ORGANIC SYNTHESES

I

ALLANTOIN

$$\begin{array}{c}
\text{NH-CO} \\
\text{CO} \quad \text{C-NH} \\
\text{NH-C-NH}
\end{array} \Big\rangle \text{CO} + \text{H}_2\text{O} + [\text{O}] \ (\text{KMnO}_4) \longrightarrow
\begin{array}{c}
\text{CO}_2\text{K} \\
\text{NH-C-NH} \\
\text{CO} \quad \text{CO} \\
\text{NH-C-NH} \\
\text{OH}
\end{array}$$

$$\xrightarrow{\text{CH}_3\text{CO}_2\text{H}} \text{CO}_2 +
\begin{array}{c}
\text{H} \\
\text{NH-C-NH} \\
\text{CO} \quad \text{CO} \\
\text{NH-C-NH} \\
\text{OH}
\end{array}
\begin{array}{c} \rightarrow \\ \leftarrow \end{array}
\begin{array}{c}
\text{H} \\
\text{NH-C-NHCONH}_2 \\
\text{CO} \\
\text{NH-C} \\
\text{O}
\end{array}$$
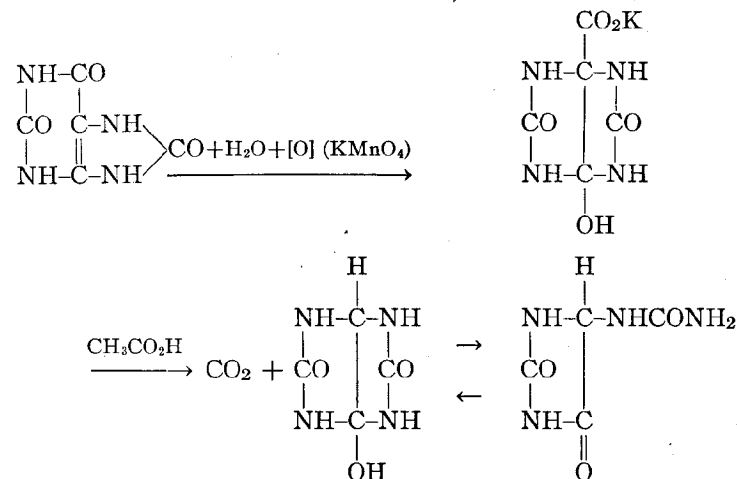
Submitted by W. W. HARTMAN, E. W. MOFFETT, and J. B. DICKEY.
Checked by W. H. CAROTHERS and W. L. McEWEN.

1. Procedure

ONE HUNDRED grams of uric acid (0.595 mole) and 4.5 l. of hot (70–85°) water are placed in a 12-l. round-bottomed flask equipped with a mechanical stirrer. The stirrer is started, and a solution of 80 g. (2 moles) (Note 1) of commercial sodium hydroxide in 120 cc. of water is added. Stirring is continued until the uric acid is in solution (Note 2), after which the solution is cooled by means of a stream of water directed against the flask. When the temperature has fallen to 25–30°, 50 g. (0.316

1

mole) (Note 3) of potassium permanganate is added all at once (Note 4) to the vigorously stirred solution. Stirring is continued for fifteen to twenty minutes (Note 5), and the mixture is filtered (Note 6) at once through a 19-cm. Büchner funnel. The first fraction of the filtrate contains a small amount of manganese dioxide. This fraction must be collected separately and returned to the funnel. As soon as the filtrate becomes clear it is collected in a 12-l. round-bottomed flask which contains 130 cc. (137 g., 2.2 moles) of glacial acetic acid. The filtrate is tested with litmus to be sure that it is acid, and evaporated to a volume of 1.5–2 l. on a steam bath under reduced pressure (20–30 mm.). The solution thus obtained is allowed to stand in a cool place over-night, and the allantoin which crystallizes is filtered off on a 9-cm. Büchner funnel (Note 7). The allantoin is dissolved in 800–900 cc. of boiling water, treated with 5 g. of norite (decolor-izing carbon), and filtered rapidly through a fluted filter paper in a steam funnel. The filtrate is allowed to stand in a cool place overnight (Note 8), and the white crystals of allantoin are separated by filtration with suction. The yield of product melting at 230–231° (uncorr.) (Note 9) is 60–71 g. (63.8–75.5 per cent of the theoretical amount). If the filtrate from the purifica-tion liquors is concentrated to 100 cc., there is obtained an addi-tional 3–5 g. of allantoin.

2. Notes

1. The use of more than 80 g. of sodium hydroxide does not increase the yield, but, if not neutralized immediately upon com-pletion of the reaction, it causes decomposition of some allantoin.

2. It is essential that the uric acid be completely in solution; otherwise all of it will not be oxidized. When the solution is cooled a small amount of white precipitate sometimes separates, but this does not affect the yield.

3. The amount of potassium permanganate can be varied between 50 and 62 g. (0.316–0.392 mole) without changing the yield.

4. The potassium permanganate must be added rapidly (one to five minutes).

5. If the period of stirring is reduced to ten minutes, some unchanged uric acid is recovered. The period can be extended slightly beyond twenty minutes without decreasing the yield of allantoin, but if it is extended beyond one hour the yield is appreciably decreased.

6. Filtration must be as rapid as possible; this necessitates the use of a large Büchner funnel.

7. The filtrate is discarded since the amount of allantoin is not sufficient to repay attempts to separate it from the various other compounds present.

8. Crystallization can be hastened by stirring in an ice bath.

9. The melting point appears to depend somewhat on the rate of heating. The melting point 228–230° is observed in a capillary tube in a bath heated up slowly from room temperature. If the capillary is placed in a bath already heated to 228°, the specimen melts at 233–234°. On a copper block still higher melting points are obtained.

3. Methods of Preparation

Allantoin has been prepared by the oxidation of uric acid with potassium permanganate,[1] lead dioxide,[2] potassium ferri-cyanide,[3] oxygen,[4] manganese dioxide,[5] ozone,[6] hydrogen per-oxide,[7] and by the electrolytic oxidation of lithium urate.[8] It is also formed by heating glyoxylic acid with urea.[9]

[1] Claus, Ber. 7, 226 (1874); Sundwik, Z. physiol. Chem. 41, 343 (1904); Behrend, Ann. 333, 141 (1904); Biltz, Ber. 43, 1999 (1910); Biltz and Giesler, ibid. 46, 3410 (1913); Biltz and Max, ibid. 54, 2451 (1921); Neubauer, Ann. 99, 206 (1856).
[2] Wöhler and Liebig, Ann. 26, 241 (1838); Mulder, Ann. 159, 349 (1871).
[3] Schlieper, Ann. 67, 214 (1848).
[4] Biltz and Max, Ber. 54, 2451 (1921).
[5] Wheeler, Z. Chem., 746 (1866).
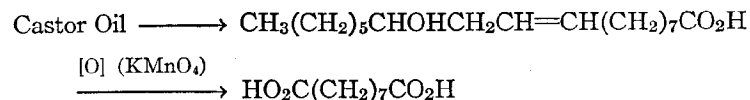[6] Gorup-Besanez, Ann. 110, 86 (1859).
[7] Venable, J. Am. Chem. Soc. 40, 1099 (1918).
[8] Fichter and Kern, Helv. Chim. Acta 9, 429 (1926).
[9] Grimaux, Ann. chim. phys. [5] 11, 356 (1877).

II

AZELAIC ACID

Castor Oil $\longrightarrow$ $CH_3(CH_2)_5CHOHCH_2CH{=}CH(CH_2)_7CO_2H$

$$\overset{\text{[O] (KMnO}_4\text{)}}{\longrightarrow} HO_2C(CH_2)_7CO_2H$$

Submitted by JULIAN W. HILL and W. L. McEWEN.
Checked by REYNOLD C. FUSON and CHARLES F. WOODWARD.

1. Procedure

FIVE HUNDRED grams of castor oil (Note 1) is added to a solution of 100 g. of potassium hydroxide in 1 l. of 95 per cent alcohol. The mixture is placed in a 3-l. flask equipped with a reflux condenser and is boiled for three hours. The solution is then poured into 3 l. of water and acidified by the addition of a solution of 100 cc. of concentrated sulfuric acid in 300 cc. of water. The acid which separates is washed twice with warm water, shaken intermittently for one hour with 100 g. of anhydrous magnesium sulfate, and then filtered with suction. The yield of crude ricinoleic acid thus obtained is 480 g. The acid should be oxidized at once (Note 2).

Two hundred and forty grams (0.8 mole) of the dried ricinoleic acid is dissolved in 1600 cc. of water containing 64 g. of potassium hydroxide. A 12-l. round-bottomed flask is equipped with a powerful mechanical stirrer, and in it are placed 625 g. (3.5 moles) of potassium permanganate and 7.5 l. of water at 35°. The mixture is stirred to facilitate solution of the permanganate, and, if necessary, heat is applied to maintain the temperature at 35°. When the permanganate has completely dissolved, the alkaline solution of ricinoleic acid is added in a single portion with vigorous stirring (Note 3). The temperature rises rapidly to about 75°. Stirring is continued for a half hour,

4

or until a test portion added to water shows no permanganate color.

The oxidation mixture is now divided into two equal portions and each portion is treated as follows: To the mixture is added a solution of 200 g. of concentrated sulfuric acid in 600 cc. of water (Note 4). The mixture is heated on a steam bath for 15 minutes to coagulate the manganese dioxide which is filtered while still very hot (Note 5). After filtration the manganese dioxide is placed in a 4-l. beaker and boiled with 2 l. of water to dissolve any azelaic acid that may adhere to it. This mixture is filtered while hot, and the filtrate is added to the main portion.

The combined filtrates and washings for the two portions of the oxidation mixture are evaporated to a volume of about 4 l., and this solution is cooled in ice. The crystals which separate are filtered with suction, washed once with cold water, and dried. The yield is 70–80 g. of material having a melting point that may vary from 95 to 105°.

The crude substance is dissolved in 1200 cc. of boiling water, filtered with suction, and allowed to cool. The crystals are filtered, washed with water, and dried. There is obtained 48–55 g. of product (32–36 per cent of the theoretical amount, based upon the amount of crude ricinoleic acid taken for oxidation). The melting point of the purified azelaic acid is 104–106°.

2. Notes

1. The castor oil used was a commercial grade designated as " Crystal." It was obtained from the Baker Castor Oil Company, New York City.

2. If ricinoleic acid is allowed to stand, polymerization occurs; Baker and Ingold report [1] that the polymerized acid gives very poor yields in the oxidation by nitric acid.

3. At this point the mixture tends to froth quite badly, and if stirring is not vigorous, material may be lost. Addition of a small quantity of ether or benzene may be resorted to but is unnecessary if stirring is efficient.

4. The acid must be added slowly and carefully to prevent too rapid evolution of carbon dioxide with consequent foaming.

If possible, each of the two portions should be placed in a large container, such as a 12-l. flask.

5. For this purpose it is advisable to use three 20-cm. Büchner funnels supported in 2-l. filter flasks.

3. Methods of Preparation

Azelaic acid can be prepared by the oxidation of castor oil with nitric acid; [2] by the oxidation of ricinoleic acid with nitric acid [1] and with alkaline permanganate; [3] by the oxidation of methyl oleate with alkaline permanganate; [4] by the ozonization of oleic acid and decomposition of the ozonide; [5] by the ozonization of methyl ricinoleate and decomposition of the ozonide; [6] by the action of carbon dioxide upon 1,7-heptamethylene magnesium bromide; [7] by the hydrolysis of 1,7-dicyanoheptane.[8]

[1] Baker and Ingold, J. Chem. Soc. **123**, 122 (1923); Verkade, Rec. trav. chim. **46**, 137 (1927).

[2] Arppe, Ann. **120**, 288 (1861); **124**, 86 (1862); Dale and Schorlemmer, ibid. **199**, 144 (1879); Kiliani, Ber. **54**, 469 (1921); Day, Kon, and Stevenson, J. Chem. Soc. **117**, 642 (1920); Böeseken and Lutgerhorst, Rec. trav. chim. **51**, 164 (1932).

[3] Maquenne, Bull. soc. chim. [3] **21**, 1061 (1899).

[4] Armstrong and Hilditch, J. Soc. Chem. Ind. **44**, 43 (T) (1925).

[5] Harries and Tank, Ber. **40**, 4556 (1907).

[6] Haller and Brochet, Compt. rend. **150**, 500 (1910).

[7] v. Braun and Sobecki, Ber. **44**, 1926 (1911).

[8] Dionneau, Ann. chim. [9] **3**, 249 (1915).

and washed on the filter with two 100-cc. portions of ice-cold alcohol and finally with two 100-cc. portions of boiling water. After drying, the product weighs 205–215 g. (69–73 per cent of the theoretical amount) and melts at 149–150°. This material is sufficiently pure for many purposes; it can be purified further by crystallization from hot benzene. In this way, using 1200 cc. of benzene, there is obtained 180–190 g. of the pure azlactone, melting at 151–152°.

2. Notes

1. The veratric aldehyde obtained by methylating vanillin (p. 102) may be used without further purification.

2. The mixture should become completely liquid at a temperature of about 110°. Overheating should be avoided, since this causes the product to become colored red instead of bright yellow.

3. Methods of Preparation

The azlactones of α-benzoylaminocinnamic acids have always been prepared by the action of hippuric acid and acetic anhydride upon aromatic aldehydes,[1] usually in the presence of sodium acetate.[2] The procedure given here is essentially that of Kropp and Decker.[3]
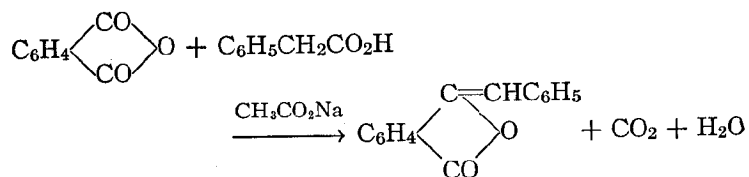
[1] Plöchl, Ber. **16**, 2815 (1883).
[2] Erlenmeyer, Ann. **275**, 3 (1893).
[3] Kropp and Decker, Ber. **42**, 1184 (1909).

III

AZLACTONE OF
α-BENZOYLAMINO-β-(3,4-DIMETHOXYPHENYL)-ACRYLIC ACID [2-PHENYL-4-(3',4'-DIMETHOXYBENZAL)-OXAZOLONE]
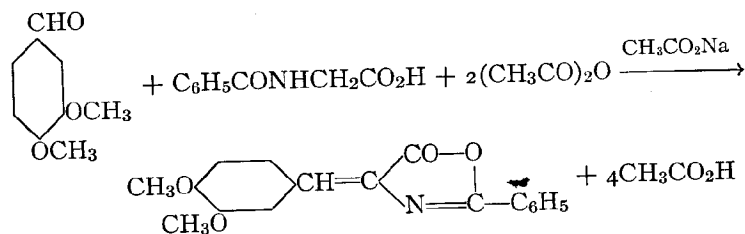
Submitted by JOHANNES S. BUCK and WALTER S. IDE.
Checked by JOHN R. JOHNSON and H. R. SNYDER.

1. Procedure

IN a 2-l. Erlenmeyer flask, a mixture of 160 g. (0.96 mole) of veratric aldehyde (Note 1), 192 g. (1.07 moles) of powdered, dry hippuric acid (Org. Syn. **12**, 40), 80 g. (0.98 mole) of powdered, freshly fused sodium acetate, and 300 g. (280 cc., 3 moles) of high-grade acetic anhydride is heated on an electric hot plate, with constant shaking. The mixture becomes almost solid and then, as the temperature rises, it gradually liquefies and becomes deep yellow in color (Note 2). As soon as the material has liquefied completely the flask is transferred to a steam bath and heated for two hours. During this time a part of the product separates as deep yellow crystals. At the end of the heating 400 cc. of alcohol is added slowly to the contents of flask. During this addition the flask is cooled slightly to moderate the vigor of the reaction. After allowing the reaction mixture to stand overnight, the yellow crystalline product is filtered with suction

IV

BENZALPHTHALIDE

$$C_6H_4\underset{CO}{\overset{CO}{<}}O + C_6H_5CH_2CO_2H$$

$$\xrightarrow{CH_3CO_2Na} C_6H_4\underset{CO}{\overset{C=CHC_6H_5}{<}}O + CO_2 + H_2O$$

Submitted by RICHARD WEISS.
Checked by JOHN R. JOHNSON and H. R. SNYDER.

1. Procedure

IN a 500-cc. round-bottomed flask with a short neck (not longer than 3 cm.) are placed 100 g. (0.67 mole) of phthalic anhydride (Note 1), 110 g. (0.8 mole) of phenylacetic acid (Coll. Vol. 1, 427), and 2.6 g. of freshly fused sodium acetate. A few chips of porous plate are added, and the flask is provided with a cork bearing a thermometer, which reaches almost to the bottom, and a wide, bent glass tube leading to a condenser. The tube ends just at the lower edge of the cork and does not protrude into the neck of the flask. The flask is imbedded up to the neck in a sand bath and is heated rapidly until the thermometer reaches 230°; after this point the temperature is raised slowly until the water produced in the reaction (and some entrained organic matter) passes out through the exit tube. The water is collected in a small vessel and its quantity noted from time to time in order to follow the progress of the reaction. The operation should be conducted so that the temperature rises from 230 to 240° in the course of about two hours. The reaction is maintained at 240° until the distillation of water ceases; this requires about one additional hour.

The flask now contains a brown mass covered with a film. The stopper is removed, and a test portion is taken out by means of a glass rod. The test portion is placed in a test tube or small beaker, treated with a little alcohol, and heated to boiling. When the reaction is complete, the material dissolves readily in the hot alcohol and crystallizes on cooling.

When this test has been found to be satisfactory, the flask is allowed to cool to 90–95°, and the product is dissolved in 400 cc. of boiling alcohol. The solution is filtered from insoluble matter and allowed to cool. The yellow crystals of benzalphthalide are filtered with suction and washed with 40–50 cc. of cold alcohol. The product weighs 115–116 g. and melts at 95–97°; for purification it is recrystallized from 370–380 cc. of alcohol. The yield of pure benzalphthalide, m.p. 100–101°, is 106–110 g. (71–74 per cent of the theoretical amount).

2. Notes

1. A good grade of sublimed phthalic anhydride should be used (m.p. 129–131°); if this is not available the ordinary phthalic anhydride can be purified by sublimation.
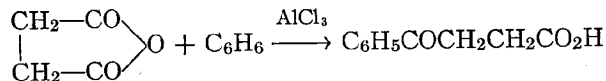
3. Methods of Preparation

Benzalphthalide has been prepared only from phthalic anhydride and phenylacetic acid in the presence of sodium acetate. The procedure given here is essentially that of Gabriel.[1]

[1] Gabriel, Ber. 18, 3470 (1885).

V

β-BENZOYLPROPIONIC ACID

$$\begin{array}{c} CH_2-CO \\ | \qquad\quad >O + C_6H_6 \xrightarrow{\ AlCl_3\ } C_6H_5COCH_2CH_2CO_2H \\ CH_2-CO \end{array}$$

Submitted by L. F. Somerville and C. F. H. Allen.
Checked by Reynold C. Fuson and Don B. Forman.

