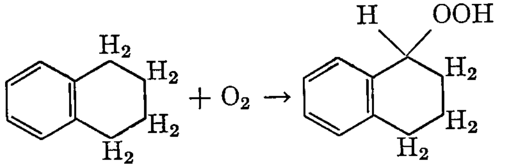
[2] Bordwell, Suter, Holbert, and Rondestvedt, Jr., *J. Am. Chem. Soc.*, **68**, 139 (1946); Bordwell and Rondestvedt, Jr., *J. Am. Chem. Soc.*, **70**, 2429 (1948).

[3] Quilico and Fleischner, *Atti acad. Lincei*, **7**, 1050 (1928) [*C. A.*, **23**, 1628 (1929)].

[4] Kharasch, Schenck, and Mayo, *J. Am. Chem. Soc.*, **61**, 3092 (1939).

TETRALIN HYDROPEROXIDE

[Hydroperoxide, (1,2,3,4-tetrahydro-1-naphthyl)-]



Submitted by H. B. Knight and Daniel Swern.[1]
Checked by John C. Sheehan and Curt W. Beck.

1. Procedure

In a 1-l. round-bottomed three-necked flask, equipped with a thermometer, a reflux condenser, and two fritted-glass gas dispersion tubes (Note 1), is placed 600 g. (4.54 moles) of pure tetralin (Note 2). The flask is placed in a constant-temperature bath at 70°, and a finely dispersed stream of oxygen is passed through the tetralin until the peroxide content of the reaction mixture is 25–30% as shown by an active oxygen content of 2.4–2.9% (Note 3). This oxidation requires 24–48 hours. The reaction mixture is then distilled (Note 4) in an all-glass apparatus at 0.2–0.4 mm. through a 60 by 2.5 cm. Vigreux column, until a pot temperature of 70° is reached. About 370–380 g. of unoxidized tetralin, boiling at 32–45°/0.2–0.4 mm., is recovered. The pot residue is a slightly viscous amber-colored oil which weighs 225–235 g. and consists of about 80% tetralin hydroperoxide (Note 5). To obtain the pure hydroperoxide the residue is dissolved in 450 ml. of toluene and the solution is cooled to −50° with stirring (Note 6). After standing at −50° for 1 hour, the slurry is separated by suction filtration (Note 7) and the precipitate is dried at room temperature at 1–2 mm. There is thus obtained 120–125 g. of moderately pure tetralin hydroperoxide, m.p. 50.2–52.0°, active oxygen content 9.20% (Note 8). Recrystallization from 480 ml. of toluene at −30° yields 80–85 g. (44–57% yield based on the peroxide content of the oxidized tetralin) of pure tetralin hydroperoxide as a colorless solid, m.p. 54.0–54.5°, active oxygen content, 9.70% (Note 9).

2. Notes

1. Rubber connections must be avoided because rubber is rapidly attacked by tetralin. Convenient gas dispersion tubes are Pyrex No. 39533.

2. Pure tetralin was prepared from the practical grade supplied by the Eastman Kodak Company by the procedure of George and Robertson:[2] Three kilograms was fractionally distilled through a packed column, the fraction boiling at 204–207° being retained (2.7 kg). This was gently shaken with 1 lb. of mercury, and the upper layer was carefully decanted through fluted filter paper. The crude tetralin was next shaken with saturated aqueous mercuric acetate solution, and the aqueous layer and a

small amount of orange precipitate were discarded. The hydrocarbon was then shaken with 5 successive 300-ml. portions of concentrated sulfuric acid, once with 10% sodium hydroxide, and finally with water until the washings were neutral. The tetralin was dried over anhydrous calcium chloride and distilled through a packed column in a nitrogen atmosphere. In this way, 2 kg. of pure tetralin was obtained, b.p. 206–207°, n_D^{20} 1.5428.

3. Active oxygen content is determined iodometrically:[3] In an iodine flask, an accurately weighed sample (0.1–0.3 g.) is dissolved in 20 ml. of an acetic acid-chloroform solution (3:2 by volume), and 2 ml. of saturated aqueous potassium iodide solution is added. The flask is immediately flushed with nitrogen, stoppered, and allowed to stand at room temperature for 15 minutes. Fifty milliliters of water is then added with good mixing, and the liberated iodine is titrated with 0.1 *N* sodium thiosulfate, employing starch as indicator. A blank titration, which usually does not exceed 0.2 ml., is also run. One milliliter of 0.1 *N* sodium thiosulfate is equivalent to 0.00821 g. of tetralin hydroperoxide.