1. Procedure

In a 2-l. three-necked, round-bottomed flask fitted with a mechanical stirrer and two reflux condensers are placed 68 g. (0.68 mole) of succinic anhydride (Org. Syn. **12**, 66) and 350 g. (4.5 moles) of dry, thiophene-free benzene (Note 1). The stirrer is started and 200 g. (1.5 moles) of powdered, anhydrous aluminum chloride is added all at once. Hydrogen chloride is evolved and the mixture becomes hot (Note 2). It is heated in an oil bath and refluxed, with continued stirring, for half an hour (Note 3). The flask is then surrounded by cold water, and 300 cc. of water is slowly added from a dropping funnel inserted in the top of one of the condensers. The excess benzene is removed by steam distillation, and the hot solution is at once poured into a 2-l. beaker. After the mixture is cold the liquid is decanted from the precipitated solid and acidified with concentrated hydrochloric acid (about 20 cc. is required); 5 to 15 g. of benzoylpropionic acid separates and is filtered off (Note 4). The residual suspension in the beaker is boiled for five hours with 1500 cc. of water containing 360 g. of commercial soda ash; the resulting solution is filtered with suction, the filter cake washed with hot water, and the filtrate acidified with concentrated hydrochloric acid (about 300 cc.). The precipitated benzoylpropionic acid is filtered and washed with hot water; after drying for a day it weighs 95–100 g. (77–82 per cent of the theoretical amount) and

melts at 111–113°. If the first (colored) precipitate (weight, 5 to 15 g.) is separated as suggested it is unnecessary to purify the remainder (Notes 5, 6, 7). It may be further purified, if desired, by dissolving in dilute sodium hydroxide and precipitating with concentrated hydrochloric acid, the first portion of the precipitate being collected separately. The pure acid melts at 116° (Note 8).

2. Notes

1. Commercial benzene is shaken with concentrated sulfuric acid, then with water and dried, first with anhydrous calcium chloride and then over metallic sodium.

2. If the reaction does not start at once it is initiated by gentle heating.

3. The yield is not increased by longer heating.

4. The amount of acid isolated at this point varies according to the length of time the solution is allowed to stand before acidification.

5. The first portion of the precipitated acid is usually colored; it is best to filter it separately. The remaining acid will then be colorless and very nearly pure (m.p. 114–115°).

6. By evaporating the filtrate to a small volume and extracting with ether, a further 3 g. of acid may be obtained.

7. The acid tenaciously retains traces of water to which apparently higher yields may be due. The weights given above were obtained on material that had been dried overnight in a vacuum desiccator.

8. γ-Benzoylbutyric acid may also be prepared by this method. Glutaric anhydride (0.68 mole) dissolved in part of the benzene is added to the rest of the benzene in which the aluminum chloride is suspended; the temperature is kept below 15° for one and one-half hours, including the time of addition; an 80–85 per cent yield of γ-benzoylbutyric acid melting at 125–126° is obtained.

3. Methods of Preparation

β-Benzoylpropionic acid has been prepared by the action of succinic anhydride on benzene in the presence of anhydrous

aluminum chloride; [1,2] by long heating of cinnamic aldehyde, hydrocyanic acid, and water; [3] by reduction of benzoylacrylic acid; [4] by the ketonic hydrolysis of benzoylsuccinic or isosuccinic esters; [5] by heating phenylbromoparaconic (or phenylbromoisoparaconic) acid; [6] by heating γ-phenyl-β,γ-dibromobutyric acid with water; [7] by decomposition of the product resulting from the action of sodium malonic ester on phenacyl bromide; [8] and by hydrolysis of phenacylbenzoylacetic ester.[9]

[1] Burcker, Ann. chim. phys. [5] **26**, 435 (1882).

[2] Kohler and Engelbrecht, J. Am. Chem. Soc. **41**, 768 (1919).

[3] Matsmoto, Ber. **8**, 1145 (1875); Peine, *ibid*. **17**, 2114 (1884).

[4] von Pechmann, Ber. **15**, 889 (1882).

[5] Perkin, J. Chem. Soc. **47**, 276 (1885); Kues and Paal, Ber. **18**, 3325 (1885).

[6] Fittig and Leoni, Ann. **256**, 81 (1890).

[7] Fittig, Obermüller, and Schiffer, Ann. **268**, 74 (1892).

[8] Barbier and Locquin, Bull. soc. chim. [4] **13**, 227 (1913).

[9] Kapf and Paal, Ber. **21**, 1487 (1888).

VI

n-BUTYL BORATE

$$3C_4H_9OH + B(OH)_3 \rightarrow B(OC_4H_9)_3 + 3H_2O$$
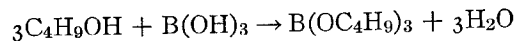
Submitted by JOHN R. JOHNSON and S. W. TOMPKINS.
Checked by W. W. HARTMAN and J. B. DICKEY.

1. Procedure

IN a 2-l. round-bottomed flask equipped with a 200-cc. dropping funnel and a 30-cm. column filled with glass beads (Note 1) and connected to a 40–50 cm. condenser, are placed 124 g. (2 moles) of boric acid, 666 g. (9 moles) of technical *n*-butyl alcohol, and a few chips of porous plate. The reaction mixture is heated to gentle boiling, and the rate of heating is adjusted so that 90–100 cc. of distillate is collected per hour. The temperature of the vapor at the top of the column remains constant at 91° over a period of three to three and one-half hours while the azeotropic mixture of *n*-butyl alcohol and water distils (Note 2). After two hours, the upper layer of *n*-butyl alcohol in the distillate is separated from the water, dried with a little anhydrous potassium carbonate or magnesium sulfate, and returned to the reaction mixture through the separatory funnel. Likewise, after the third hour of heating, the *n*-butyl alcohol in the distillate is separated, dried, and returned to the reaction flask.

During the third hour of heating, the temperature at the top of the column rises slowly as the removal of the water approaches completion. After the fourth hour, when the temperature of the distilling vapor has attained 110–112°, the heating is discontinued, and the reaction mixture is transferred to a 2-l. Claisen flask with the least possible exposure to atmospheric moisture (Note 3). The unreacted *n*-butyl alcohol is distilled off under reduced pressure (Note 4) until the thermometer

registers a sudden rise in temperature. The receiver is then changed, and the main fraction of *n*-butyl borate distils almost entirely at 103–105°/8 mm. or 114–115°/15 mm. A negligible residue remains in the distilling flask. The weight of the distilled *n*-butyl borate, which contains a small amount of *n*-butyl alcohol, is 410–435 g. (89–94 per cent of the theoretical amount). From the aqueous distillate and the fore-run of the vacuum distillation, 190–210 g. of *n*-butyl alcohol is recovered.

The main fraction of *n*-butyl borate is redistilled from a Claisen flask provided with an indented fractionating column (Note 5), and the first 4–6 cc. of distillate is rejected. The purified product, b.p. 103–105°/8 mm. or 114–115°/15 mm., weighs 400–425 g. (87–92 per cent of the theoretical amount).

2. Notes

1. Any reasonably effective type of fractionating column can be used. Columns longer than 30 cm. and of the most efficient types were found to give no better results than a simple Hempel column filled with glass beads or broken glass.

2. The distillate collected while the temperature remains at 91° separates into two layers; 100 cc. of this distillate contains 72 cc. of a supernatant layer of wet *n*-butyl alcohol.

3. Since *n*-butyl borate is hydrolyzed readily by atmospheric moisture, it is necessary to manipulate the reaction product so as to minimize exposure to the air.

4. *n*-Butyl borate can be purified by distillation at atmospheric pressure, but the separation from *n*-butyl alcohol is effected more readily under reduced pressure. *n*-Butyl borate is stated [1] to boil at 190°/200 mm. and 230–235° at atmospheric pressure.

5. It is advantageous to use a Claisen flask with a 25–30 cm. side arm bearing a condenser jacket and connected to a device for collecting the fractions without interruption of the distillation or exposure to moist air.

6. *n*-Amyl borate can be prepared in a similar manner. From 792 g. (9 moles) of *n*-amyl alcohol and 124 g. (2 moles) of boric acid there is obtained 510–525 g. (93–96 per cent of the

theoretical amount) of *n*-amyl borate, b.p. 146–148°/16 mm.; 210–215 g. of *n*-amyl alcohol is recovered. In this preparation the temperature of the distilling vapor remains at 95° during the first two hours and the distillate contains relatively more water (100 cc. of distillate contains 56 cc. of water and 44 cc. of *n*-amyl alcohol). After the second hour the temperature rises slowly to 136–137°. It is unnecessary, and not advantageous, to return the recovered *n*-amyl alcohol to the reaction mixture.

3. Methods of Preparation

The procedure described is essentially that given in a recent patent.[1] *n*-Butyl borate can also be prepared by the action of *n*-butyl alcohol on boron triacetate or boric anhydride.

[1] W. J. Bannister, U. S. pat. 1,668,797, May 8, 1928 [C. A. **22**, 2172 (1928)].

VII

iso-BUTYL BROMIDE

$$3(CH_3)_2CHCH_2OH + PBr_3 \rightarrow 3(CH_3)_2CHCH_2Br + P(OH)_3$$
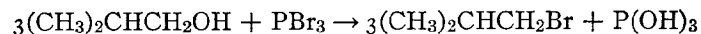
Submitted by C. R. Noller and R. Dinsmore.
Checked by F. C. Whitmore, D. E. Badertscher, and A. R. Lux.

1. Procedure

In a 2-l. three-necked flask fitted with a mechanical stirrer, a thermometer, and a dropping funnel, is placed 518 g. (643 cc., 7 moles) of dry *iso*-butyl alcohol (b.p. 106–108°/760 mm.). This is cooled to −10° by immersing the flask in an ice-salt bath and 695 g. (244 cc., 2.56 moles) of phosphorus tribromide (Note 1) is slowly added with stirring at such a rate as to keep the temperature below 0° (about four hours). The cooling bath is removed, and stirring is continued until the mixture reaches room temperature; it is then allowed to stand overnight. The stirrer, funnel, and thermometer are removed, and the flask is fitted with a 30-cm. fractionating column and a condenser. The crude *iso*-butyl bromide is distilled from the reaction mixture under diminished pressure *e.g.* at about 50° under 200 mm. (Note 2).

The distillate is cooled to about 0° and washed three times with 50-cc. portions of concentrated sulfuric acid cooled to 0°; it is then shaken with 25 g. of anhydrous potassium carbonate until the odor of hydrobromic acid disappears. It is distilled through a 1-m. fractionating column at atmospheric pressure, collecting the portion boiling at 91–93°/760 mm., 88.5–90.5°/728 mm., or under reduced pressure through a 70 x 2-cm. total reflux, adjustable take-off, adiabatic column (Note 3), b.p. 41–43°/135 mm. The product weighs 525–570 g. (55–60 per cent of the theoretical amount) (Note 4).

2. Notes

1. The phosphorus tribromide boiled at 171–173°/760 mm., 168–170°/725 mm., and was prepared in 90–95 per cent yield by adding bromine to a stirred suspension of red phosphorus in carbon tetrachloride. A good fractionating column is necessary. Old red phosphorus containing acids of phosphorus gives a poorer yield.

2. In some runs, the crude bromide was successfully distilled at atmospheric pressures; in others it decomposed violently. When reduced pressure was used no difficulty was experienced. A water pump with an adjustable leak in the vacuum line was used.

3. The column used with reduced pressure was similar to those described by Whitmore and Lux, J. Am. Chem. Soc. **54**, 3451 (1932). The product, fractionated under reduced pressure using a reflux ratio of 5 : 1, contained less than 1 per cent of tertiary butyl bromide.

4. Using similar procedures, the following can be prepared in the yields indicated: *sec.*-butyl bromide, b.p. 90–93°, 80 per cent; *n*-propyl bromide, b.p. 70–73°, 95 per cent; *iso*-propyl bromide, b.p. 60–63°, 68 per cent.

In attempting to prepare *iso*-butyl bromide by the hydrobromic, or hydrobromic-sulfuric, acid methods, the yields were always poor and not reproducible. In all the above cases the product is purer and the yields better than when the hydrobromic, or hydrobromic-sulfuric, acid method is used. When tertiary butyl bromide is prepared by the above method it is difficult to get a pure product.

3. Methods of Preparation

iso-Butyl bromide has been prepared from *iso*-butyl alcohol by the action of bromine and phosphorus,[1] of aqueous hydrobromic acid,[2] and of gaseous hydrobromic acid;[3] from *iso*-butylene and gaseous hydrogen bromide;[4] or hydrogen bromide in glacial acetic acid;[5] and by the rearrangement of tertiary butyl bromide at 210–220°.[6] A number of bromides, including *iso*-

butyl bromide, have recently been prepared by the action of phosphorus tribromide on alcohols.[7]   The above procedure is a modification of one used for preparing cyclopentyl bromide.[8]

[1] Wurtz, Ann. **93**, 114 (1855).

[2] Norris, Am. Chem. J. **38**, 640 (1907).

[3] Fournier, Bull. soc. chim. [3] **35**, 623 (1906).

[4] Brunel, J. Am. Chem. Soc. **39**, 1978 (1917).

[5] Ipatiew and Ogonowsky, Ber. **36**, 1988 (1903).

[6] Faworsky, Ann. **354**, 343 (1907).

[7] Reynolds and Adkins, J. Am. Chem. Soc. **51**, 280 (1929).

[8] Adams and Noller, J. Am. Chem. Soc. **48**, 1080 (1926).

BUTYROIN

$$2C_3H_7CO_2C_2H_5 + 4Na \longrightarrow \begin{matrix} C_3H_7CONa \\ \| \\ C_3H_7CONa \end{matrix} + 2C_2H_5ONa$$

$$\begin{matrix} C_3H_7CONa \\ \| \\ C_3H_7CONa \end{matrix} \xrightarrow[\quad]{H_2SO_4} \begin{matrix} C_3H_7COH \\ \| \\ C_3H_7COH \end{matrix} \longrightarrow \begin{matrix} C_3H_7C{=}O \\ | \\ C_3H_7CHOH \end{matrix}$$
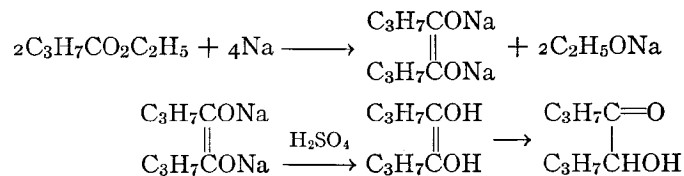
Submitted by John M. Snell and S. M. McElvain.
Checked by C. S. Marvel and M. R. Lehman.

1. Procedure

In a 3-l. three-necked, round-bottomed flask fitted with a long reflux condenser and an efficient mechanical stirrer are placed 92 g. (4 gram atoms) of clean metallic sodium and about 150 cc. of xylene. The sodium is finely powdered by heating the flask until the sodium melts and then cooling with very vigorous stirring. The cooled xylene is decanted, and the powdered sodium is thoroughly washed with four or five portions of dry, alcohol-free ether. About 1200 cc. of absolute ether is added, and the flask is fitted with a reflux condenser, a 250-cc. separatory funnel, and a mechanical stirrer (Note 1).

The stirrer is started, and 232 g. (2 moles) of purified ethyl *n*-butyrate (Note 2) is slowly run in from the separatory funnel. It is advisable to add first a portion of about 25 cc.; the heat of reaction soon causes the ether to boil; the rest of the ester is then run in at such a rate that gentle ebullition is maintained. Stirring is continued until there is no further reaction and practically all of the sodium has been converted into the voluminous yellow-white solid which begins to appear almost at once (Note 3).

The reaction flask is now surrounded by an ice bath, and the contents are vigorously stirred while a cooled solution of 210 g.

of sulfuric acid (sp. gr. 1.84) in 350 cc. of water is carefully run in from the separatory funnel. The stirrer is now removed and the flask is allowed to stand in the ice bath until the lower layer of hydrated sodium sulfate ($Na_2SO_4 \cdot 10H_2O$) has solidified. The ether solution is decanted and the sodium sulfate crystals washed with 100–200 cc. of ether.

The combined solution and washings are shaken with about 100 cc. of 20 per cent sodium carbonate solution (Note 4) and are then dried over anhydrous potassium carbonate. The ether and alcohol are removed rapidly by distillation, and the residue is fractionated under reduced pressure in a 250-cc. modified Claisen flask (Note 5). The main fraction boils at 80–86° at 12 mm.; a fraction boiling up to about 15° above the main fraction should also be collected. The low-boiling and high-boiling fractions can be refractionated for recovery of a small additional amount of butyroin. The total yield is 94–101 g. (65–70 per cent of theoretical amount). The product thus prepared is colored yellow by traces of the diketone.

2. Notes

1. For powdering the sodium a small, rapid stirrer is best; for stirring the reaction mixture, a fairly large, slower stirrer is best.

2. The ester is purified as follows: It is washed once with 10 per cent sodium carbonate solution and twice with an equal volume of saturated sodium chloride solution; it is then dried twenty-four hours over anhydrous potassium carbonate. The potassium carbonate is filtered off and the ester allowed to stand overnight with about 2 per cent of its weight of phosphorus pentoxide. The ester is then distilled through a column directly from the phosphorus pentoxide; a fraction that distils over a range of two degrees or less should be taken. Lower yields of butyroin may be obtained from less carefully purified ester.

3. Addition of the ester requires one and one-half to two hours, and the mixture should then be refluxed an hour longer.

4. Small amounts of butyric acid and dipropylglycollic acid are present in the reaction mixture.

5. The ether should be removed rapidly and the distillation should not be too slow, for long heating favors the formation of a high-boiling by-product of unknown structure at the expense of the butyroin.

6. The reaction can be run in benzene, but it is much slower than in ether.

7. Usually the amount of diketone present is negligible. The diketone may be removed by shaking the butyroin vigorously from time to time during one hour with 100 cc. of a saturated sodium bisulfite solution, washing with strong sodium chloride solution, and then redistilling.

8. These directions have been used for the following acyloins:

Propionoin b.p. 60–65°/12 mm.; 50–55 per cent yield.

Iso-butyroin b.p. 70–75°/14 mm.; 70–75 per cent yield.

Pivaloin m.p. 80–81°; b.p. 85–95°/12 mm.; 52–60 per cent yield.

3. Methods of Preparation

Aliphatic acyloins can be obtained by the saponification of the reaction product of sodium on moist ethereal solutions of acid chlorides, the first product being the di-ester of the di-enolic modification of the acyloin.[1] Of greater preparative interest, however, is the reaction between ethereal solutions of aliphatic esters and sodium [2] or potassium.[3]

[1] Klinger and Schmitz, Ber. 24, 1273 (1891); Basse and Klinger, Ber. 31, 1218 (1898); Anderlini, Gazz. chim. ital. 25, II, 51, 128 (1895); Egorova, J. Russ. Phys.-Chem. Soc. 60, 1199 (1928) [C. A. 23, 2935 (1929)].

[2] Bouveault and Locquin, Bull. soc. chim. [3] 35, 629 (1906); Feigl, Ber. 58, 2299 (1925); Corson, Benson, and Goodwin, J. Am. Chem. Soc. 52, 3988 (1930).

[3] Scheibler and Emden, Ann. 434, 265 (1923).

IX

m-CHLOROBENZALDEHYDE

$$m\text{-}NO_2C_6H_4CHO + 3SnCl_2 + 6HCl$$
$$\rightarrow m\text{-}NH_2C_6H_4CHO + 3SnCl_4 + 2H_2O$$

$$m\text{-}NH_2C_6H_4CHO + NaNO_2 + 2HCl$$
$$\rightarrow m\text{-}CHOC_6H_4N_2Cl + NaCl + 2H_2O$$

$$m\text{-}CHOC_6H_4N_2Cl$$
$$\xrightarrow[]{(CuCl + HCl)} m\text{-}CHOC_6H_4Cl + N_2$$
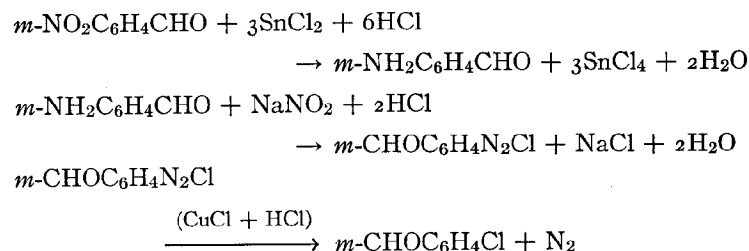
Submitted by JOHANNES S. BUCK and WALTER S. IDE.
Checked by JOHN R. JOHNSON and PAUL W. VITTUM.