4. The distillation should be conducted behind a safety shield.

5. Peroxide loss up to this point is negligible provided an all-glass apparatus has been used throughout and the distillation temperature has not exceeded 70°.

6. A Dry Ice-ethanol bath is convenient for cooling the solution.

7. Filtration may be carried out in a suction funnel surrounded by a Dry Ice-ethanol cooling bath, or using a cold box maintained at −50°.

8. Pure tetralin hydroperoxide has an active oxygen content of 9.74%.

9. Tetralin hydroperoxide is a convenient model compound for many studies in peroxide chemistry. It remains colorless and does not decrease in peroxide content for months if stored in the dark at or below 0°. Storage under warm summer conditions for several months results in decomposition to a dark, viscous liquid.

3. Methods of Preparation

The present procedure is adapted from that reported by Hartmann and Seiberth[4] and Hock and Susemihl.[5] Robertson and Waters[6] employed cobalt naphthenate as a catalyst, but this is not required.

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[1] Eastern Regional Research Laboratory, U. S. Department of Agriculture, Philadelphia, Pennsylvania.

[2] George and Robertson, *Trans. Faraday Soc.*, **42**, 227 (1946).

[3] Wheeler, *J. Am. Oil Chemists' Soc.*, **9**, 89 (1932).

[4] Hartmann and Seiberth, *Helv. Chim. Acta*, **15**, 1390 (1932).

[5] Hock and Susemihl, *Ber.*, **66**, 61 (1933).

[6] Robertson and Waters, *J. Chem. Soc.*, **1948**, 1578.

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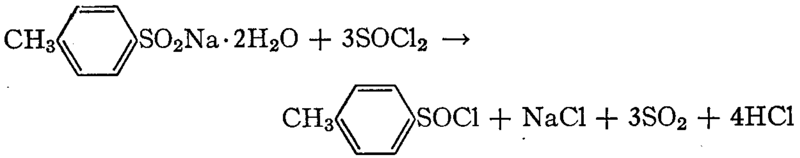
p-TOLUENESULFINYL CHLORIDE



Submitted by Frederick Kurzer.[1]
Checked by Richard S. Schreiber and Fred Kagan.

1. Procedure

Caution! This reaction should be conducted in a hood to avoid exposure to sulfur dioxide and hydrogen chloride.

To 179 g. (108 ml., 1.5 moles) of thionyl chloride (Note 1) contained in a 250-ml. round-bottomed flask, 42.8 g. (0.2 mole) of powdered sodium *p*-toluenesulfinate dihydrate[2] (Note 1) is added in portions at room temperature over a 10- to 15-minute period. A vigorous reaction occurs with the evolution of hydrogen chloride and sulfur dioxide. As the first portions of the sulfinate are added, the temperature of the reaction mixture rises, but it soon drops to approximately 0° as the addition proceeds (Note 2).

The resulting reaction mixture, a clear yellow liquid containing a white opaque solid, is protected from atmospheric moisture by means of a calcium chloride drying tube and is set aside at room temperature for 1.5–2 hours. During this time slight effervescence continues (Note 3) and the white opaque suspended material gradually disintegrates to a finely divided translucent deposit.

The excess thionyl chloride is removed by distillation under reduced pressure (15–20 mm.) with the bath temperature below 50°, and the last traces are eliminated by one or two evaporations under reduced pressure after the addition of 50-ml. portions of anhydrous ether (Note 4). The residue consists of a viscous yellow oil containing a suspension of white granular inorganic solid. The crude sulfinyl chloride is readily dissolved by three successive treatments with portions of anhydrous ether (50, 30, and 30 ml., respectively) which are decanted without difficulty from most of the inorganic residue (Note 5). Removal of the solvent by distillation at reduced pressure leaves the sulfinyl chloride as a clear, pale, straw-yellow oil. The yield is 30–32 g. (86–92%) (Note 6). Distillation at reduced pressure (Note 5) yields *p*-toluenesulfinyl chloride as a deep yellow mobile oil, b.p. 113–115°/3.5 mm. or 99–102°/0.5 mm. (Note 7). The yield of redistilled material is 23–26 g. (66–74%). A small quantity (2–3 g.) of a dark tarry residue remains in the distilling flask.