1. Procedure

A SOLUTION of 450 g. (2 moles) of stannous chloride crystals (Note 1) in 600 cc. of concentrated hydrochloric acid is placed in a 3-l. beaker provided with an efficient mechanical stirrer and cooled in an ice bath. When the temperature of the solution has fallen to $+5°$, 100 g. (0.66 mole) of *m*-nitrobenzaldehyde (Note 2) is added in one portion. The temperature rises slowly at first, reaching $25-30°$ in about five minutes, then rises very rapidly to about $100°$. Stirring must be vigorous or the reaction mixture may be forced out of the beaker (Note 3). During the reaction the nitrobenzaldehyde dissolves, and an almost clear, red solution is obtained. The solution is cooled in an ice-salt mixture until the temperature has fallen to about $+2°$. During the cooling, orange-red crystals separate, and a pasty suspension results.

A 250-cc. separatory funnel is fixed so that its stem extends below the surface of the pasty suspension. A solution of 46 g. (0.67 mole) of sodium nitrite in 150 cc. of water is placed in the funnel and is slowly added to the well-stirred mixture until it

shows a positive starch-iodide test for nitrous acid. The temperature of the mixture is maintained between o and $+5°$ (Note 4) throughout the addition of the nitrite solution, which requires about ninety minutes. Usually, all but 5–8 cc. of the nitrite solution must be added before a positive test for nitrous acid appears.

During the latter part of the diazotization of the aminobenzaldehyde, a hot solution of cuprous chloride is prepared. In a 5-l. round-bottomed flask, 189 g. (0.75 mole) of powdered copper sulfate crystals and 161 g. of sodium chloride are dissolved in 600 cc. of hot water, and to this solution is added a solution of 41 g. (0.22 mole) of sodium metabisulfite ($Na_2S_2O_5$) and 27 g. (0.67 mole) of sodium hydroxide in 300 cc. of water. The final temperature of the resulting cuprous chloride solution should be about $75°$.

The diazonium solution is added to the hot cuprous chloride solution while the latter is shaken by hand but is not cooled. After the solutions are thoroughly mixed, 840 cc. of concentrated hydrochloric acid is added, and the mixture is allowed to stand overnight. The reaction mixture is steam-distilled to separate the *m*-chlorobenzaldehyde, which is collected practically completely in the first 1500 cc. of distillate. The *m*-chlorobenzaldehyde is removed from the aqueous distillate by extraction with two 150-cc. portions of ether, and the ethereal solution is dried with 10–15 g. of anhydrous calcium chloride. After being decanted from the drying agent, the ether is distilled, and the residual liquid is distilled under diminished pressure. The *m*-chlorobenzaldehyde boils at $84-86°/8$ mm., $107-109°/26$ mm. (Note 5). The yield is 70–74 g. (75–79 per cent of the theoretical amount) (Note 6).

2. Notes

1. A chemically pure grade of stannous chloride crystals ($SnCl_2 \cdot 2H_2O$) was used. Lower yields were obtained when technical stannous chloride was used.

2. A practical grade of *m*-nitrobenzaldehyde was used; m.p. $52-55°$.

3. During the vigorous reaction it is advisable to keep the cooling bath and the reaction mixture well stirred. Less satisfactory yields were obtained when the reaction was moderated by adding the nitrobenzaldehyde in several portions.

4. At temperatures below 0° the speed of diazotization is markedly decreased. Above +5° some decomposition of the diazonium salt takes place.

5. Since m-chlorobenzaldehyde is oxidized easily by atmospheric oxygen, it should be stored in a tightly corked or sealed container.

6. m-Bromobenzaldehyde can be prepared by the same general procedure, using, in place of cuprous chloride, a solution of cuprous bromide prepared from 189 g. of copper sulfate, 91 g. of sodium bromide, 41 g. of sodium metabisulfite, and 27 g. of sodium hydroxide. Instead of 840 cc. of concentrated hydrochloric acid, 200 cc. of 48 per cent hydrobromic acid is added after the diazonium solution has been mixed with the cuprous bromide. The m-bromobenzaldehyde boils at 93–98°/8 mm. The yield is 80 g. or 65 per cent of the theoretical amount (Johannes S. Buck and Walter S. Ide).

3. Methods of Preparation

m-Chlorobenzaldehyde has been prepared by the chlorination of benzaldehyde [1] and by the oxidation of m-chlorobenzyl alcohol [2] and of m-chlorotoluene.[3] It is most conveniently prepared from m-nitrobenzaldehyde through m-aminobenzaldehyde and the diazonium reaction.[4] The procedure given above is essentially that described in the patent literature.[4]

[1] Müller, Ger. pat. 30,329; 33,064 [Frdl. 1, 143, 146 (1877–87)].
[2] Mettler, Ber. 38, 2812 (1905).
[3] Law and Perkin, J. Chem. Soc. 93, 1636 (1908).
[4] Farbw. Meister, Lucius and Brüning, Ger. pat. 31,842 [Frdl. 1, 144 (1877–87)]; Erdmann and Schwechten, Ann. 260, 59 (1890); Eichengrün and Einhorn, ibid. 262, 135 (1891).

ICE

ice bath is removed, and stirring is continued for two hours at room temperature (Note 2).

The solution is then poured slowly, with constant stirring, into a mixture of 1 kg. of cracked ice and 200 cc. of concentrated hydrochloric acid in a 5-l. flask. There should be a small quantity of ice remaining after decomposition is complete. When the ice has melted, the mixture of water, precipitated dibenzoylbutane, and benzene is divided into two equal portions, and 1–1.25 l. of benzene is added to each. The solid is dissolved by shaking and gentle warming on the steam bath; the benzene layers are separated and washed, first with an equal volume of dilute sodium carbonate solution, and then with water.

The benzene solution is placed in a 5-l. flask and 3–3.5 l. of benzene is removed by distillation. The residual liquid is set aside and allowed to cool. The dibenzoylbutane crystallizes after several hours and is filtered (Note 3). The product melts at 104–107° without recrystallization (Note 4). An equal volume of ether is added to the light-brown filtrate and a second crop of crystals is obtained (Note 5).

The yield of crude product is 199–216 g. (75–81 per cent of the theoretical amount). The material may be recrystallized by dissolving it in 1 l. of hot 95 per cent ethyl alcohol. Upon cooling, crystals which melt at 106–107° separate. The yield of recrystallized product is 190–210 g.

2. Notes

1. It is very important to keep the reaction mixture cold during the addition of the acid chloride, otherwise there will be charring which will lead to a discolored product.

2. If the reaction mixture is allowed to stand at this point the yield is materially decreased.

3. Sometimes the product has a brown color. This color may be completely removed by washing the final product with a few cubic centimeters of cold ether in which the diketone is only slightly soluble.

4. The melting point of the crude product seems to be influ-

X

1,4-DIBENZOYLBUTANE

$$\begin{array}{l} CH_2CH_2COOH \\ | \\ CH_2CH_2COOH \end{array} + 2SOCl_2 \longrightarrow \begin{array}{l} CH_2CH_2COCl \\ | \\ CH_2CH_2COCl \end{array} + 2SO_2 + 2HCl$$

$$\begin{array}{l} CH_2CH_2COCl \\ | \\ CH_2CH_2COCl \end{array} + 2C_6H_6 \xrightarrow{AlCl_3} \begin{array}{l} CH_2CH_2COC_6H_5 \\ | \\ CH_2CH_2COC_6H_5 \end{array} + 2HCl$$

Submitted by Reynold C. Fuson and Joseph T. Walker.
Checked by Wallace H. Carothers and W. L. McEwen.

1. Procedure

One mole (146 g.) of adipic acid (Coll. Vol. 1, 18) previously dried over sulfuric acid in a vacuum is placed in a 1-l. round-bottomed flask equipped with a condenser, and 357 g. (217 cc., 3 moles) of thionyl chloride is added at once. The mixture is heated gently on a water bath held at a temperature of 50–60°. After about four hours, solution is complete and evolution of hydrogen chloride has ceased. The flask is now connected to a downward condenser and heated under diminished pressure by a water bath to remove any excess of thionyl chloride. The light yellow residue of adipyl chloride is ready for use.

A mixture of 300 g. (2.25 moles) of anhydrous aluminum chloride and 1500 cc. (17 moles) of benzene (dried over sodium and distilled) is placed in a 3-l. three-necked flask equipped with a mercury-sealed stirrer, a reflux condenser, and a dropping funnel. The reaction mixture is cooled in an ice bath and, with rapid stirring, the adipyl chloride is added through the dropping funnel at an *even rate* during the course of forty-five minutes (Note 1). The reaction mixture darkens slowly but does not become black. After the adipyl chloride has been added, the

enced by the quality of the aluminum chloride. That used by the checkers was of high purity; the crude product obtained always melted at 106–108°; and the melting point was not raised by one recrystallization from alcohol. Furthermore, the color of the reaction mixture got no darker than a bright orange, and the crude product was always pure white.

5. The checkers found that only 5–6 g. of material was precipitated by the addition of ether. For this reason it scarcely seems worth while to carry out this part of the procedure.

3. Methods of Preparation

Dibenzoylbutane has been prepared by the action of aluminum chloride on a mixture of benzene and adipyl chloride [1] or benzene and polymeric adipic anhydride.[2] It has also been obtained as a by-product in the action of zinc and alcohol on α, β-dibromopropiophenone.[3] The melting points recorded are 102°,[1] 105–106°,[2] and 112°.[3]

[1] Etaix, Ann. chim. phys. [7] **9**, 372 (1896).
[2] Hill, J. Am. Chem. Soc. **54**, 4105 (1932).
[3] Kohler, Am. Chem. J. **42**, 384 (1909).

XI

2,4-DINITROPHENYLHYDRAZINE

$$C_6H_3(NO_2)_2Cl + 3CH_3CO_2K + NH_2NH_2 \cdot H_2SO_4$$

$$\rightarrow C_6H_3(NO_2)_2NHNH_2 + K_2SO_4 + KCl + 3CH_3CO_2H$$
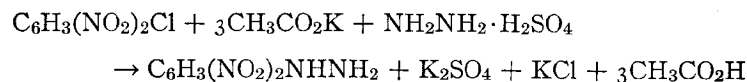
Submitted by C. F. H. Allen.
Checked by Reynold C. Fuson and Mark W. Farlow.

1. Procedure

Thirty-five grams (0.27 mole) of hydrazine sulfate (Coll. Vol. I, 302) is suspended in 125 cc. of hot water in a 400-cc. beaker and stirred by hand during the addition of 85 g. (0.87 mole) of potassium acetate (Note 1). The mixture is boiled five minutes and then cooled to about 70°; 75 cc. of alcohol is added, and the solid is filtered with suction and washed with 75 cc. of hot alcohol. The filtered hydrazine solution is saved for the next step.

In a 1-l. flask fitted with a stirrer and reflux condenser, 50.5 g. (0.25 mole) of technical 2,4-dinitrochlorobenzene is dissolved in 250 cc. of alcohol; the hydrazine solution is added, and the mixture is refluxed with stirring for an hour. Most of the product separates during the first ten minutes (Note 2); it is cooled well, filtered, and washed once with 50 cc. of warm alcohol (60°) to remove unchanged halide and then with 50 cc. of hot water. The solid weighs 30 g. and melts at 190–192° with evolution of gas (Note 3); it is pure enough for most purposes. By distilling half the alcohol from the filtrate a less pure second crop is obtained; this is recrystallized from n-butyl alcohol (30 cc. per g.) (Note 4). The total yield is 40–42 g. (80–85 per cent of the theoretical amount) (Notes 5–10).

36

2. Notes

1. An equivalent amount of sodium acetate may be substituted for the potassium acetate.

2. Considerable heat is evolved during the separation.

3. The melting point is not sharp; in the capillary tube the sample shrinks about 10° below the melting point.

4. For recrystallization, n-butyl alcohol is the best solvent in spite of the large amount required, but tetralin, pyridine, or dioxane (10 cc. per g.) may be used where large quantities are involved. Fortunately, most of the material as prepared does not need further purification.

5. Complete evaporation of the filtrate yields a gummy residue; the amount of dinitrochlorobenzene present is too small to justify recovery.

6. By substituting 10 g. of sodium hydroxide for every 35 g. of potassium acetate and boiling for five minutes without filtering the salt, a 70 per cent yield of dinitrophenylhydrazine results; the quality is not quite as good as that obtained by the use of potassium acetate.

7. A slightly higher yield is obtained by starting with hydrazine hydrate.

8. 2,4-Dinitrophenylhydrazine is used in qualitative organic analysis for preparing solid derivatives of carbonyl compounds.[1,4]

9. By this procedure 2,6-dinitrophenylhydrazine can be prepared from 2,6-dinitrochlorobenzene; picryl chloride gives 2,4,6-trinitrophenylhydrazine.

10. These directions have been used equally successfully with twice, and with five times, the amounts specified.

3. Methods of Preparation

2,4-Dinitrophenylhydrazine has been prepared from hydrazine hydrate and 2,4-dinitrochlorobenzene[2,4] or 2,4-dinitrobromobenzene,[3] and from the same halogen compounds and hydrazine acetate.[1]

[1] Allen, J. Am. Chem. Soc. 52, 2955 (1930).
[2] Purgotti, Gazz. chim. ital. 24, I, 555 (1894).
[3] Curtius and Dedichen, J. prakt. chem. [2] 50, 258 (1894).
[4] Brady and Elsmie, Analyst 51, 77 (1926); Brady, J. Chem. Soc. 757 (1931).

XII

DIPHENYL-TRIKETONE

$C_6H_5COCH_2COC_6H_5 + 2Br_2$

$\rightarrow C_6H_5COCBr_2COC_6H_5 + 2HBr$

$C_6H_5COCBr_2COC_6H_5 + CH_3CO_2Na + 2H_2O$

$\rightarrow C_6H_5COC(OH)_2COC_6H_5 + 2NaBr + 2CH_3CO_2H$

$C_6H_5COC(OH)_2COC_6H_5$

$\xrightarrow{\text{Heat}} C_6H_5COCOCOC_6H_5 + H_2O$
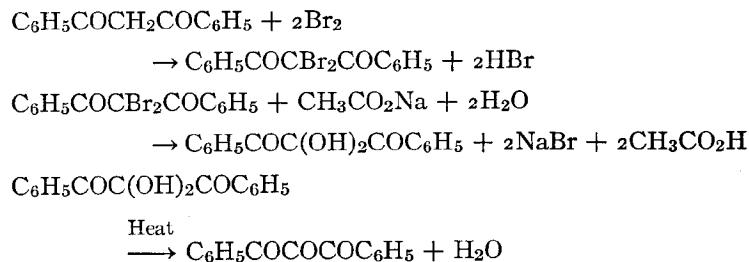
Submitted by Lucius A. Bigelow and Roy S. Hanslick.
Checked by W. W. Hartman and Lloyd A. Smith.

1. Procedure

A. Dibenzoyldibromomethane: In a 1-l. three-necked flask equipped with a mechanical stirrer, a dropping funnel, and a thermometer, are placed 56 g. (0.25 mole) of dibenzoylmethane (Coll. Vol. I, 199) and 14 cc. of chloroform. The flask is surrounded by an ice bath, the stirrer is started, and a solution of 28.5 cc. (88 g., 0.55 mole) of dry bromine (Note 1) in 230 cc. of chloroform is added slowly from the dropping funnel during a period of about thirty minutes. The temperature of the mixture should not exceed 15° during the bromination; the hydrogen bromide evolved is continuously removed by aspirating a gentle stream of air over the surface of the solution. After all the bromine has been added, stirring is continued for about fifteen minutes. The solution is then transferred to a distilling flask, and the solvent is completely removed under diminished pressure at room temperature (Note 2). The slightly colored residue is crystallized from 125 cc. of hot 95 per cent ethyl alcohol. The dibenzoyldibromomethane is obtained in the form of white crystals melting at 94–95°. The yield is 72.4 g. (76 per cent of the theoretical amount) (Note 3).

B. Diphenyl Triketone Hydrate: A solution of 34.3 g. (0.42 mole) of fused sodium acetate in 142 cc. of hot glacial acetic acid is prepared in a 1-l. round-bottomed flask; 72.4 g. (0.19 mole) of dibenzoyldibromomethane is added, and the mixture is refluxed until the precipitation of sodium bromide ceases (one and one-half to two hours). The mixture is then cooled to room temperature and diluted with 150–200 cc. of water with constant shaking to dissolve the inorganic salt and to precipitate the triketone hydrate, which separates as a white, curdy mass (Note 4). This is separated by filtration, washed well with water, and dried in an oven at 60°. The melting point varies from 65 to 90°, depending upon the extent of dehydration that occurs during the drying operation. The yield is 41.5 g. (86 per cent of the theoretical amount based on the dibenzoyldibromomethane).

C. Diphenyl Triketone: The 41.5 g. (0.16 mole) of triketone hydrate is distilled in vacuum from a Claisen flask heated by means of a sand bath. A distilling flask is used as a receiver, and no condenser is necessary. The neck of the receiving flask must be warmed, however, to prevent clogging of the apparatus by crystallization of the distillate. The anhydrous triketone distils at 174–176°/2 mm. as a reddish oil that solidifies to a light yellow, crystalline mass. This is dissolved in 70 cc. of hot ligroin (b.p. 90–120°); it separates on cooling in light yellow needles which melt at 68–70°. The yield is 35 g. (91 per cent of the theoretical amount based on the triketone hydrate; 59 per cent based on the dibenzoylmethane) (Note 5).

2. Notes

1. The bromine should be dried by washing it with concentrated sulfuric acid.

2. If the solvent is removed by heat at ordinary pressure, there is a decrease both in the yield and the purity of the product.

3. If the recrystallization is omitted, a lower yield of the triketone hydrate is obtained.

4. If the hydrate separates in part in an oily condition, it may be dissolved in a small amount of glacial acetic acid and reprecipitated with an equal volume of water.

5. The triketone is hygroscopic and must be kept in a vacuum desiccator or sealed tube.

3. Methods of Preparation

The two general methods known for the preparation of diphenyltriketone involve the treatment of dibenzoylmethane with bromine [1] and with oxides of nitrogen. [2] De Neufville and v. Pechmann, who originated the first method, recommended [1] conversion of the diketone to dibenzoylbromomethane and transformation of this to the acetate and then to dibenzoylbromocarbinol acetate which was split to the triketone. This sequence has lately been used with success by Kohler and Erickson [3] to prepare the triketone in good yields, but the present method, mentioned but not described by De Neufville and v. Pechmann, [1] is simpler and more direct.

[1] De Neufville and v. Pechmann, Ber. **23**, 3375, 3379 (1890).
[2] Wieland and Bloch, Ber. **37**, 1524, 1531 (1904).
[3] Kohler and Erickson, J. Am. Chem. Soc. **53**, 2301 (1931).

XIII

ETHOXYACETIC ACID AND ETHYL ETHOXYACETATE

$$ClCH_2CO_2H + 2C_2H_5ONa$$
$$\rightarrow C_2H_5OCH_2CO_2Na + NaCl + C_2H_5OH$$

$$C_2H_5OCH_2CO_2Na + HCl$$
$$\rightarrow C_2H_5OCH_2CO_2H + NaCl$$

$$C_2H_5OCH_2CO_2H + C_2H_5OH$$
$$\rightarrow C_2H_5OCH_2CO_2C_2H_5 + H_2O$$
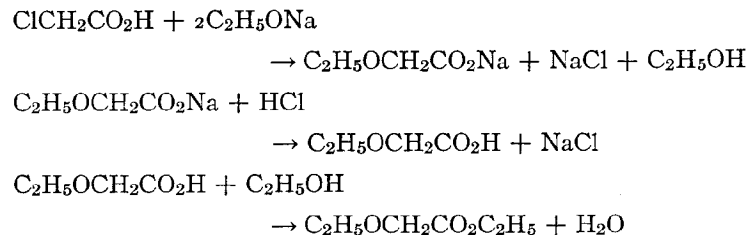
Submitted by REYNOLD C. FUSON and BRUNO H. WOJCIK.
Checked by C. R. NOLLER and J. J. GORDON.

1. Procedure

A. Ethoxyacetic Acid: In a 2-l. round-bottomed flask provided with a reflux condenser (70–80 cm.) is placed 1250 cc. of absolute ethyl alcohol (Note 1). Through the condenser tube 69 g. (3 gram atoms) of metallic sodium is added rapidly enough to keep the alcohol refluxing gently. When the sodium has completely dissolved, a solution of 142 g. (1.5 moles) of chloroacetic acid in 180 cc. of absolute alcohol is added slowly in 20-cc. portions to the sodium ethylate solution (Note 2). After all of the acid has been added, the mixture is heated gently for ten minutes. The excess alcohol is removed as completely as possible by distilling from a steam bath and finally by passing steam into the residue. The aqueous solution is cooled, and 140 cc. (1.7 moles) of concentrated hydrochloric acid (sp. gr. 1.19) is added. The sodium chloride is removed by filtration with suction and is washed with two 50-cc. portions of ether. The original filtrate is saturated with dry sodium sulfate (30–35 g.) and is then extracted with the ether which was used for washing the precipitate, together with an additional 100 cc. of ether. The ether is

separated from the aqueous layer, and the latter is extracted four times with 100-cc. portions of fresh ether. The ether is removed by distillation from a steam bath, and the residue is distilled under reduced pressure, using a 500-cc. Claisen flask equipped with a 500-cc. receiver. The acid boils at 109–111°/17–18 mm. and weighs 115–116 g. (73–74 per cent of the theoretical amount). By redistilling the low-boiling fraction and collecting the portion boiling at 150–210°, there is obtained an additional 7–10 g. of material which is chiefly ethoxyacetic acid and may be combined with the main fraction for conversion to the ester.

B. Ethyl Ethoxyacetate: The ethoxyacetic acid, which should amount to about 125 g. (1.2 moles), is placed in a 750-cc. Erlenmeyer flask containing 230 cc. (3.9 moles) of absolute ethyl alcohol. The flask is set in a pan filled with cold water (Note 3), and dry hydrogen chloride is passed into the mixture. After the mixture becomes saturated (Note 4) it is allowed to stand twenty-four hours to insure the completion of the reaction at room temperature (Note 5). The solution is cooled, and a saturated solution of sodium carbonate is added cautiously and with stirring to avoid excessive foaming. The addition is continued until the mixture is faintly alkaline to litmus; an excess of sodium carbonate lowers the yield and should be avoided. The ester is extracted with four 100-cc. portions of ether; the extract is dried with 25 g. of anhydrous potassium carbonate, and the ether is distilled from a steam bath. The residue is distilled at ordinary pressure. The yield of ester boiling at 153–155° is 110–115 g. (55–58 per cent of the theoretical amount based on the chloroacetic acid, or 69–72 per cent based on the ethoxyacetic acid).

2. Notes

1. Alcohol dried over quicklime is satisfactory.
2. The chloroacetic acid should be added fast enough to keep the solution boiling.
3. Heat is evolved during the reaction, and, unless the flask

is kept in cold water, an insufficient amount of hydrogen chloride will be absorbed. This lowers the yield.

4. A considerable quantity of dry hydrogen chloride is required. The gas should be allowed to bubble through the mixture for at least five hours.

5. The yield seems to be limited by the equilibrium between the acid and ester. At least twenty-four hours is required to reach this equilibrium.

3. Methods of Preparation

Ethoxyacetic acid was first prepared by Heintz [1] by the reaction of chloroacetic acid with sodium ethylate. The procedure described above is essentially that of Sommelet. [2] Ethoxyacetic acid has also been prepared by hydrolysis of ethoxyacetonitrile with concentrated hydrochloric acid [3] and by the action of excess sodium ethylate on 1,1,1,2-tetrachlorethane and on α,β-dichlorovinyl ethyl ether. [4] A recent patent reports a synthesis from diethyl ether and carbon dioxide [5] at high pressure.

Ethyl ethoxyacetate has been prepared by the action of ethyl iodide on sodium ethoxyacetate, [6] of sodium ethylate on ethyl chloroacetate, [7] of alcohol on crude diazoacetic ester, [8] and by the alcoholysis of ethoxyacetonitrile using alcoholic hydrogen chloride. [3,9]

[1] Heintz, Ann. Physik. 109, 331 (1860); 111, 555 (1860).
[2] Sommelet, Ann. chim. phys. [8] 9, 489 (1906).
[3] Gauthier, Ann. chim. phys. [8] 16, 304 (1909).
[4] Geuther and Brockhoff, J. prakt. Chem. [2] 7, 113 (1873).
[5] Dreyfus, Fr. pat. 671,103 [C. A. 24, 1867 (1930)].
[6] Heintz, Ann. 129, 40 (1864).
[7] Henry, Ber. 4, 706 (1871).
[8] Curtius, J. prakt. Chem. [2] 38, 424 (1888).
[9] Sommelet, Ann. chim. phys. [8] 9, 501 (1906).

tion is carried out in two 3-l. flasks coated with wax (Note 5) which are shaken and kept cold by immersion in iced water. The temperature of the acid should not be allowed to rise above 20–25°.

The ice-cold solution of fluoboric acid is then poured into the diazonium solution, which has been cooled below 0°. The temperature should remain under 10° during the addition, which is carried out fairly rapidly. Powerful stirring is required to agitate the thick magma at this stage (Note 1). After twenty to thirty minutes' stirring, the brown-colored mass is filtered with suction, using two 24-cm. Büchner funnels. The yellowish crystalline solid is washed with iced water (about 800 cc.), with methyl alcohol (800 cc.), and with commercial ethyl ether (900 cc.). It should be sucked as free as possible from liquid after each washing. This washing is important, since it improves the stability of the product (Note 6).

The light-brown, fluffy salt is spread out on absorbent paper overnight in a current of air (a table placed near a hood is effective), and is then placed in a 12-l. flask (Note 7). This is connected by a wide bent tube through a long, wide condenser to three 2-l. Erlenmeyer flasks arranged in series and immersed in ice-salt mixtures. The last flask is fitted with an exit tube leading to a good hood, to carry off the voluminous fumes of boron fluoride, or to an absorption system containing ice and water or soda solution. The solid is heated gently at one point near its surface with a small flame until decomposition begins. The flame is then withdrawn and the reaction allowed to continue spontaneously as long as it will. If the reaction becomes too vigorous, it may be necessary to cool the flask by rubbing it with a piece of ice (Note 8). The mixture is heated cautiously from time to time, as may be necessary to keep the reaction going. At the last it should be heated vigorously until no more fumes of boron fluoride are evolved. The last traces of fluorobenzene may be removed from the reaction flask by applying a slight suction to the receiving flask.

The combined distillate is separated from any phenol which may have settled out. It is washed four or five times with 10

XIV

FLUOROBENZENE

$$C_6H_5NH_2 \cdot HCl + HNO_2 \rightarrow C_6H_5N_2Cl + 2H_2O$$

$$C_6H_5N_2Cl + HBF_4 \rightarrow C_6H_5N_2BF_4 + HCl$$

$$C_6H_5N_2BF_4 \rightarrow C_6H_5F + N_2 + BF_3$$

Submitted by D. T. Flood.
Checked by W. W. Hartman and J. R. Byers.

1. Procedure

A mixture of 1350 cc. of water and 1650 cc. (20 moles) of concentrated hydrochloric acid (sp. gr. 1.19) is placed in a large glass jar (30 by 30 cm.) or a 40-l. crock and stirred mechanically (Note 1) while strongly cooled by an ice-salt mixture. Two thousand and seventy-five grams (16 moles) of aniline hydrochloride (Note 2) and a solution of 1200 g. (17 moles) of sodium nitrite in 1500 cc. of water are made ready. When the temperature of the acid has reached 5° or below, about one-third of the aniline hydrochloride is added to it, and diazotization is begun by the slow addition of the nitrite solution, the temperature being held below 7°. Additional aniline hydrochloride is added from time to time in such amounts that an excess of crystals is always present. The entire amount may be added by the time that half of the nitrite has been added. The diazotization is stopped when a positive test for free nitrous acid is obtained with potassium iodide starch paper. This should require nearly all of the nitrite solution.

Fluoboric acid is made concurrently with the diazotization by the addition, in small amounts, of 1000 g. (16.2 moles) of boric acid (u. s. p. crystals) to 2150 g. (65 moles) of 60 per cent hydrofluoric acid. (Handle with care; Note 3) (Note 4). The addi-

per cent sodium hydroxide solution until the washings are almost colorless and then once with water (Note 10). It is dried by shaking with crushed calcium chloride, and then distilled from a 2-l. flask through a short column at a fairly rapid rate. The first runnings may contain a little water and can be further dried. The product is a colorless liquid with an odor resembling that of benzene. The yield of fluorobenzene boiling at 84–85° is 780–870 g. (50–56 per cent of the theoretical amount) (Note 11).

2. Notes

1. A slow-speed, paddle stirrer with several blades is preferable because of the large amount of suspended matter present at several times in the process. A stirrer of wood or metal protected with acid-proof paint is satisfactory, although the paint does not last well. Rubber-covered stirrers may also be used.

2. Aniline (1485 g.) and hydrochloric acid (3000 cc.) without any added water can be used in place of the aniline hydrochloride, water, and acid. The separation of aniline hydrochloride in a hard cake on the side of the jar, however, leads to difficulty in cooling and stirring.

3. Hydrofluoric acid in contact with the skin produces extremely painful burns. It is therefore necessary to use every precaution to protect exposed parts of the body, especially the hands and eyes. Long acid-resisting rubber gloves and rubber goggles should be worn. If one is burned by the acid, the burned surface, which has become white, is held under running water until the natural color returns. Prompt application of a paste made from magnesium oxide and glycerin is said to be helpful in preventing burns from becoming serious [Fredenhagen and Wellmann, Angew. Chem. 45, 537 (1932)].

4. A corresponding amount of 48 per cent or of 52 per cent hydrofluoric acid may also be used. The quantities given represent an excess of fluoboric acid. A larger excess may be taken but does not appreciably influence the yield. Fluoboric acid (40 per cent) is now a commercial product.

5. The fluoboric acid may be more conveniently prepared in

a lead jar with mechanical stirring. Such a jar can be readily made from sheet lead by bending to shape and soldering. A piece of iron rod fitted into some narrow lead pipe and having a strip of lead soldered on at the bottom makes an effective stirrer, and a wooden lid covered on the under side with a sheet of lead may serve as a cover. The solder is slowly attacked by the acid and can be protected with an acid-proof grease. The fluoboric acid is siphoned from the jar by means of a rubber tube.

6. The presence of moisture affects the stability of benzene diazonium fluoborate. The moist product, if allowed to stand packed together, may undergo spontaneous decomposition. In damp weather, when spread out on paper, it becomes dark and slowly decomposes. The same result is observed if it is not sufficiently washed.

7. The decomposition may also be carried out in two batches from 5-l. flasks. It is more easily controlled in this way.

8. Normally the decomposition proceeds smoothly under the intermittent heating. If the salt is moist, however, the reaction proceeds more rapidly, and, unless the flask is cooled, it may pass beyond control (see Note 6).

9. On account of the large volume of gas evolved, all connections should be made with wide tubing.

10. Since the density of fluorobenzene is about 1.025, it is important that the right strength of caustic soda solution be used in order to effect clean separation of the two layers. Before washing with water, the caustic soda should be completely removed.

11. Preparations have been successfully carried out with two times and three times the quantities here stated and with almost proportionate yields. A large stoneware filter in addition to the lead pot (Note 5) is then desirable to handle the larger quantities of material.

12. Technical grades of all raw materials are employed.

3. Methods of Preparation

The above method for the preparation of fluorobenzene is adapted from that of Balz and Schiemann.[1] Fluorobenzene has

also been prepared in 50 per cent yield from benzene diazopiperi-
dide and hydrofluoric acid,[2] although the reaction is said to pro-
ceed violently and cannot be used with quantities greater than
10–15 g. of piperidide.   Other methods depend on the formation
of benzene diazonium fluoride and its decomposition into fluoro-
benzene when heated.[3,4,5] The claim of Valentiner and
Schwarz [3] that this reaction proceeds in aqueous solution could
not be substantiated by the author.

[1] Balz and Schiemann, Ber. **60**, 1188 (1927).

[2] Wallach, Ann. **235**, 258 (1886); Wallach and Heusler, Ann. **243**, 219 (1888).

[3] Valentiner and Schwarz, Ger. pat. 96,153 [Frdl. **5**, 910 (1897–1900); Chem.
Zentr. I, 1224 (1898)].

[4] Holleman and Beekman, Rec. trav. chim. **23**, 225 (1904).

[5] Swarts, ibid. **27**, 120 (1908).

XV

p-FLUOROBENZOIC ACID

$$C_2H_5O_2CC_6H_4NH_2 + NaNO_2 + 2HCl$$
$$\rightarrow C_2H_5O_2CC_6H_4N_2Cl + NaCl + 2H_2O$$
$$C_2H_5O_2CC_6H_4N_2Cl + HBF_4$$
$$\rightarrow C_2H_5O_2CC_6H_4N_2BF_4 + HCl$$
$$C_2H_5O_2CC_6H_4N_2BF_4 \rightarrow C_2H_5O_2CC_6H_4F + N_2 + BF_3$$
$$C_2H_5O_2CC_6H_4F + H_2O \rightarrow FC_6H_4CO_2H + C_2H_5OH$$
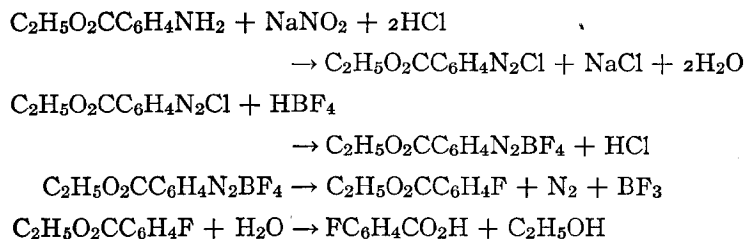
Submitted by G. SCHIEMANN and W. WINKELMÜLLER.
Checked by W. W. HARTMAN, J. R. BYERS, and J. B. DICKEY.

1. Procedure

IN a 5-l. round-bottomed flask are placed 165 g. (1 mole) of ethyl *p*-aminobenzoate (Coll. Vol. 1, 235), 300 cc. of water, and 204 cc. (2.5 moles) of concentrated hydrochloric acid (sp. gr. 1.19) (Note 1). This mixture is warmed on a steam bath for an hour with occasional shaking. The flask containing the resulting white paste of *p*-carbethoxyaniline hydrochloride is placed in an ice-salt bath and cooled to 0°. The mixture is stirred mechanically, and a solution of 72.6 g. (1 mole) of 95 per cent sodium nitrite in a minimum quantity of water is run in slowly while the temperature is kept below 7°. The diazotization is complete when a faint positive test for nitrous acid with starch-iodide paper persists for ten minutes.

While the diazotization is in process, 68 g. (1.1 moles) of boric acid is dissolved in 133 g. (4 moles) of 60 per cent hydrofluoric acid (Note 2) in a beaker coated with paraffin-wax. The temperature is kept below 25° to avoid melting the paraffin-wax (Note 3).

The ice-cold fluoboric acid solution (Note 4) is added rather rapidly, with stirring, to the diazonium solution while the temperature is kept below 10°. A thick paste of *p*-carbethoxybenzenediazonium fluoborate precipitates; stirring is continued for twenty to thirty minutes. The solid is filtered on an 18.5-cm. Büchner funnel and washed consecutively with 300 cc. of cold water, 300 cc. of commercial methyl alcohol, and 200 cc. of commercial ether; it is sucked as dry as possible between washings. The fluoborate is then dried over concentrated sulfuric acid (sp. gr. 1.84) in a vacuum desiccator (Note 5). The yield of the dried fluoborate is 198–205 g. (75–78 per cent of the theoretical amount); the decomposition point is 93–94°.

The thermal decomposition may be conveniently carried out in a 2-l. distilling flask. A second distilling flask of 1-l. capacity is connected directly to the side arm of the first to serve as a receiver. Attached to the side arm of the receiver is a rubber tube arranged to lead the escaping gases over 2 l. of water in a 5-l. round-bottomed flask. The boron trifluoride dissolves in the water, and the other gases are led into a good hood (Note 6). The *p*-carbethoxybenzenediazonium fluoborate is placed in the decomposition flask and heated at its upper edge with a Bunsen flame. When the white fumes of boron trifluoride commence to appear, the flame is removed and the decomposition is permitted to proceed spontaneously. The heat is applied as necessary, and finally the flask is strongly heated to completely decompose and melt the solid. Some of the ethyl ester, b.p. 105–106°/25 mm., of *p*-fluorobenzoic acid is collected in the receiver, where it is carried by the gases, but the larger part is left in the decomposition flask. The ester is washed from the decomposition flask and the receiver with ether, and the ether is distilled from a steam bath. The residue is refluxed for one hour on a steam bath with a solution of 56 g. (1 mole) of potassium hydroxide in 80 cc. of 95 per cent ethyl alcohol and 120 cc. of water. The solution is then filtered while still hot. The *p*-fluorobenzoic acid is precipitated by adding concentrated hydrochloric acid to the hot filtrate until the mixture is acid to Congo paper. After the mixture has cooled, the solid is filtered off and allowed to dry.

To purify the *p*-fluorobenzoic acid, it is dissolved in hot dilute potassium carbonate solution (40 g. in 400 cc.) and the solution is treated with norite (decolorizing carbon) and filtered hot. Hydrochloric acid is added with stirring to precipitate the fluorobenzoic acid, which is then cooled, filtered, and dried.

When 85 g. (0.32 mole) of *p*-carbethoxybenzenediazonium fluoborate is thus decomposed, there is obtained 38–40 g. of *p*-fluorobenzoic acid (84–89 per cent of the theoretical amount, based on the fluoborate; 63–69 per cent, based on the ester of *p*-aminobenzoic acid). The melting point of the purified acid is 186°. The crude acid melts at 183–184°.

2. Notes

1. Ethyl *p*-aminobenzoate may be prepared by adding 274 g. (2 moles) of *p*-aminobenzoic acid to 1400 g. of ethyl alcohol which has been saturated with dry hydrogen chloride, and then refluxing the mixture for twenty-four hours. The reaction mixture is poured into water, neutralized with sodium carbonate, and the insoluble ester is separated by filtration. The yield is 80 per cent of the theoretical amount.

2. Hydrofluoric acid produces exceedingly painful burns when it comes in contact with the skin. (See Note 3, p. 48.)

3. A lead jar may be conveniently used instead of the beaker lined with paraffin-wax. By using a lead stirrer of the usual shape, mechanical stirring may be substituted. The stirrer should be thrust through a hole in a lead cover of sufficient size to prevent spattering of the hydrofluoric acid.

4. Fluoboric acid (40 per cent) is now a commercial product. Two hundred grams of this acid may be used in the above method.

5. It is very important that the fluoborate be dry. If this solid is wet, the decomposition is very violent, tar is formed, and the yield is lowered.

6. A simple apparatus for the decomposition is a 2-l. round-bottomed decomposition flask connected by means of a wide (2-cm.) bent tube to a 1-l. flask containing 500 cc. of water. The gases from the second flask are led to a good hood.