2. Notes

1. Redistilled thionyl chloride is recommended. No difficulties were encountered when the color of the reagent was deep yellow. The sodium *p*-toluenesulfinate dihydrate should be thoroughly air-dried to remove mechanically bound water.

2. When smaller quantities are used the thionyl chloride may be added to the sulfinate in one portion. After an initial rise, the temperature drops to about 0°. With larger quantities this procedure is not practicable.

3. If the sodium *p*-toluenesulfinate is not finely powdered, reaction occurs more slowly with emission of slight crackling sounds.

4. The ether was dried over calcium chloride and finally over phosphorus pentoxide. The checkers found that after the ether evaporations the odor of thionyl chloride was still present. The last traces of thionyl chloride were best removed at a pressure of 1–2 mm. When free of thionyl chloride the residue no longer has the pungent odor of either hydrogen chloride or sulfur dioxide but has a faint odor typical of sulfonyl chlorides.

5. If it is desired to distil the sulfinyl chloride subsequently, any traces of suspended material must be removed by filtration of the ethereal solution through a small filter, preferably into the distilling flask. It is advantageous to concentrate the ethereal solution to a small volume before filtering since more concentrated solutions of sulfinyl chloride in ether have less tendency to take up moisture from the atmosphere. The filter is rinsed with a little anhydrous ether.

The checkers used an inverted funnel connected to a source of dry nitrogen to provide an inert atmosphere for the filtration. The filtration was carried out as completely as possible directly beneath the inverted funnel through which a rapid stream of nitrogen flowed.

6. The sulfinyl chloride thus obtained is satisfactory for further preparative work. The checkers found that the average yield of crude material after removal of inorganic salts by filtration was about 81%.

7. On being heated, the sulfinyl chloride undergoes transient color changes (green), and the redistilled material may be darker in color than the pale yellow residue obtained after the removal of the ether.

For distillation the checkers employed a Claisen head with a fraction cutter. Approximately 90% of the product distilled at 93–96°/1.1 mm., $n_D^{23.5}$ 1.6004, and 10% distilled at 98–100°/1.3–1.6 mm., $n_D^{23.5}$ 1.5998. The total yield of distilled material in two runs averaged 74%.

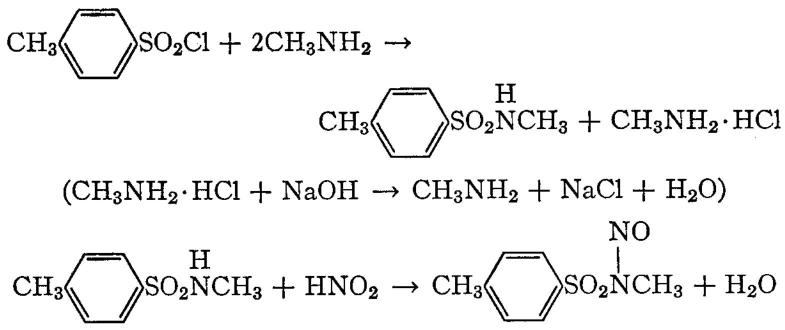
3. Methods of Preparation

Arylsulfinyl chlorides have been prepared by treating the corresponding arylsulfinic acids with an excess of thionyl chloride in the absence of solvents, either with gentle heating[3–8] or at room temperature.[9] The use of nearly equimolecular proportions of the reactants, and of ether as diluent in this reaction, has been claimed[10,11] to yield a cleaner product. *p*-Toluenesulfinyl chloride may be obtained directly from the hydrated sodium salt of *p*-toluenesulfinic acid by the action of a large excess of thionyl chloride, and the present procedure is based on this variation.[12]

[1] University of London, London, England.
[2] *Org. Syntheses* Coll. Vol. **1**, 492 (1941).
[3] Hilditch and Smiles, *Ber.*, **41**, 4115 (1908).
[4] von Braun and Kaiser, *Ber.*, **56**, 549 (1923).
[5] Whalen and Jones, *J. Am. Chem. Soc.*, **47**, 1353 (1925).
[6] Hunter and Sorenson, *J. Am. Chem. Soc.*, **54**, 3368 (1932).
[7] Courtot and Frenkiel, *Compt. rend.*, **199**, 557 (1934).
[8] Burton and Davy, *J. Chem. Soc.*, **1948**, 528.
[9] Raiford and Hazlet, *J. Am. Chem. Soc.*, **57**, 2172 (1935).
[10] Hilditch, *J. Chem. Soc.*, **97**, 2585 (1910).
[11] Phillips, *J. Chem. Soc.*, **1925**, 2569.
[12] Kurzer, *J. Chem. Soc.*, **1953**, 552.