3. Methods of Preparation

p-Fluorobenzoic acid has been prepared by the oxidation of *p*-fluorotoluene with chromic acid in dilute sulfuric acid at 160°;[1] by the oxidation of *p*-fluorotoluene with potassium permanganate;[2] by heating *p*-carboxybenzenediazonium chloride with fuming hydrofluoric acid;[3] by the oxidation of *p*-fluorobenzaldehyde;[4] by the oxidation of *p,p'*-difluorostilbene with potassium permanganate;[5] by the oxidation of 4,4'-difluorobiphenyl with nitric acid;[6] and by the oxidation of 4,4'-difluorobiphenyl with chromic acid.[7] The above method is adapted from that of Balz and Schiemann.[8]

[1] Wallach, Ann. **235**, 263 (1886).

[2] Slothouwer, Rec. trav. chim. **33**, 324 (1914); Holleman, ibid. **25**, 332 (1906); Holleman and Slothouwer, Proc. K. Acad. Wetensch. Amsterdam **19**, 497, 500 (1910) [Chem. Zentr. I, 74 (1911)]; Koopal, Rec. trav. chim. **34**, 152 (1915); Meyer and Hub, Monatsh. **31**, 933 (1910).

[3] Schmitt and Gehren, J. prakt. Chem. [2] **1**, 394 (1870); Paterno and Oliveri, Gazz. chim. ital. **12**, 87 (1882).

[4] Rinkes, Chem. Weekblad **16**, 206 (1919).

[5] Meyer and Hoffmann, Monatsh. **38**, 154 (1917).

[6] Th. van Hove, Chem. Zentr. I, 884 (1927).

[7] Schiemann and Bolstad, Ber. **61**, 1403 (1928); Schiemann and Roselius, Ber. **62**, 1805 (1929).

[8] Balz and Schiemann, Ber. **60**, 1189 (1927).

XVI

METHOXYACETONITRILE

$$NaCN + CH_2O + H_2O \rightarrow HOCH_2CN + NaOH$$

$$HOCH_2CN + (CH_3)_2SO_4 + NaOH$$

$$\rightarrow CH_3OCH_2CN + CH_3NaSO_4 + H_2O$$
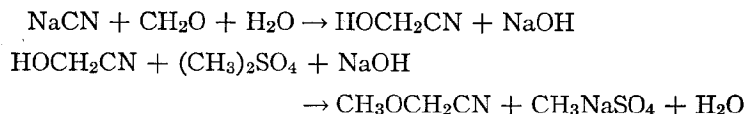
Submitted by J. A. SCARROW and C. F. H. ALLEN.
Checked by REYNOLD C. FUSON and CHARLES F. WOODWARD.

1. Procedure

THIS preparation must be carried out in a hood having good suction. Dimethyl sulfate has a high vapor pressure in spite of its high boiling point and is very poisonous. Ammonia is a specific antidote and should be kept on hand to destroy any of the ester accidentally spilled. It is advisable to wash the hands in dilute ammonium hydroxide frequently.

In a 1-l. three-necked, round-bottomed flask, fitted with a stirrer, a thermometer for reading low temperatures (Note 1), and a dropping funnel, are placed 98 g. (2 moles) of pulverized sodium cyanide (Note 2) and 200 cc. of water. The stirrer is started, and 60 g. of paraformaldehyde (2 moles) (Note 3) is added in small quantities until the temperature rises to 20–25° and the sodium cyanide has dissolved. The flask is then surrounded by a freezing mixture, and the temperature is kept below 25° during the introduction of the remaining paraformaldehyde.

Two hundred cubic centimeters (270 g., 2.1 moles) of technical dimethyl sulfate is placed in the dropping funnel, and when the temperature inside the flask has dropped to 13°, a 20- to 30-cc. portion of the sulfate is added. An exothermic reaction should set in; the ice bath is removed, if necessary, to get the reaction

to start (Note 4). When the temperature begins to fall, the remainder of the dimethyl sulfate is admitted at such a rate as to keep the temperature at 12–15°; this takes at least twenty minutes. When the addition is complete the mixture is stirred an additional forty minutes; during this time the temperature will drop to about 5°. The stirrer is stopped, and the oily, upper layer is separated at once (Note 5). The lower, aqueous layer is returned to the flask and methylated as before with a second 200-cc. portion of dimethyl sulfate (Note 6).

The oily, upper layer is dried with 10 g. of anhydrous sodium sulfate (Note 7) and is distilled under diminished pressure. For this purpose an efficient fractioning column (Note 8) is used. The portion boiling below 70° at 15 mm. is mainly methoxyacetonitrile, and weighs 60–70 g. The upper layer from the second methylation is treated in a similar manner; the distillate weighs 55–60 g. The residue in the distilling flask is dimethyl sulfate and is used in a subsequent run (Note 9).

The crude fractions are combined and distilled at atmospheric pressure through a good column; about 95 per cent distils at 118–122° as a colorless liquid. The methoxyacetonitrile so prepared weighs 100–110 g. (70–77 per cent of the theoretical amount).

2. Notes

1. A 30- to 35-cm. thermometer reading from −50 to +50° is most convenient since the graduations used are then outside the flask.

2. Potassium cyanide gives poorer results.

3. An equivalent amount of commercial formalin solution can be used with equally good results, provided allowance is made for the volume of water—the total volume must not exceed 200 cc.

4. The reaction usually starts immediately; occasionally it does not start until the mixture becomes warm.

5. If the mixture is allowed to stand, the temperature rises to 40–50°, a red color develops, and the yield drops to almost nothing.

6. Recovered dimethyl sulfate can be used without purification.

7. No drying agent is completely satisfactory; sodium sulfate does the least harm.

8. The authors found a Glinsky column most satisfactory. A capillary tube reaching to the bottom of the flask for the admission of air is essential to prevent bumping. In the redistillation a piece of porous plate is sufficient for this purpose.

9. The density of the residual liquid in two runs was found to be 1.31, 1.32. The pure ester has a density of 1.35.

10. This procedure is based on the results of thirty-four runs.

3. Methods of Preparation

This method is a modification of Robinson's [1] adaptation of that of Polstorff and Meyer.[2] Methoxyacetonitrile has been made by methylating hydroxyacetonitrile with dimethyl sulfate;[1,2,3] by treatment of copper, mercury, or silver cyanide with chloromethyl ether;[4] and by dehydration of methoxyacetamide with phosphorus pentoxide.[5]

[1] Pratt and Robinson, J. Chem. Soc. **123**, 748 (1923).

[2] Polstorff and Meyer, Ber. **45**, 1911 (1912).

[3] Rule, J. Chem. Soc. **113**, 9 (1918); Slater and Stephen, ibid. **117**, 314 (1920); Malkin and Robinson, ibid. **127**, 372 (1925); Dufraisse and Chaux, Bull. soc. chim. **39**, 443 (1926).

[4] Gauthier, Ann. chim. phys. [8] **16**, 302 (1909); Wedekind, Ber. **36**, 1383 (1903)

[5] Kilpi, Z. physik. Chem. **80**, 165 (1912); **86**, 662 (1914).

XVII

METHYL IODIDE

$$3CH_3OH + PI_3 \rightarrow 3CH_3I + H_3PO_3$$
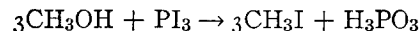
Submitted by HAROLD S. KING.
Checked by LOUIS F. FIESER.

1. Procedure

IODINE is slowly washed by means of condensed liquid into a mixture of methyl alcohol and phosphorus. The apparatus employed by the author, Fig. 1, is rendered more flexible by the use of a three-necked flask, as shown in Fig. 2, and a further improvement is in the provision of a side tube for the addition of iodine to the separatory funnel, A (Note 1). In the following description reference is made to the simpler apparatus, Fig. 1; the changes required for the modified assembly will be obvious.

The cylindrical separatory funnel A has a volume of 1200 cc. and holds 2 kg. (15.75 gram atoms) of iodine crystals (Note 2). A piece of perforated platinum foil B, or a loose plug of glass wool, is placed in the bottom to prevent clogging of the stopcock by iodine crystals or solid impurities. Stopcock C is as large as 5 mm. in bore as a further precaution. For the production of up to 4 kg. of methyl iodide, a 5-l. round-bottomed Pyrex flask D is used (Note 3). It is partly submerged in a water bath. Tube E, fitted into the reaction flask by a rubber stopper, is at least 2.5 cm. in internal diameter in order to allow the vapor to rise without interrupting the return of the excess distillate. Tube F is 4 cm. in diameter to allow for preliminary condensation. A space (13 cm.) is left above stopcock G as a reservoir for the distillate. Stopcock G has a bore of 2 or 3 mm. (Note 4). The bottom of the tube from this stopcock is flush with the bottom of the rubber stopper to the iodine container, so that the

liquid will flow down the sides of the container instead of forming a channel through the middle of the iodine. Condenser H, 2.5 cm. in diameter and at least 200 cm. long, is attached by a rubber stopper and is well cooled with a strong stream of water (Notes 5 and 6).

In container A are placed 2 kg. of iodine, no crystals being allowed to fall below the platinum foil or glass wool. The iodine is covered with part of 2000 cc. (50 moles) of methanol (Note 7), the rest of which is added to 200 g. each of red and yellow phosphorus (12.8 gram atoms) in reaction flask D. The apparatus is assembled as illustrated in Fig. 1. The water bath is heated to 70–75°; stopcock G is opened wide and stopcock C part way to allow the solution of iodine to flow slowly into the reaction flask. By the time that all the alcohol has been added, enough methyl iodide will have been formed to start the refluxing. Stopcock C is then opened wide and stopcock G partly closed so that only a small stream of methyl iodide flows through the iodine container. The temperature is adjusted so that little of the reflux flows back through tube E. This will require the progressive lowering of the water bath
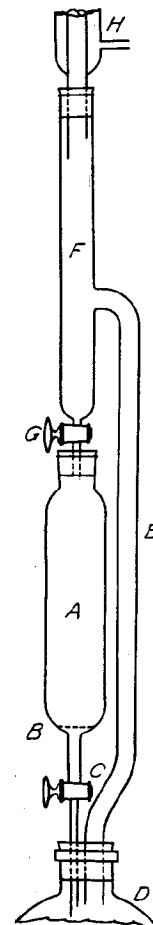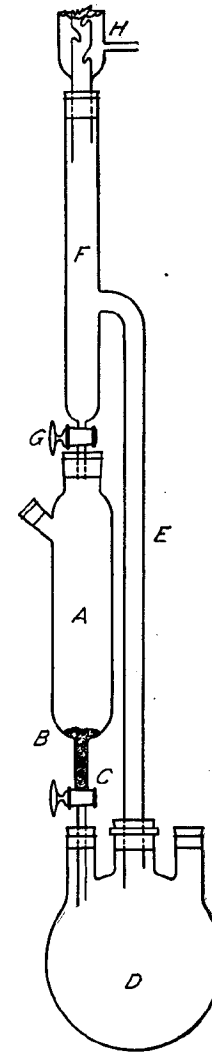
FIG. 1.

FIG. 2.

temperature as the reaction proceeds (Note 8); a temperature of about 55° is sufficient to promote even boiling after the first portion of iodine has been introduced. If for any reason refluxing becomes too violent, both stopcocks are closed. When the reaction has been brought under control, stopcock G is partly opened and then stopcock C part way, until any liquid in A has run out, after which C is opened wide. When all the iodine has been extracted (about two and one-half hours) both stopcocks are closed, the separatory funnel is lowered with a rotary motion, filled with a second charge of 2 kg. (15.75 gram atoms) of iodine, and raised to its former position. Stopcock C is opened wide and stopcock G part way as before.

After the extraction of this second charge of iodine, the flask is cooled, and a condenser arranged for downward distillation is fitted in place of the special apparatus. To the lower end of the condenser is tightly attached an adapter dipping under a slush of ice and water. When all the methyl iodide has distilled (b.p. 40–42.5°), it is separated from the water, dried by shaking with anhydrous calcium chloride, filtered through glass wool, stored for use in a sealed flask or tubes and kept in the dark (Note 9). The yield is 4150–4250 g. (93–95 per cent of the theoretical amount based on iodine), and the crude product is colorless and sufficiently pure for many purposes. Redistillation gives, in 95.5 per cent yield, a product boiling at 41.0–42.0°. Because of the high vapor pressure of methyl iodide, special precautions should be taken to prevent loss of material. Two different devices that have been found satisfactory are described in Notes 10 and 11.

The discoloration of purified methyl iodide is greatly retarded by the addition of a drop of mercury, and traces of iodine in an old sample may be removed by shaking with mercury (Note 12). A very highly colored product is best washed with very dilute sodium thiosulfate, then with water, before drying.

With minor modifications, this method is suitable for the preparation of ethyl, *n*-propyl, *n*- and *iso*-butyl and *n*- and *iso*-amyl iodides with yields above 90 per cent. A somewhat lower yield is obtained in the preparation of *sec.*-butyl iodide owing to the formation of hydrogen iodide.

2. Notes

1. The upper opening of the funnel A (Fig. 2) should be the same size as that of tube F, so that the funnel may be used as a receiver in the distillation described below (Note 11).

2. A funnel of this volume and shape is not essential but has been found convenient. Even if a globular separatory funnel is used, the liquid flowing through it has been found to wet the walls.

3. For larger quantities a flask up to 12 l. in capacity may be substituted.

4. The stopcock from a small, broken, separatory funnel serves the purpose.

5. In hot weather there is usually some loss of methyl iodide through the condenser. This can be recovered by a trap made by bending the mouth end of a 50-cc. pipette into a U, which is stoppered into the end of the condenser, the delivery end being just below the surface of a slush of ice and water.

6. In place of the very long condenser, the checker used a modified West condenser with staggered indentures, as shown in Fig. 2. The jacket was 90 cm. in length, the inner tube was 2.2 cm. (i.d.), the opening at the top was 3.3 cm. (i.d.). At the top of this condenser there was attached a 30-cm. bulb condenser which could be cooled with ice water. With the tap water at 5°, there was no difficulty in effecting complete condensation, and the trap described in Note 5 was not required. In warm weather it will probably be necessary to run the water to each condenser through a large bottle of ice.

7. The methanol need not be absolute. In one experiment it was diluted with 10 per cent of its weight of water. The yield of methyl iodide was identical with that of a check run in which absolute methanol was used.

The refluxing starts more smoothly if the iodine crystals are covered with methanol. The alcoholic solution of iodine forms sufficient methyl iodide to start the refluxing at a lower temperature than would otherwise be necessary.

8. The increased speed of the reaction is largely due to the fact that iodine is more soluble in methyl iodide than in methanol

and is therefore more rapidly introduced as the reaction progresses. The reaction is exothermic.

9. Care should be taken in disposing of the residues left in the reaction flask because they contain yellow phosphorus. They should be covered at once with water.

10. One end of a coil of 2-mm. glass tubing is sealed to the end of the inner tube of the condenser. The other end of the coil is sealed to a tube leading through the stopper of the collecting vessel, which also carries a Bunsen valve to prevent the entrance of moisture from the air. Both the coil and the collecting vessel are cooled with ice and salt, or with carbon dioxide snow.

11. Another convenient assembly for the distillation is furnished by using the condenser shown in Fig. 2, together with the separatory funnel, A. The methyl iodide is distilled from a 3-l. flask through an inverted U-tube (22 mm.); this brings the vapor down into the condenser, which is also clamped in a vertical position. The separatory funnel serves as the receiver and permits the easy removal of fractions. The side opening is equipped with a small condenser carrying a calcium chloride tube. A simple and adequate method of recording the boiling temperature is to insert in the U-tube in an inverted position a long thermometer with its head imbedded in a small cork, which rests on the bottom of the flask.

12. *Caution.* Methyl iodide in contact with mercury when exposed to the sunlight readily forms methylmercuric iodide, which is exceedingly poisonous.

3. Methods of Preparation

Methyl iodide has been prepared by the action of methyl sulfate on an aqueous solution of potassium iodide;[1] by the slow distillation of a mixture of methanol with a large excess of constant-boiling hydriodic acid;[2] by the electrolysis of an aqueous solution of potassium acetate in the presence of iodine or potassium iodide;[3] by the action of an aqueous solution of potassium iodide on methyl-*p*-toluenesulfonate;[4] and by the action of metha-

nol on a solution of phosphorus pentaiodide in methyl iodide.[5] The most generally employed method of preparing methyl iodide has been the interaction of methanol and phosphorus triiodide (or a mixture of iodine and phosphorus, red, yellow or both).[6] Many modifications of this method have been proposed and certain variants have been suggested for the preparation of the higher alkyl iodides which are applicable to the preparation of methyl iodide.[7] The procedure here adopted is a modification of Walker's method.[8] The method of introducing a soluble substance gradually into a reaction flask, here described, is applicable to other reactions, such as the preparation of mercury dialkyls.[9]

[1] Weinland and Schmid, Ber. **38**, 2327 (1905); Ger. pat. 175,209 [Frdl. **8**, 17 (1905–07)].

[2] Norris, Am. Chem. J. **38**, 639 (1907).

[3] Kaufler and Herzog, Ber. **42**, 3860 (1909).

[4] Peacock and Menon, Quart. J. Indian Chem. Soc. **2**, 240 (1925); Rodionow, Bull. soc. chim., **39**, 305 (1926).

[5] Walker and Johnson, J. Chem. Soc. **87**, 1595 (1905).

[6] Dumas and Peligot, Ann. **15**, 20 (1835); Ipatiew, J. Russ. Phys.-Chem. Soc. **27**, I, 364 (1895) [Ber. **29** (R) 90 (1896)]; J. prakt. Chem. [2] **53**, 275 (1896); Crismer, Ber. **17**, 649 (1884); Walker and Johnson, J. Chem. Soc. **87**, 1592 (1905); Haywood, J. Chem. Soc. **121**, 1911 (1922).

[7] Hunt, J. Chem. Soc. **117**, 1592 (1920); Bogert and Slocum, J. Am. Chem. Soc. **46**, 763 (1924).

[8] Walker, J. Chem. Soc. **61**, 717 (1892); Nagai, J. Pharm. Soc. Japan, 1, No. 407 (1916); Adams and Voorhees, J. Am. Chem. Soc. **41**, 796 (1919); Adams, Kamm, and Marvel, "Organic Chemical Reagents," Univ. of Ill. Bull., Urbana, 1, 19 (1919); Reynolds and Adkins, J. Am. Chem. Soc. **51**, 280 (1929); King, Proc. Trans. Nova Scotian Inst. Sci. **16** [2] 87 (1924).

[9] Gilman and Brown, J. Am. Chem. Soc. **51**, 928 (1929).

hydrazine boiling at 106–109°/13 mm. is 46–50 g. (52–56 per cent of the theoretical amount).

2. Notes

1. α-Methyl-α-phenylhydrazine darkens on standing.

3. Methods of Preparation

α-Methyl-α-phenylhydrazine has been obtained by reducing nitrosomethylaniline with zinc and acetic acid;[1,2] by reducing N-methylnitroformaldehyde phenylhydrazone with the same reagents;[3] and by heating methylbenzoylphenylhydrazine with concentrated hydrochloric acid.[4]

[1] Fischer, Ann. **190**, 152 (1878).
[2] Fischer, Ann. **236**, 198 (1886).
[3] Bamberger and Schmidt, Ber. **34**, 574 (1901).
[4] Tafel, Ber. **18**, 1739 (1885).

XVIII
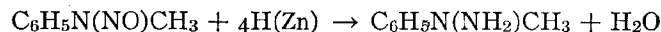
α-METHYL-α-PHENYLHYDRAZINE

$$C_6H_5N(NO)CH_3 + 4H(Zn) \rightarrow C_6H_5N(NH_2)CH_3 + H_2O$$

Submitted by W. W. HARTMAN and L. J. ROLL.
Checked by LOUIS F. FIESER and J. T. WALKER.

1. Procedure

A MIXTURE of 200 g. (3 gram atoms) of zinc dust and 300 cc. of water is placed in a 2-l. three-necked flask equipped with an efficient mechanical stirrer, a thermometer, and a dropping funnel. The suspension is then stirred vigorously, while a solution of 100 g. (0.73 mole) of N-nitrosomethylaniline (p. 82) in 200 cc. (210 g., 3.5 moles) of glacial acetic acid is added in a slow stream. The temperature is maintained between 10 and 20° by external cooling or by the addition of finely crushed ice. When all of the acid solution has been added (about one and one-half to two hours is required, depending upon the rate of cooling) the mixture is stirred for an hour longer at room temperature and then warmed to 80° on the steam bath. The hot solution is filtered from the unreacted zinc, and the latter is washed with three 100-cc. portions of a warm 5 per cent hydrochloric acid solution. The combined filtrate and washings are cooled and treated with sufficient 40 per cent sodium hydroxide solution to redissolve the zinc hydroxide precipitated. (About 1200 cc. is required.) The oily layer is separated and the aqueous layer extracted with two or three 100-cc. portions of ether. The combined oil and extracts are distilled from a steam bath until the ether is removed; the residue is then distilled under reduced pressure. The yield of colorless (Note 1) α-methyl-α-phenyl-

XIX

METHYL *iso*-PROPYL KETONE

$$(CH_3)_2C(OH)CH_2CH_3 + Br_2 \rightarrow (CH_3)_2CBrCHBrCH_3 + H_2O$$

$$(CH_3)_2CBrCHBrCH_3 + H_2O \rightarrow (CH_3)_2CHCOCH_3 + 2HBr$$
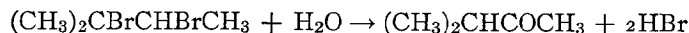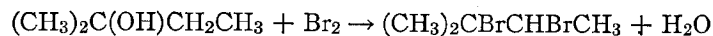
Submitted by F. C. Whitmore, W. L. Evers, and H. S. Rothrock.
Checked by W. W. Hartman and L. J. Roll.

1. Procedure

In a 1.5-l. round-bottomed Pyrex flask fitted with a dropping funnel, an efficient mechanical stirrer, and a thermometer, is placed 176 g. (2 moles) of *tert.*-amyl alcohol (redistilled, b.p. range 0.5°). The flask is surrounded by a water bath, and the temperature of the alcohol is held at 50–60° while 320 g. (103 cc., 2 moles) of bromine is slowly added with stirring during about two hours (Notes 1 and 2). The stirring is continued for a few minutes until the bromine color has disappeared.

To the reaction flask containing the crude trimethylethylene dibromide is added 540 cc. of water, and the flask is fitted with a long reflux condenser and a mercury-sealed stirrer (Notes 3 and 4). The mixture is refluxed with stirring for three to five hours until hydrolysis is practically complete (Note 5). The reflux condenser is then replaced by a condenser for distillation, and the crude methyl *iso*-propyl ketone is removed from the reaction mixture by direct distillation, with stirring, until the temperature rises (Note 6) and the oil nearly stops coming over (about one and one-half hours), or until the oil coming over is heavier than water. The residue in the flask can be distilled to yield about 380 cc. of constant-boiling hydrobromic acid.

To the distillate, consisting of a yellow oil with a small lower water layer, powdered sodium carbonate (about 10 g.) is added, and the mixture is shaken until the water layer is alkaline and nearly saturated (Note 7). The layers are separated, and the

oil is refluxed for about sixteen hours with 20 g. of powdered potassium carbonate and 5 cc. of water (Note 8). The oily layer is again separated and dried over about 6 g. of anhydrous calcium chloride or potassium carbonate (Note 9). It is then placed in a flask containing 2 g. of dry sodium carbonate and distilled through an efficient column. The yield of methyl *iso*-propyl ketone boiling at 92–94°/760 mm. (Note 10) is about 102 g. (59 per cent of the theoretical amount). The product is slightly yellow.

2. Notes

1. The bromine is added at such a rate that only a small amount is present at any time, as shown by an orange-red color. The speed of the reaction depends on the temperature and efficiency of stirring. The temperature of the reaction mixture remains a few degrees above that of the water bath.

2. After about half the bromine has been added, the mixture becomes cloudy owing to the separation of water, and a somewhat lower temperature (40–45°) suffices to prevent the accumulation of unreacted bromine.

3. The crude trimethylethylene dibromide can be purified by washing with sodium carbonate solution and water, drying, and distilling under reduced pressure; b.p. 49–51°/11 mm.; 60–70 per cent yield. The losses in purification, however, result in a slightly decreased over-all yield of ketone; hydrolysis of the purified dibromide gave a 78 per cent yield of ketone.

4. The quantity of water used is 50 per cent more than the theoretical amount for hydrolyzing the dibromide and converting all the bromine to constant-boiling (47.3 per cent) hydrobromic acid. Less water can be used, but more darkening of the reaction mixture occurs, and the yield of ketone is slightly decreased.

5. Efficient stirring lessens the time required for hydrolysis and avoids loss of material by intermittent sudden boiling. To be sure of complete hydrolysis, the refluxing should be continued for at least an hour after the specific gravity of the oily layer becomes less than that of the water layer.

6. The distillate and residue contain a very powerful lachrymator and should be handled under a good hood.

7. The ketone is somewhat soluble in water, and the sodium carbonate serves to salt it out as well as to remove any hydrobromic acid.

8. The crude ketone contains small amounts of bromides, and it darkens even after repeated distillation unless first refluxed over potassium carbonate.

9. It is necessary to dry the ketone thoroughly since water distils with it at about 78°. This fraction can be dried again to recover the ketone.

10. A column 55 cm. high packed with glass tubes 6 mm. in length and diameter was employed with good results. A few grams of trimethylethylene, b.p. 34–36°/735 mm., is always obtained if adequate condensers have been used throughout the preparation. The presence of a little sodium carbonate during the final distillation hinders decomposition.

3. Methods of Preparation

Trimethylethylene dibromide has been obtained by adding bromine to trimethylethylene[1] and to tertiary amyl alcohol.[2] Methyl *iso*-propyl ketone has been prepared by heating trimethylethylene glycol (2-methyl-2,3-dihydroxybutane) with dilute hydrochloric acid,[3] by heating trimethylethylene chlorohydrin (2-methyl-2-hydroxy-3-chlorobutane) in a sealed tube with water,[4] by boiling trimethylethylene dibromide with lead oxide (PbO) and water,[5] by heating trimethylethylene dibromide with water,[6] by the action of *iso*-propylmagnesium bromide on acetic anhydride,[7] and by a variety of other methods not particularly related to the one here described.[8]

[1] Michailenko, J. Russ. Phys.-Chem. Soc. **27**, 56 (1895) [Ber. **28** (R) 852 (1895)]; Froebe and Hochstetter, Monatsh. **23**, 1075 (1902).

[2] Ipatiew, J. prakt. Chem. [2] **53**, 266 (1896).

[3] Bauer, Ann. **115**, 91 (1860).

[4] Krassuski, J. Russ. Phys.-Chem. Soc. **34**, 287 (1902) [Chem. Zentr. **73**, II, 19 (1902)].

[5] Ipatiew, J. Russ. Phys.-Chem. Soc. **27**, 359 (1895) [Ber. **29** (R) 90 (1896)].

[6] Froebe and Hochstetter, Monatsh. **23**, 1075 (1902).

[7] Sweet and Marvel, J. Am. Chem. Soc. **54**, 1188 (1932).

[8] Beilstein's Handbuch, 4th ed., **1**, 682 (1918).

XX

1-NITRO-2-ACETYLAMINONAPHTHALENE
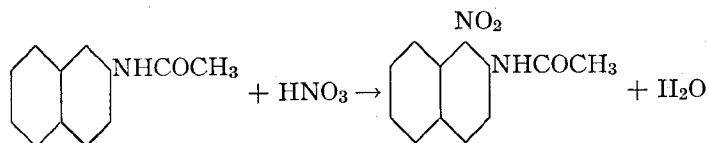
Submitted by W. W. HARTMAN and LLOYD A. SMITH.
Checked by LOUIS F. FIESER and J. T. WALKER.

1. Procedure

IN a 2-l. round-bottomed flask equipped with a mechanical stirrer, a thermometer, and a dropping funnel, and clamped in a position such that it may be surrounded by a bath of water and ice when desired, are placed 300 g. (1.62 moles) of acetyl-β-amino-naphthalene (m.p. 131–132°) and 500 cc. of glacial acetic acid. With the mixture at room temperature, the stirrer is set in motion, and 200 g. (143 cc., 2.1 moles) of concentrated nitric acid (sp. gr. 1.4) is added dropwise over a period of forty-five minutes; the temperature is kept below 40° by occasionally immersing the flask in the cooling bath. After about one-tenth of the nitric acid has been added, the reaction mixture sets to a mass that is stirred with difficulty. The addition of nitric acid is stopped at this point. In a short time (three to five minutes) the mass becomes fluid, and the addition of nitric acid is resumed. When about one-fourth of the nitric acid has been added, the solid material all dissolves. Considerable heat is evolved at this point, and good cooling is required to keep the temperature from rising above 40°; the mixture must be cooled during the addition of the remainder of the acid. After the addition is complete, stirring is continued for ten minutes longer.

72

The flask is stoppered and cooled in a bath of ice and water for three hours; the reaction product should then separate in the form of a yellow, crystalline paste (Notes 1, 2). The crystals are collected on a Büchner funnel (19-cm.) and washed with 200 cc. of 50 per cent acetic acid, and subsequently with 400 cc. of ordinary ether. This crude, dry product, weighing 270–290 g., is placed in a 3-l. flask and heated under a reflux condenser with 1700 cc. of benzene for twenty minutes. The mixture is then allowed to cool to 40–45° and filtered through a Büchner funnel (19-cm.). The residue is a mixture of sparingly soluble isomers, chiefly 5- and 8-nitro-2-acetylaminonaphthalene. On further cooling of the filtered solution, there is obtained 190–200 g. of 1-nitro-2-acetylaminonaphthalene melting at 117–119°. This material is recrystallized from about 500 cc. of hot 95 per cent ethyl alcohol. Fine yellow crystals melting at 123–124° are obtained. The yield is 175–182 g. (47–49 per cent of the theoretical amount).

2. Notes

1. The material is sometimes slow in crystallizing, and it is then advisable to scratch the walls of the container with a stirring rod. If this fails to induce crystallization, seed may be obtained by diluting a small portion of the solution with water.

2. Crystallization is nearly, but not entirely, complete after this period of time. When the mother liquor was allowed to stand for five days, an additional quantity of material separated, but it yielded only 3 g. of pure 1-nitro-2-acetylaminonaphthalene.

3. Methods of Preparation

This procedure is based upon previous studies of the nitration of 2-acetyl-β-aminonaphthalene.[1]

[1] Jacobson, Ber. **14**, 803 (1881); Liebermann and Jacobson, Ann. **211**, 36 (1882); Friedlaender and Littner, Ber. **48**, 328 (1915).

XXI

2-NITROFLUORENE AND 2-AMINOFLUORENE
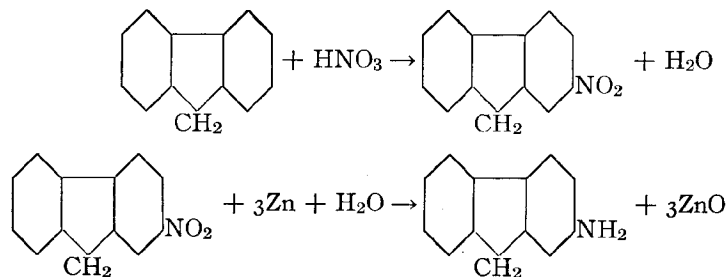
Submitted by W. E. KUHN.
Checked by LOUIS F. FIESER and J. T. WALKER.

1. Procedure

A. 2-Nitrofluorene: Sixty grams (0.36 mole) of fluorene (Note 1) is dissolved in 500 cc. of warm glacial acetic acid in a 1-l. three-necked flask fitted with a thermometer, a mechanical stirrer, and a dropping funnel, and supported in a water bath. The temperature is brought to 50°, and 80 cc. (1.3 moles) of concentrated nitric acid (sp. gr. 1.42) is added with stirring in the course of fifteen minutes. During the addition, the solution becomes slightly yellow, and a small amount of material precipitates. The water bath is slowly brought to a temperature of 60-65°, when the precipitate dissolves and the color of the solution deepens. Stirring is continued, and heat is applied continuously until the temperature of the mixture reaches 80° (Note 2). After five minutes, the water bath is removed, and the mixture, which now consists of a semi-solid paste of fine, yellow needles, is allowed to cool to room temperature during two hours. The product is collected on a Büchner funnel, sucked

74

as dry as possible, and washed with two 25-cc. portions of cold glacial acetic acid containing 0.5 g. of potassium acetate. It is then washed several times with water and dried. The 2-nitrofluorene so obtained melts at 155-156° and is sufficiently pure for most purposes. The yield is 60 g. (79 per cent of the theoretical amount).

If a purer product is desired, the above material may be crystallized from 200 cc. of glacial acetic acid. The purified product melts at 157° and weighs 56 g.

B. 2-Aminofluorene: In a 2-l. round-bottomed flask, 30 g. (0.14 mole) of dried and powdered 2-nitrofluorene is made into a thin paste with 1 l. of 78 per cent alcohol (820 cc. of 95 per cent alcohol and 180 cc. of water). A solution of 10 g. of calcium chloride in 15 cc. of water, together with 300 g. of zinc dust, is added to the suspension, and the whole is thoroughly mixed. The flask is fitted with an effective reflux condenser, and the mixture is refluxed for two hours.

The sludge of zinc dust and zinc oxide is filtered from the boiling solution and extracted (Note 3) with 50 cc. of boiling 78 per cent alcohol. The combined filtrates are then poured into 2 l. of water, whereupon a white, flocculent precipitate is obtained. This is filtered with suction and recrystallized from 400 cc. of hot 50 per cent alcohol. The purified 2-aminofluorene crystallizes in needles melting at 127.5°. The yield is 20-21 g. (78-80 per cent of the theoretical amount).

2. Notes

1. The fluorene used had a melting point of 113-114° and was obtained from the Gesellschaft für Teerverwertung, Duisberg-Meiderich.

2. The reaction is exothermic at this point, and the temperature of the reaction mixture may be expected to rise 10-15° above that of the surrounding bath. If the temperature is allowed to rise above 85°, the 2-nitrofluorene will be highly colored and impure.

3. The sludge of zinc dust and zinc oxide is filtered while hot,

through a previously warmed filter. Unless the solution is kept near the boiling point, some of the compound will crystallize out during the filtration. If a small amount of zinc dust runs through the filter paper, it is advisable to heat the filtrate to the boiling point, and refilter without suction, through a folded filter paper in a hot water or steam jacket.

3. Methods of Preparation

The procedures given are essentially those of Diels.[1]

[1] Diels, Ber. **34**, 1758 (1901).

XXII

1-NITRO-2-NAPHTHOL
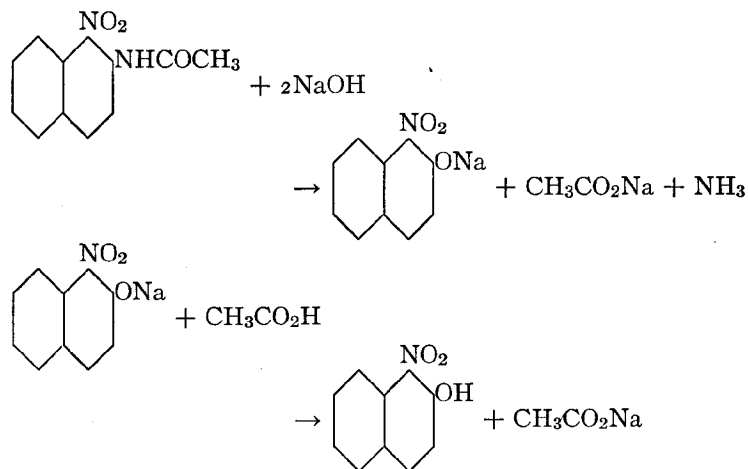
Submitted by W. W. Hartman, J. R. Byers, and J. B. Dickey.
Checked by Louis F. Fieser and J. T. Walker.

1. Procedure

In a 3-l. round-bottomed flask, fitted with a reflux condenser, are placed 100 g. (0.435 mole) of 1-nitro-2-acetylaminonaphthalene (p. 72) and a solution of 112 g. (2.8 moles) of sodium hydroxide in 2.7 l. of water (Note 1). The mixture is boiled until ammonia is no longer evolved (six to seven hours). The solution becomes deep red in color. It contains suspended crystals of sodium nitronaptholate; these are dissolved by the addition of 1 l. of hot water. The small amount of insoluble material is removed by filtration, washed with hot water until the washings are colorless, and then discarded, although it contains a little nitronaphthylamine. The combined washings and filtrate are

78

made acid by adding 500 cc. of glacial acetic acid. The nitronaphthol precipitates as small, bright yellow crystals which are filtered on a 10-cm. Büchner funnel, washed with water, and dried. The yield of material melting at 101–103° is 76–81 g. (92–98 per cent of the theoretical amount).

The product is purified by recrystallization from 500 cc. of methyl alcohol containing 5 cc. of concentrated hydrochloric acid. The first crop of crystals amounts to 60 g. and melts at 103–104°. The mother liquors are concentrated to 150 cc., and a second crop weighing 12–13 g. is collected. The total yield of recrystallized material is 72–73 g. (88–89 per cent of the theoretical amount).

2. Notes

1. This concentration of alkali was found to be very satisfactory. The hydrolysis takes place rather rapidly at first when stronger alkali is used, with the precipitation of the sodium salt, which forms a thick paste and causes bumping. When more dilute alkali is used a much longer time is required to complete the hydrolysis.

3. Methods of Preparation

1-Nitro-2-naphthol has been prepared by the nitration of β-naphthol ethyl ether;[1,2] by the oxidation of 1-nitroso-2-naphthol;[3] and by the treatment of β-naphthol with diacetylnitric acid.[4] It has also been prepared by the treatment of β-naphthylamine with sodium nitrite;[5] by the decomposition of benzeneazo-β-naphthol with nitric acid;[6] by heating the nitrate of pseudo cumeneazo-β-naphthol under reduced pressure;[6] by the treatment of 1-bromo-2-naphthol in acetic acid with nitric acid;[7] and by the reaction of nitrogen dioxide with β-naphthol.[7] It

[1] Wittkampf, Ber. 17, 393 (1884).

[2] Gaess, J. prakt. Chem. [2] 43, 22 (1891).

[3] Stenhouse and Groves, Ann. 189, 145 (1877).

[4] Pictet and Krijanowski, Arch. sc. phys. nat. Genève [4] 16, 191 (1903) [Chem. Zentr. II, 1109 (1903)].

[5] Deninger, J. prakt. Chem. [2] 40, 296 (1889).

[6] Charrier and Ferreri, Chem. Zentr. II, 218 (1914).

[7] Armstrong and Rossiter, Ber. 24 (R), 720 (1891).

has been prepared from 1-nitro-1-bromo-2-ketodihydronaphthalene by treatment with caustic alkali,[8] and by the fusion of α-nitronaphthalene with sodium hydroxide.[9]

The method on which this procedure is based has been described by Andreoni and Biedermann and by others.[10]

[8] Fries, Ann. **389**, 315 (1912).

[9] Wohl, Ger. pat. 116,790 [Frdl. **6**, 114 (1900)].

[10] Andreoni and Biedermann, Ber. **6**, 342 (1873); Jacobson, ibid. **14**, 803 (1881); Liebermann and Jacobson, Ann. **211**, 36 (1882).

XXIII

N-NITROSOMETHYLANILINE
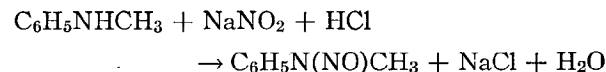
$$C_6H_5NHCH_3 + NaNO_2 + HCl$$
$$\rightarrow C_6H_5N(NO)CH_3 + NaCl + H_2O$$

Submitted by W. W. Hartman and L. J. Roll.
Checked by Louis F. Fieser and J. T. Walker.