p-TOLYLSULFONYLMETHYLNITROSAMIDE

(*p*-Toluenesulfonamide, N-methyl-N-nitroso-)



$(CH_3NH_2 \cdot HCl + NaOH \rightarrow CH_3NH_2 + NaCl + H_2O)$

Submitted by Th. J. de Boer and H. J. Backer.[1]
Checked by James Cason, John B. Rogan, and Wm. G. Dauben.

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1. Procedure

A total of 320 g. (1.68 moles) of *p*-toluenesulfonyl chloride (Note 1) is divided into three portions of 190, 90, and 40 g.; and a solution of alkali is prepared by dissolving 70 g. of sodium hydroxide in 70 ml. of water with cooling. The 190-g. portion of the sulfonyl chloride is added with swirling during about 5 minutes to 210 ml. (2.1 moles) of 33% aqueous methylamine (or 174 ml. of the 40% solution) contained in a 1-l. round-bottomed flask. The mixture is allowed to heat up to 80–90° in order to maintain the sulfonylmethylamide (m.p. 78°) in a molten condition (Note 2). After all this portion of the sulfonyl chloride has been added, the mixture is shaken vigorously. Boiling is prevented by mild cooling with water in order to avoid an excessive loss of methylamine.

As soon as the mixture has become acidic (Note 3), as indicated by testing a drop on litmus paper, 50 ml. of the 50% sodium hydroxide solution is added carefully with swirling. This is followed immediately by gradual addition of the 90-g. portion of the sulfonyl chloride as before. When the mixture has again become acidic (Note 3), 25 ml. of the sodium hydroxide solution is added, followed by the final 40 g. of the sulfonyl chloride. After the mixture has again become acidic, the remainder of the sodium hydroxide solution is added. The liquid phase of the final mixture should be alkaline (Note 4).

After the walls of the flask have been rinsed with a little water, the reaction is completed by heating the mixture, consisting of two layers and a precipitate of sodium chloride, on a steam bath for 15 minutes with vigorous mechanical stirring. The hot reaction mixture (Notes 2 and 5) is then poured into 1.5 l. of glacial acetic acid contained in a 5-l. round-bottomed flask, and the smaller flask is rinsed clean with 250 ml. of acetic acid (Note 6). The solution is cooled in an ice bath to about 5° (Note 7) and stirred mechanically as a solution of 124 g. (1.8 moles) of sodium nitrite in 250 ml. of water is added from a dropping funnel during about 45 minutes. The temperature of the mixture is kept below 10°, and stirring is continued for 15 minutes after addition is complete. During the reaction, the nitroso compound separates as a yellow crystalline product.

One liter of water is added to the mixture; then the precipitate is separated by suction filtration, pressed on the funnel, and washed with about 500 ml. of water. The product is transferred to a beaker, stirred well with about 500 ml. of cold water, then filtered and washed again on the funnel. This process is again repeated if necessary to remove the odor of acetic acid. After drying to constant weight in a vacuum desiccator over sulfuric acid, the product melts in the range between 55° and 60° (Note 8). The yield is 306–324 g. (85–90%) (Notes 9 and 10).

2. Notes

1. The *p*-toluenesulfonyl chloride used by the submitters was a product recrystallized from a 1:20 mixture of benzene:60–80° petroleum ether, and it melted at 67.5–69°. The checkers employed material obtained from Distillation Products Industries. Sulfonic acid may be removed from old samples of the sulfonyl chloride by thorough washing with cold water followed by immediate drying in a vacuum desiccator over sulfuric acid.

2. At lower temperatures, the sulfonylmethylamide is likely to form a hard cake. In smaller runs, e.g. 0.2 mole, the mixture heats up considerably less; therefore, the reaction mixture should be warmed on a steam bath after the first addition of sulfonyl chloride and thereafter as necessary.