1. Procedure

A mixture of 107 g. (1 mole) of methylaniline (Note 1), 145 cc. of concentrated hydrochloric acid, and 400 g. of ice is placed in a 3-l. flask equipped with a mechanical stirrer. The mixture is stirred vigorously and the temperature is maintained at 10° or below by the addition of more ice as required, while a solution of 70 g. (1 mole) of sodium nitrite in 250 cc. of water is added during the course of five or ten minutes. Stirring is then continued for one hour more. The oily layer is separated, and the aqueous portion is extracted with two 100-cc. portions of benzene. The benzene is removed by distillation at ordinary pressure, and the residue is fractionated under reduced pressure. The main fraction of the nitrosomethylaniline distils as a light yellow liquid boiling at 135–137°/13 mm. The yield (Note 1) is 118–127 g. (87–93 per cent of the theoretical amount).

2. Notes

1. The yield is dependent upon the quality of the methylaniline used. The higher yield reported was obtained with pure material, b.p. 81–82°/14 mm.

3. Methods of Preparation

N-Nitrosomethylaniline was first prepared by the action of nitrous acid on methylaniline.[1] It has been obtained also by the action of methyl iodide on the sodium salt of benzene diazoic acid followed by reduction;[2] by treating dimethylaniline with tetranitromethane;[3] or with phenylnitrocarbinol;[4] by the acid hydrolysis of nitrosophenylglycine;[5] and by oxidizing dimethyldiphenylhydrazine with nitric oxide.[6]

[1] Hepp, Ber. **10**, 329 (1877).

[2] Bamberger, Ber. **27**, 359 (1894).
[3] Schmidt and Fischer, Ber. **53**, 1538 (1920).
[4] Cohen and Calvert, J. Chem. Soc. **73**, 164 (1898).
[5] Fischer, Ber. **32**, 249 (1899).
[6] Wieland and Fressel, Ann. **392**, 146 (1912).

XXIV

NITROSOMETHYLURETHANE
(ETHYL N-NITROSO-N-METHYLCARBAMATE)

$$CH_3NHCO_2C_2H_5 + HNO_2 \rightarrow CH_3N(NO)CO_2C_2H_5 + H_2O$$
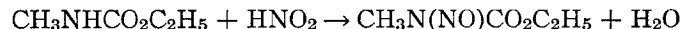
Submitted by W. W. Hartman and Ross Phillips.
Checked by Louis F. Fieser and J. T. Walker.

1. Procedure

To 206 g. (2 moles) of ethyl N-methylcarbamate (Org. Syn. 12, 38) and 600 cc. of ordinary ethyl ether in a 5-l. flask is added, along with 200 g. of ice, 650 g. (9 moles) of 96 per cent sodium nitrite (Note 1) dissolved in 1 l. of cold water. The flask is provided with a stopper carrying a thermometer, a tube to lead off evolved nitric oxide, and a separatory funnel with an extension tube reaching to the bottom of the flask. A solution of 1200 g. (6.7 moles) of cold 35 per cent nitric acid, prepared by pouring 600 g. (426 cc.) of concentrated acid onto 600 g. of ice, is then cautiously added through the funnel in the course of one and one-half hours. The flask is given an occasional swirl to insure some mixing, but most of the stirring is done by the evolved gases. Ice is added as required to keep the temperature below 15°. The ether layer first becomes pale red and gradually changes to a blue-green. As soon as the color has changed to green, the ether layer is separated (Note 2) and washed twice with cold water and then with cold potassium carbonate solution until carbon dioxide is no longer evolved. The solution is dried with solid potassium carbonate, and the ether is distilled from a water bath using a 1-l. flask with a 30-cm. column arranged for vacuum distillation. The vacuum is applied as soon as most of the ether has been removed, and the flask is heated gently so that the temperature of the liquid does not exceed 45–50°

(Note 3) until the pressure has been reduced below 20 mm. The yield of nitrosomethylurethane boiling at 59–61°/10 mm. is 200 g. (75 per cent of the theoretical amount). The density is 1.133 at 20°.

2. Notes

1. A large excess of sodium nitrite is required to give a satisfactory yield. This may be due to reaction according to the following equations:

(1) $$2HNO_2 \rightarrow NO_2 + NO + H_2O$$

(2) $CH_3NHCO_2C_2H_5 + 2NO_2 \rightarrow CH_3N(NO)CO_2C_2H_5 + HNO_3$

(1) plus (2)

$$CH_3NHCO_2C_2H_5 + 4HNO_2 \rightarrow CH_3N(NO)CO_2C_2H_5 + 2NO + HNO_3 + 2H_2O$$
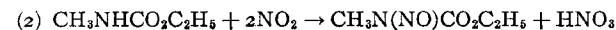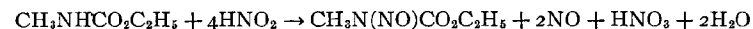
Nitric oxide (NO) is lost during the reaction. It is not thought advisable to use this by passing in oxygen, because of the danger of an explosion, nor by passing in air, because of the loss of material by evaporation.

2. Nitrosomethylurethane irritates the skin.

3. According to the literature, nitrosomethylurethane explodes when attempts are made to distil it at normal pressure.

3. Methods of Preparation

Nitrosomethylurethane has been prepared by treating ethyl methylcarbamate with sodium nitrite and sulfuric acid,[1] and by passing the gases generated from arsenious oxide and nitric acid into an ethereal solution of ethyl methylcarbamate.[2]

[1] Klobbie, Rec. trav. chim. 9, 139 (1890).
[2] v. Pechmann, Ber. 28, 856 (1895); Schmidt, ibid. 36, 2477 (1903); Brühl, ibid. 36, 3635 (1903).

XXV

PERBENZOIC ACID

$$(C_6H_5CO)_2O_2 + CH_3ONa \rightarrow C_6H_5COO_2Na + C_6H_5CO_2CH_3$$

$$C_6H_5COO_2Na + H_2SO_4 \rightarrow C_6H_5COO_2H + NaHSO_4$$
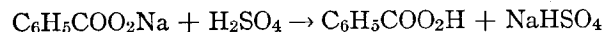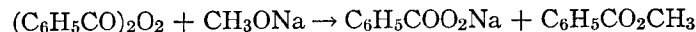
Submitted by Géza Braun.
Checked by C. R. Noller and Poe Liang.

1. Procedure

In a 500-cc. Erlenmeyer flask (Note 1), 5.2 g. (0.22 gram atom) of sodium is dissolved in 100 cc. of absolute methyl alcohol with moderate cooling. The resulting solution of sodium methylate (Note 2) is cooled to $-5°$ in a freezing mixture. A solution of 50 g. (0.21 mole) of pure commercial benzoyl peroxide (m.p. 104°) (Note 3) in 200 cc. of chloroform (Note 4) is prepared, cooled to 0°, and added without delay to the sodium methylate solution (Note 2) with shaking and cooling at such a rate that the temperature does not rise above 0°. The mixture is kept for four or five minutes in an ice-salt bath with continuous shaking; it turns milky, but no precipitate appears. The reaction mixture is now transferred to a 1-l. separatory funnel, and the sodium perbenzoate is extracted with 500 cc. of water containing much chopped ice (Note 5). The chloroform layer is then separated and the aqueous layer is extracted twice with 100-cc. portions of cold chloroform to remove the methyl benzoate. The aqueous solution contains the sodium salt of perbenzoic acid. The perbenzoic acid is liberated by the addition of 225 cc. of cold 1 N sulfuric acid and is removed from solution by extracting three times with 100-cc. portions of cold chloroform (Note 6). The united chloroform solutions are washed twice with 50-cc. portions of water, and the chloroform layer is carefully separated.

The volume of the moist (milky) chloroform solution is about 308 cc., and iodometric titration indicates that it contains 23.5–24.5 g. of perbenzoic acid (82.5–86 per cent of the theoretical amount) (Notes 7, 8, and 9). Water is the only impurity present in the moist solution; the solution may therefore be used as such for oxidations that are to be carried out in the presence of water.

To obtain crystalline perbenzoic acid, the moist chloroform solution is dried with a small amount of anhydrous sodium sulfate for an hour (Note 6). Then the sodium sulfate is removed by filtration and washed with dry chloroform; from the filtrate the chloroform is completely removed under reduced pressure while carbon dioxide is introduced through a capillary tube. The white or pale yellow residue is dried for several hours under 10 mm. pressure at 30–35°. The yield is 22–23 g. of crystalline mass which contains several per cent less active oxygen than the theoretical owing to a slight contamination with benzoic acid (Notes 8 and 9). The perbenzoic acid is very soluble in the usual organic solvents, such as chloroform, ether, ethyl acetate; slightly soluble in cold water and in cold ligroin.

2. Notes

1. All the glassware used in the preparation should be carefully cleaned. Either cork or thoroughly cleaned rubber stoppers may be used.

2. Sodium methylate is preferred to sodium ethylate because it is more soluble in the excess of alcohol, and does not precipitate provided the solution is not cooled below $-5°$. If sodium ethylate is used the sodium perbenzoate precipitates immediately as a white powder when the sodium ethylate is added to the chloroform solution of benzoyl peroxide. In the case of sodium methylate the solution turns milky, but no precipitate appears.

3. The commercial (Eastman) benzoyl peroxide may be used if it gives a colorless or pale yellow chloroform solution; otherwise it should be recrystallized from a small amount of hot chloroform. It should always be analyzed before use, since the melting point is not a safe criterion of purity. The following method of analysis is convenient and satisfactory:

In a 300-cc. Erlenmeyer flask, 0.5 g. of benzoyl peroxide is dissolved in 15 cc. of chloroform. The solution is cooled to $-5°$ and 25 cc. of 0.1 N ice-cold sodium methylate solution is added at once with cooling and shaking. After four to five minutes at $-5°$, 100 cc. of iced water, 5 cc. of 10 per cent sulfuric acid, and 2 g. of potassium iodide in 20 cc. of 10 per cent sulfuric acid are added in the order mentioned with violent stirring. The liberated iodine is titrated with 0.1 N sodium thiosulfate solution. One cubic centimeter of 0.1 N sodium thiosulfate solution is equivalent to 0.0121 g. of benzoyl peroxide.

4. The chloroform (U. S. P. grade) used in the preparation can be recovered by careful drying with anhydrous sodium sulfate and subsequent fractional distillation and used over and over again. The by-product is methyl benzoate, which is purified by vacuum distillation.

5. The preparation should be carried out as quickly as possible; the temperature must be kept around $0°$ by the addition of chopped ice, especially before the free acid is liberated from the sodium salt. Failure to observe this precaution leads to very uncertain results, whereas under correct conditions the yield of perbenzoic acid is invariably as high as 82–86 per cent of the theoretical amount.

6. After the perbenzoic acid is liberated with sulfuric acid, it may be extracted from the aqueous solution with any appropriate organic solvent (*e.g.* ether or ethyl acetate). Even if concentrated solutions of perbenzoic acid are required, it is better to apply the amount of solvent specified (or more) and then to concentrate the solution under reduced pressure at a temperature not above $30–35°$. The solution may, but need not, be dried before concentration. Anhydrous sodium sulfate is the only satisfactory drying agent. Calcium chloride sometimes causes a sudden decomposition of the peracid.

7. The yield is calculated on the benzoyl peroxide content of the material used. These directions are equally satisfactory for the preparation of perbenzoic acid on a smaller or larger scale. Experiments in which the amount of benzoyl peroxide used ranged from 10 to 250 g. gave an average yield of 85 per cent of

the theoretical. However, amounts from 25 to 50 g. are preferred because the experiments can easily be completed in a short time.

8. The perbenzoic acid thus prepared is fairly stable, especially when kept in the dark in a cold place. A sample kept in moist chloroform solution showed the following change in active oxygen:

1 cc. of the solution required:
Immediately after preparation.... 13.2 cc. of 0.1 N $Na_2S_2O_3$
After 21 days at $2°$ in the dark.... 12.5 cc. of 0.1 N $Na_2S_2O_3$
After 5 days more at room temperature..................... 7.8 cc. of 0.1 N $Na_2S_2O_3$

9. The amount of active oxygen is estimated by iodometric titration. One or two grams of sodium iodide is dissolved in 50 cc. of water, and then about 5 cc. of glacial acetic acid and 5 cc. of chloroform are added. To this mixture a chloroform solution of perbenzoic acid is added with violent shaking. The iodine liberated is titrated with 0.1 N sodium thiosulfate solution, of which 1 cc. is equivalent to 0.0069 g. of perbenzoic acid.

3. Methods of Preparation

The above procedure is a considerable improvement, especially in ease of manipulation and time required, over that given in Coll. Vol. 1, 422. It has been found [1] that chloroform is more suitable than ether or toluene as a solvent for the benzoyl peroxide. A further improvement in the present method consists in the substitution of sodium methylate for sodium ethylate. The sodium methylate is much more soluble in the excess of alcohol, and the sodium perbenzoate remains in solution, thus assuring a quantitative conversion. The directions given in Coll. Vol. 1, 422 contain two errors: The amount of sodium specified (23 g.) is twice the correct amount, and the percentage yield stated as 90 is actually only 65.

[1] Braun, J. Am. Chem. Soc. **51,** 239 (1929).

of water (Note 8), whereupon a black oil collects at the surface. After standing overnight in the ice box, a large portion of this layer solidifies and can be separated by filtration. This solid (*p*-propiophenol) is recrystallized from 400 cc. of methyl alcohol. The yield is 129–148 g. (34–39 per cent of the theoretical amount) of a light yellow product melting at 145–147°. A second recrystallization raises the melting point to 147–148°.

The oily filtrate combined with the concentrated mother liquors of the above recrystallization is dissolved in 500 cc. of 10 per cent sodium hydroxide and extracted with two 100-cc. portions of ether to remove non-phenolic products. The alkaline solution is acidified with hydrochloric acid and the oily layer is separated, dried over anhydrous magnesium sulfate, and distilled. The *o*-propiophenol boils at 110–115°/6 mm. The yield is 120–132 g. (32–35 per cent of the theoretical amount). About 40 g. of *p*-propiophenol boiling at 135–150°/11 mm. is obtained. The total yield of crude *p*-propiophenol is thus 169–188 g. (45–50 per cent of the theoretical amount).

2. Notes

1. The stirrer should be made of sturdy glass rod, bent preferably in the shape of a golf-club head, to provide for heavy duty when the reaction mass becomes thick.

2. When nitrobenzene was used as a solvent the products were always tarry.

3. Crude, undistilled phenyl propionate, made by gently heating a mixture of equivalent quantities of phenol and propionyl chloride until hydrogen chloride evolution ceases, is satisfactory for rearrangement. The ester can also be made conveniently by slowly adding one mole of thionyl chloride to a mixture of 1.05 moles each of phenol and propionic acid, driving off all of the hydrogen chloride and sulfur dioxide, and distilling.

4. Because of the large volume of hydrogen chloride evolved, it is desirable to work under a good hood. If this is not available, the gas may be absorbed in a train of water bottles connected with a water vacuum pump.

XXVI

o-PROPIOPHENOL AND *p*-PROPIOPHENOL

$$C_6H_5OCOC_2H_5 \xrightarrow[\text{CS}_2]{\text{AlCl}_3} \text{ } o\text{- and } p\text{-}C_6H_4(OH)COC_2H_5$$

Submitted by ELLIS MILLER and WALTER H. HARTUNG.
Checked by W. W. HARTMAN and L. J. ROLL.

1. Procedure

IN a 2-l. three-necked, round-bottomed flask fitted with a reflux condenser, a mechanical stirrer (Note 1), and a 100-cc. dropping funnel, are placed 374 g. (2.8 moles) of anhydrous aluminum chloride and 400 cc. of carbon bisulfide (Note 2). To the stirred suspension is added slowly through the dropping funnel 375 g. (2.5 moles) of phenyl propionate (Note 3). Reaction sets in almost at once with the evolution of hydrogen chloride (Note 4), and the carbon bisulfide begins to reflux from the heat of reaction (Note 5). When the propionate is all in (one and one-half hours are required), the mixture is further heated to gentle refluxing on a steam bath until the evolution of hydrogen chloride has practically ceased (about two hours). The reflux condenser is then turned downward and the carbon bisulfide is distilled. The steam bath is replaced by an oil bath which is heated to 140° and maintained at 140–150° for three hours (Note 6). During this period a fresh evolution of hydrogen chloride takes place. The mixture thickens and finally congeals to a brown resinous mass. Stirring is continued as long as possible (Note 7).

The solid is then allowed to cool, and the aluminum complex is decomposed by slowly adding first a mixture of 300 cc. of concentrated hydrochloric acid with 300 cc. of water and then 500 cc.

5. The rate of addition of the phenyl propionate is regulated by the degree of refluxing. This should not become too violent.

6. The temperature of the reaction mixture is about 10° lower than the bath temperature, or 130–135°. The reaction temperature determines the yield ratio of the two isomers. In general, higher temperature (above 160–170°) favors the formation of the ortho isomer.

7. It is necessary to stir the thickening mass continuously to permit the escape of hydrogen chloride formed during the heating; otherwise it may swell rapidly and choke the outlets of the flask.

8. This decomposition is strongly exothermic, and the dilute acid should be added slowly.

9. The above procedure has been found satisfactory for the preparation of a number of the homologues of *o*- and *p*-propiophenol, such as aceto-, butyro-, caprophenol, etc.

3. Methods of Preparation

Ortho and para propiophenols have been previously prepared by condensing propionic acid and phenol in the presence of zinc chloride,[1] and from phenol and propionyl chloride.[2] The procedure described above is an adaptation of one described by Cox[3] and Hartung, Munch, Miller, and Crossley.[4]

[1] Goldzweig and Kaiser, J. prakt. Chem. [2] **43**, 86 (1891).
[2] Perkin, J. Chem. Soc. **55**, 547 (1889).
[3] Cox, J. Am. Chem. Soc. **49**, 1028 (1927).
[4] Hartung, Munch, Miller, and Crossley, J. Am. Chem. Soc. **53**, 4149 (1931).

XXVII

o-TOLUAMIDE

$$2\ o\text{-}CH_3C_6H_4CN + 2H_2O_2 \rightarrow 2\ o\text{-}CH_3C_6H_4CONH_2 + O_2$$
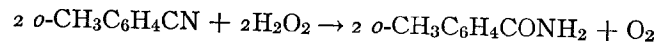
Submitted by C. R. NOLLER.
Checked by W. W. HARTMAN and L. A. SMITH.

1. Procedure

IN a 2-l. round-bottomed flask are placed 88 g. (0.75 mole) of o-tolunitrile (Coll. Vol. 1, 500), 300 cc. (2.6 moles) of 30 per cent hydrogen peroxide, 400 cc. of 95 per cent alcohol, and 30 cc. of 6 N sodium hydroxide solution (Note 1). The mixture evolves oxygen and soon warms up owing to the heat of reaction; the temperature is kept at 40–50° by external cooling (Note 2). After about one hour, heat is no longer evolved; the temperature is then maintained at 50° by external heating for an additional three hours. The mixture, while still warm, is made exactly neutral to litmus with 5 per cent sulfuric acid and subjected to steam distillation. One liter of distillate is collected, and the residue, which has a volume of about 600 cc. (Note 3), is poured while hot into a 1-l. beaker and cooled to 20°. The crystals are filtered with suction. They are transferred to a mortar and ground to a paste with 100 cc. of cold water, filtered again, and then washed on the filter with an additional 100 cc. of cold water. The o-toluamide is obtained in the form of white crystals melting at 141–141.5°. The yield of air-dried product is 91–93 g. (90–92 per cent of the theoretical amount) (Note 4). The product may be recrystallized from water (10 g. per 100 cc.). The recovery is 92 per cent, and the melting point is not changed.