3. The reaction mixture may not become acidic after a given addition of sulfonyl chloride, especially the first one. If such is the case, no more than 5 minutes need be allowed between successive sulfonyl chloride and alkali additions. The whole procedure requires about 30 minutes.

4. If the final mixture is acidic, indicating excessive loss of methylamine, sufficient methylamine should be added to render the mixture basic. This situation is more likely to occur in smaller runs (0.1–0.2 mole).

5. The precipitate of sodium chloride need not be removed before nitrosation; it dissolves when the final product is washed with water.

6. The total amount of 1750 ml. of acetic acid is necessary to dissolve the amide completely at lower temperatures. With less acetic acid, it is difficult to secure complete nitrosation, even with very efficient stirring of the suspension.

In one experiment with 750 ml. of acetic acid, the resulting impure product was washed first with water to remove acetic acid and then with 1 *N* sodium hydroxide to remove *p*-tolylsulfonylmethylamide (the nitroso compound is not attacked by cold aqueous sodium hydroxide). The yield of *p*-tolylsulfonylmethylnitrosamide was 76%, m.p. 58–60°. Acidification of the alkaline wash yielded (9% recovery) the *p*-tolylsulfonylmethylamide, m.p. 77.5–78.5°.

7. An ice-salt mixture may be used for more efficient cooling, but reaction temperatures below 0° should be avoided because the total amount of acetic acid is just sufficient to keep the sulfonylmethylamide in solution above 0°.

8. A melting point in the lower part of this range generally indicates contamination with *p*-tolylsulfonylmethylamide, which may be removed as described in Note 6; however, this purification is not necessary since the presence of this amide does not interfere in the preparation of diazomethane.

9. This product may be kept at room temperature for years without significant change. For long periods of storage, a dark bottle is recommended; also, recrystallized samples are more stable. Recrystallization is best accomplished by dissolution in boiling ether (1 ml./g.), addition of an equal volume of low-boiling petroleum ether (technical pentane), and cooling overnight in a refrigerator. Other solvents (benzene, carbon tetrachloride, chloroform) may be used for recrystallization, but the maximum temperature should not exceed 45°.

10. *p*-Tolylsulfonylmethylnitrosamide is a useful substance for the preparation of diazomethane.[2] It is apparently of low toxicity. An explosive decomposition has never been encountered by the submitters during its preparation, recrystallization, storage, or the reaction with alkali to form diazomethane. These properties afford advantages over other nitroso compounds which have been used for preparation of diazomethane.

3. Methods of Preparation

p-Tolylsulfonylmethylnitrosamide has been prepared previously by adding sodium nitrite to an acid aqueous suspension of *p*-tolylsulfonylmethylamide.[3,4] The present method is more rapid and gives higher yields.

---

[1] De Rijks-Universiteit, Groningen, the Netherlands.

[2] Cf. *Org. Syntheses*, **34**, 24 (1954).

[3] Friedlander, *Fortschritte der Teerfarbenfabrikation*, **10**, 1216 (1910); Bayer Co. D.R.P. 224,388 [*Chem. Zentr.*, **1910**, II, 609].

[4] Takizawa, *J. Pharm. Soc. Japan*, **70**, 490 (1950) [*C. A.*, **46**, 454 (1952)].

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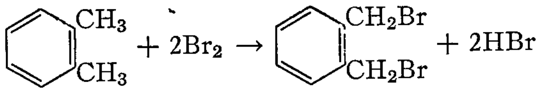
o-XYLYLENE DIBROMIDE

(*o*-Xylene, α,α′-dibromo-)



Submitted by Emily F. M. Stephenson.[1]
Checked by William S. Johnson, C. W. Taylor, and William DeAcetis.

1. Procedure

Caution! o-Xylylene dibromide is a powerful and persistent lachrymator. The preparation and all subsequent handling of this substance should, therefore, be carried out in an efficient hood with adequate protection by rubber gloves. A gas mask should be at hand for emergency. All apparatus coming in contact with the dibromide should be immersed in alcoholic alkali contained in a large crock with a lid. A period of 24 hours is sufficient for decontamination. Waste substances such as filter paper and corks usually require several days of such soaking before they can be safely discarded.

A 1-l. three-necked round-bottomed flask is fitted with a rubber slip-sleeve-sealed stirrer, a dropping funnel with the tip extended to reach almost to the bottom of the flask (Note 1), and an efficient condenser leading to a gas absorption trap.[2] *o*-Xylene (106 g., 1 mole) (Note 2) is placed in the flask, which is heated with an oil bath and illuminated with a sun lamp (Note 3) placed 1–5 cm. from the upper portion of the flask. When the temperature of the *o*-xylene reaches 125°, the dropwise addition of 352 g. (2.2 moles) of bromine is commenced with stirring. The rate of addition is regulated so that all the bromine is introduced in 1.5 hours. The mixture is stirred at 125° under illumination for an additional 30 minutes. It is then allowed to cool to 60° and poured into 100 ml. of boiling 60–68° petroleum ether contained in a beaker, the transfer being assisted with small amounts of warm solvent. As the homogeneous solution cools slowly to room temperature it is stirred frequently to prevent caking of the brown crystalline product that separates. After the mixture is cool and the bulk of the dibromide has crystallized, the beaker is placed in a refrigerator for 12 hours (Note 4). The product is then separated by suction filtration, washed twice with 25-ml. portions of cold petroleum ether, and then pressed on the filter until nearly dry. Final drying is effected in a vacuum desiccator containing solid potassium hydroxide. The brown crystalline product amounts to 123–140 g. (48–53% yield), the melting point ranging between 89° and 94° (Note 5).

2. Notes

1. It is convenient to seal a short inner tube inside the stem of the dropping funnel so that the rate of addition can be observed readily. The introduction of the bromine below the surface of the *o*-xylene through an extended stem, about 4-mm. inside diameter, results in better mixing of reactants and less loss of bromine vapors.

2. The submitters used *o*-xylene obtained from Light and Company, Wraysbury, Middlesex, England. It was refluxed with sodium, then distilled from sodium, b.p. 144–144.5°, and stored over sodium.

The checkers employed the "white label" grade of *o*-xylene supplied by the Eastman Kodak Company without further purification.

3. The submitters employed a 600-watt lamp, and the checkers used a 275-watt General Electric sun lamp.

4. Occasional stirring during the first 3–4 hours of this chilling period helps to prevent caking of the product on the side of the beaker.

5. This product is satisfactory for most preparative work. Further purification may be effected by recrystallization from 95% ethanol (3 ml./g.), to give material melting at 93–94° in 80–85% recovery. Other solvents that have been used for recrystallization are petroleum ether (British Drug House, "Analar," b.p. 60–80°) (19 ml./g.), and chloroform (1 ml./g.).

3. Methods of Preparation

o-Xylylene dibromide has been prepared by the bromination of *o*-xylene [3] and of *o*-xylyl bromide.[4] It has also been produced by the action of concentrated hydrobromic acid on the monophenyl ether of α,α'-dihydroxy-*o*-xylene.[5] The present procedure is essentially that of Perkin [3] as modified by Cope and Fenton.[6]

[1] Chemistry Department, University of Melbourne, Melbourne, Australia.

[2] *Org. Syntheses* Coll. Vol. **2**, 4 (1943).

[3] Perkin, *J. Chem. Soc.*, **1888**, 5; Atkinson and Thorpe, *J. Chem. Soc.*, **1907**, 1695.

[4] von Braun and Cahn, *Ann.*, **436**, 262 (1924).

[5] von Braun and Zobel, *Ber.*, **56**, 2142 (1923).

[6] Cope and Fenton, *J. Am. Chem. Soc.*, **73**, 1668 (1951).

SUBJECT INDEX

(This cumulative index comprises material from Volumes 30, 31, 32, 33, and 34; for previous volumes see Collective Volumes 1 and 2 and Volume 29.)

Names in small capital letters refer to the titles of individual preparations. A number in ordinary bold-face type denotes the volume. A page number in bold-face italics indicates that the detailed preparative directions are given or referred to; entries so treated include principal products and major by-products, special reagents or intermediates (which may or may not be isolated), compounds mentioned in the text or Notes as having been prepared by the method given, and apparatus described in detail or illustrated by a figure. Page numbers in ordinary type indicate pages on which a compound or subject is mentioned in connection with other preparations. For example, Allylbenzene, **31**, 85, ***86***, indicates that allylbenzene is mentioned on page 85, and that directions for its preparation are given on page 86, of Volume 31.

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