2. Notes

1. This amount of alcohol is sufficient to provide a homogeneous solution.

2. If the temperature is allowed to rise much above 50° the evolution of oxygen will be sufficiently rapid to cause the mixture to foam out of the flask.

3. The volume of the solution in the flask is kept down by applying a small flame to the flask after most of the alcohol has been distilled.

4. An additional 3–4 g. of low-melting material may be obtained by concentrating the filtrate, but this is hardly worth while.

5. In general, amides may be prepared by this method from aliphatic nitriles in yields of 50–60 per cent and from aromatic nitriles in yields of 80–95 per cent. Slight variations in the above procedure may be necessary for carrying out the reaction and for isolating the amide, depending on the solubility of the nitriles and amides. Except for difficultly hydrolyzable nitriles such as the o-substituted aromatic nitriles, an equivalent amount of 6 to 12 per cent hydrogen peroxide gives better yields than the 30 per cent reagent.[4]

3. Methods of Preparation

o-Toluamide has been prepared by the action of ammonia on o-toluyl chloride,[1] and by the action of alcoholic potassium hydroxide[2] or of an alkaline solution of hydrogen peroxide[3,4] on o-tolunitrile.

[1] Remsen and Reid, Am. Chem. J. 21, 289 (1899).
[2] Weith, Ber. 6, 419 (1873).
[3] Kattwinkel and Wolffenstein, Ber. 37, 3224 (1904); Dubsky, J. prakt. Chem. [2] 93, 137 (1916).
[4] McMaster and Noller, Wash. Univ. Studies 13, 23 (1925).

aniline is filtered on a Büchner funnel, thoroughly washed with water to remove hydrobromic acid, sucked as dry as possible, and taken without further drying to the next step.

The moist tribromoaniline, together with 2100 cc. of 95 per cent alcohol and 525 cc. of benzene, is placed in a 5-l. two-necked flask. One neck of the flask bears a reflux condenser; the other is closed with a stopper that can be removed momentarily for the addition of reagents. The tribromoaniline is brought into solution by heating the flask on a steam bath. To this solution are added 140 cc. of concentrated sulfuric acid, then 140 g. (2.03 moles) of powdered sodium nitrite as rapidly as the violence of the reaction will permit. When the reaction has moderated, the solution is brought to the boiling point and maintained there as long as gas is evolved. It is then allowed to stand in a warm place for three hours more.

After the mixture has been cooled (preferably in an ice bath), the mother liquor is removed from the solid by decantation through a Büchner funnel; if necessary, a wire gauze is used to retain the solid in the flask. To the solid is then added a solution of 150 cc. of concentrated sulfuric acid in 1500 cc. of water. When the excess sodium nitrite has been decomposed, the solid is transferred to a Büchner funnel and washed first with water and then with a small amount of alcohol. The yield of crude, dry tribromobenzene is 250–260 g. (75–78 per cent of the theoretical amount). The product is reddish-brown in color, and melts at 112–116°.

For further purification, 100 g. of the crude product is dissolved in a boiling mixture of 1560 cc. of glacial acetic acid and 350 cc. of water; the solution is boiled for a few minutes with 25 g. of decolorizing carbon, filtered hot, and allowed to cool. The crystals are washed on a Büchner funnel with a small amount of chilled 95 per cent alcohol to remove the acetic acid. This gives 216–240 g. (65–72 per cent of the theoretical amount) of product, only slightly colored, and melting at 121.5–122.5° (corr.).

The yield of crude product may be increased 50–60 g.—making a total of 300–320 g. (90–96 per cent of the theoretical amount) —by working up the mother liquors. The alcoholic liquors and

XXVIII

sym.-TRIBROMOBENZENE

$$C_6H_5NH_2 + 3Br_2 \rightarrow C_6H_2Br_3NH_2 + 3HBr$$

$$C_6H_2Br_3NH_2 \cdot H_2SO_4 + HNO_2$$

$$\rightarrow C_6H_2Br_3N_2HSO_4 + 2H_2O$$

$$C_6H_2Br_3N_2HSO_4 + C_2H_5OH$$

$$\rightarrow C_6H_3Br_3 + CH_3CHO + N_2 + H_2SO_4$$

Submitted by G. H. Coleman and William F. Talbot.
Checked by Reynold C. Fuson and Charles F. Woodward.

1. Procedure

The apparatus consists of a 12-l. round-bottomed flask and a 250-cc. suction flask provided with stoppers and glass tubes as shown in Fig. 3. After the flasks have been charged, A is surrounded by an ice bath and B by a water bath heated to 40–50°. In flask A are placed 100 g. (1.06 moles) of aniline, 1 l. of water, and 100 cc. (1.2 moles) of concentrated hydrochloric acid; when the aniline has dissolved, sufficient water is added to bring the volume of the solution to 5 l. Flask B is charged with 577 g. (185 cc., 3.6 moles) of bromine; the baths are adjusted, and a rapid stream of air saturated with bromine vapor is drawn into A by applying suction at C (Notes 1 and 2).
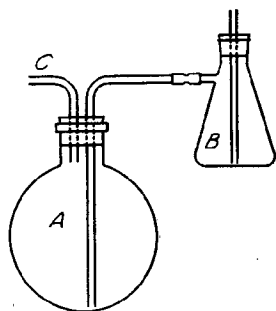
Fig. 3.

The introduction of bromine is continued until the solution assumes a distinctly yellow color (approximately three to four hours are required); reaction is then complete. The tribromo-

washings are diluted to 6 l., and the aqueous layer is separated from the heavy oil at the bottom. The benzene is then distilled from the oil in a distilling flask, care being used not to overheat the product after the benzene has been removed. The residual tribromobenzene may be recrystallized in the manner described above.

2. Notes

1. Considerable heat is generated by the reaction, and it is necessary to cool A to prevent the loss of bromine. Flask B must be kept at 40–50° to insure a high concentration of bromine vapor in the air stream; the violent agitation produced by air saturated at lower temperatures whips the reaction mixture into a light foam that is apt to overflow the flask.

2. It is well to interpose a safety flask between the reaction flask and the aspirator. The safety flask is partially filled with water through which the air stream passes after the bromine vapor has been removed. This device serves a double purpose; it enables one to gauge the rate of aspiration by the rate at which the air current bubbles through the water, and it serves to detect the escape of bromine vapors from the reaction flask. A small amount of bromine will impart to the water a distinctly yellow color. In case bromine does escape into this trap a momentary release of the suction will cause the wash water to be drawn into the reaction flask, thus returning the bromine to the reaction mixture.

3. Methods of Preparation

Sym.-tribromobenzene has been prepared from 3,5-dibromo-aniline by the replacement of the amino group by bromine;[1] from bromoacetylene by the action of light;[2] by the decomposition of 2,4,6-tribromophenylhydrazine;[3] by the reduction of 2,4,6-tri-bromobenzene diazonium sulfate;[4,5] and as a by-product in the preparation of 2,4,6-tribromobenzonitrile.[6]

[1] Körner, Gazz. chim. ital. **4**, 410 (1874).

[2] Sabancjew, J. Russ. Phys.-Chem. Soc. **17**, I, 176 (1885) [Ber. **18**, 374 (R) (1885)].

[3] Chattaway and Vonderwahl, J. Chem. Soc. **107**, 1508 (1915).

[4] Jackson and Moore, Am. Chem. J. **12**, 167 (1890).

[5] Jackson and Bentley, Am. Chem. J. **14**, 335 (1892).

[6] Montagne, Rec. trav. chim. **27**, 347 (1908).

XXIX

TRICARBOMETHOXYMETHANE

$$2CH_2(CO_2CH_3)_2 + 2Na \rightarrow 2NaCH(CO_2CH_3)_2 + H_2$$
$$NaCH(CO_2CH_3)_2 + ClCO_2CH_3 \rightarrow CH(CO_2CH_3)_3 + NaCl$$
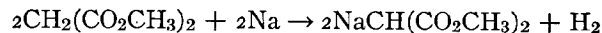
Submitted by B. B. Corson and J. L. Sayre.
Checked by Roger Adams and A. E. Knauf.

1. Procedure

In a 2-l. three-necked flask fitted with an upright condenser, a separatory funnel, and a mercury-sealed stirrer, are placed 400 cc. of dry xylene and 13 g. (0.56 gram atom) of sodium. The flask is heated in an oil bath until the sodium melts, and the mixture is stirred until the sodium is broken up into fine globules. Then 69 g. (0.57 mole) of dimethyl malonate is added over a period of five to ten minutes (Note 1).

The mixture is cooled while being well stirred, and when the temperature reaches about 65°, 57 g. (0.6 mole) of methyl chloroformate is added during five to ten minutes. The mixture is then warmed slowly so that the boiling point is reached in about fifteen to twenty minutes. Boiling and stirring are maintained for five hours.

The mixture is cooled to room temperature, the flask is filled two-thirds full with water, and stirring is continued for five minutes. The xylene solution is separated, washed with water, dried over calcium chloride, filtered, and distilled under reduced pressure. After removal of the solvent, the tricarbomethoxymethane distils at 128–142°/18 mm. The yield of crude product is 50–51 g. (47–48 per cent of the theoretical amount). This material becomes semi-solid on cooling.

The crude product is purified by dissolving it in an equal

volume of methyl alcohol and then cooling the solution in a freezing mixture until crystallization is complete. The solution is filtered with suction, and the mother liquors are again cooled in a freezing mixture. If necessary this process is repeated a third time or until no further crop of crystals separates on chilling the mother liquors. The crystals are transferred from the funnel to a beaker, stirred with about 70 cc. of petroleum ether (b.p. 32–45°), filtered, pressed dry, and washed with a little petroleum ether. The yield of fine, snow-white crystals melting at 43–45° is about 40–42 g. (37–39 per cent of the theoretical amount).

2. Notes

1. A brisk evolution of hydrogen occurs, and sodium dimethyl malonate settles as a pasty mass. Stirring should be vigorous during the addition of the malonic ester and also during the subsequent heating, to avoid caking of the sodium salt.

2. Tricarbomethoxymethane is very soluble, and only by repeated cooling and filtration can a good recovery be obtained. Owing to this excessive solubility the apparent loss on crystallization is high. However, a considerable portion of this material can be recovered from the alcoholic mother liquors.

3. Methods of Preparation

This method is very similar to the one recently published by Adickes, Brunnert, and Lücker.[1] In the older methods[2] the sodium salt of dimethyl malonate was isolated.

[1] Adickes, Brunnert, and Lücker, J. prakt. Chem. **130**, 163 (1931).
[2] Scholl and Egerer, Ann. **397**, 355 (1913); Philippi, Hanusch, and von Wacek, Ber. **54**, 901 (1921).

XXX

VERATRIC ALDEHYDE (3,4-DIMETHOXYBENZALDEHYDE)

$$CHO-C_6H_3(OCH_3)(OH) + (CH_3)_2SO_4 + NaOH$$

$$\rightarrow CHO-C_6H_3(OCH_3)(OCH_3) + CH_3SO_4Na + H_2O$$
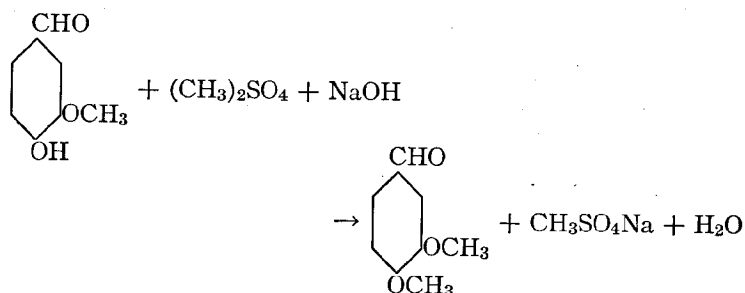
Submitted by JOHANNES S. BUCK.
Checked by JOHN R. JOHNSON and H. R. SNYDER.

1. Procedure

IN a 3-l. three-necked flask a mixture of 182 g. (1.2 moles) of vanillin (Note 1) and 450 cc. of boiling water is heated on a steam bath. A solution of sodium hydroxide is prepared by dissolving 150 g. of sodium hydroxide (U. S. P.) in 200–300 cc. of water and diluting to 750 cc. A 360-cc. portion of this solution is heated to about 100° and added in one lot to the hot mixture of vanillin and water (Note 2). The flask is now fitted with a reflux condenser, mechanical stirrer, and 250-cc. separatory funnel.

Heating is continued on a steam bath, and 189 g. (142 cc.) of dimethyl sulfate (Note 3) is added through the separatory funnel just rapidly enough to maintain the gentle ebullition which starts after the addition of the first 10–15 cc. (Note 4). After the addition of all of the dimethyl sulfate, which requires about one hour, the reaction mixture is heated for forty-five minutes longer and an additional portion of 39 g. (30 cc.) of dimethyl sulfate is added at the same rate as the first portion. At the end of this addition

102

the reaction mixture should show an acid reaction to litmus (Note 5). After ten minutes' heating the reaction mixture is rendered slightly alkaline by the addition of about 60 cc. of the sodium hydroxide solution (prepared above), and another 39-g. portion of dimethyl sulfate is added. The alternate addition of sodium hydroxide solution and of dimethyl sulfate (39-g. portions) is repeated twice more, so that a total quantity of 345 g. (2.7 moles) of dimethyl sulfate is added. The reaction mixture is then made strongly alkaline by the addition of 150 cc. of the sodium hydroxide solution and is heated for twenty minutes after the last addition of dimethyl sulfate. The reaction mixture is cooled rapidly to 25° (Note 6) with continued stirring, and the veratric aldehyde is extracted with three 300-cc. portions of ether. The combined extracts are dried over anhydrous magnesium sulfate, and the ether is distilled off. There remains a slightly yellow oil which soon solidifies. The yield is 164–173 g. (82–87 per cent of the theoretical amount) of veratric aldehyde melting at 43–44.5°. This product is sufficiently pure for many purposes. It can be purified further with slight loss by distillation under diminished pressure. From 164 g. of the above product there is obtained 156 g. of pure veratric aldehyde (b.p. 153°/8 mm.) melting at 46°. Since this aldehyde is easily oxidized in the air it should be stored in a tightly corked or sealed container.

2. Notes

1. A good grade of vanillin (m.p. 81–82°) should be used.

2. The reactants are mixed while hot in order to avoid precipitation of the sodium salt of vanillin.

3. A practical grade of dimethyl sulfate gives satisfactory results. Dimethyl sulfate is very toxic, and care should be exercised to avoid inhaling its vapors or spilling the liquid. Ammonia is a specific antidote. The preparation is preferably carried out under a good hood.

4. The yield is usually lowered if this ebullition does not occur.

5. In order to obtain a good yield it is essential that the

reaction mixture be allowed to become acid at several times. For this reason the last 156 g. is added in four small portions, and the reaction mixture is allowed to become acid after each portion is added. It is convenient to test the reaction of the solution by lowering through the condenser tube a glass tube with a piece of litmus paper attached at the end.

6. If the reaction mixture is cooled too slowly or below 25°, the veratric aldehyde may solidify at this stage. If this occurs it is advisable to remelt the product before extracting with ether.

3. Methods of Preparation

Veratric aldehyde has been prepared from vanillin by methylation with dimethyl sulfate [1] or with methyl iodide,[2] and from veratrole by reaction with hydrogen cyanide in the presence of aluminum chloride.[3]

[1] v. Kostanecki and Tambor, Ber. **39**, 4022 (1906).
[2] Tiemann, Ber. **8**, 1135 (1875); **11**, 663 (1878); Juliusberg, ibid. **40**, 119 (1907)
[3] Gattermann, Ann. **357**, 367 (1907).

APPENDIX

LATER REFERENCES TO PREPARATIONS IN THE PRECEDING VOLUMES

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

Adipic Acid (*Coll. Vol.* 1, 18):

By oxidation of cyclohexanol with alkaline permanganate. WAGNER, J. Chem. Education 10, 115 (1933).

γ-Chlorobutyronitrile (*Coll. Vol.* 1, 150):

By the addition of hydrogen chloride to allyl cyanide. BRECKPOT, Bull. soc. chim. Belg. 39, 467 (1930).

Desoxybenzoin (12, 16):

In 88 per cent yield by reducing benzoin with tin and hydrochloric acid. BALLARD and DEHN, J. Am. Chem. Soc. 54, 3970 (1932).

Dimethylglyoxime (10, 22):

Methyl ethyl ketone is converted to biacetyl monoxime in ethereal solution, and the latter is treated with sodium hydroxylamine disulfonate. SLOTTA and JACOBI, Z. anal. Chem. 83, 1 (1931).

Epichlorohydrin (*Coll. Vol.* 1, 228):

By treating dichlorohydrin with calcium hydroxide in the presence of water. BRAUN, J. Am. Chem. Soc. 54, 1248 (1932).

Furan (*Coll. Vol.* 1, 269):

By passing furfural over hot soda-lime or by dropping furfural onto a fused mixture of sodium and potassium hydroxides. HURD, GOLDSBY, and OSBORNE, J. Am. Chem. Soc. 54, 2532. (1932).

2-Furancarboxylic Acid (*Coll. Vol.* 1, 270):

In 75 per cent yield by the oxidation of furfural with potassium dichromate and sulfuric acid. HURD, GARRETT and OSBORNE, J. Am. Chem. Soc. 55, 1084 (1933).

Glutamic Acid (*Coll. Vol.* 1, 281):

From benzoylaminomalonic ester by reaction with β-bromopropionic ester followed by hydrolysis. DUNN, SMART, REDEMANN, and BROWN, J. Biol. Chem. 94, 599 (1931).

Glycine (*Coll. Vol.* 1, 292):

By the action of ammonia on copper chloroacetate. KRAUSE, Chem. Ztg. 55, 666 (1931).

Guanidine Nitrate (*Coll. Vol.* 1, 295):

Guanidine thiocyanate, prepared by passing ammonia into molten ammonium thiocyanate, is converted into the sulfate. The latter can be converted to the nitrate by the action of calcium nitrate. GLUUD, KELLER and SCHULTZE, Ber. ges. Kohlentech. 4, 21 (1931) [C. A. 26, 2017 (1932)].

Ketene (*Coll. Vol.* 1, 325):

The yields of ketene obtained by the decomposition of acetone increase as the space velocity is increased and at low conversions may exceed 75 per cent of the theoretical. Many publications and patents dealing with this reaction have appeared, and of these the following appear to be the most important. RICE, U. S. pat. 1,879,497; CLARKE, Brit. pat. 309,577; HURD

and DULL, J. Am. Chem. Soc. **54**, 3428 (1932); BERL, Ger. pat. 536,423; BERL and KULLMANN, Ber. **65**, 1114 (1932); AL, Angew. Chem. **45**, 545 (1932). The last three of these references report positive catalytic effects especially with vanadium oxide.

A new apparatus for decomposing acetone to ketene with a hot filament has also been described. OTT, SCHRÖTER and PACKENDORFF, J. prakt. Chem. **130**, 177 (1931).

A very high yield of ketene obtained by passing vapors of acetic anhydride through a platinum tube at 800° is reported. PEYTRAL, Compt. rend. **193**, 1199 (1931).

Lauryl Alcohol (10, 62):

By hydrogenation at high pressure of ethyl laurate in the presence of a copper-chromium catalyst. ADKINS and FOLKERS, J. Am. Chem. Soc. **53**, 1095 (1931).

By hydrogenation at high pressure of lauric acid in the presence of a zinc-copper-cadmium-chromium catalyst. LAZIER, U. S. pat. 1,839,974.

By the hydrogenation at high pressure of lauric acid in the presence of a nickel catalyst. NORMANN, Z. angew. Chem. **44**, 714 (1931).

By hydrogenation at high pressure of methyl laurate in the presence of a zinc-copper-chromium catalyst. SCHRAUTH, SCHENCK, and STICKDORN, Ber. **64**, 1314 (1931).

Methyl Isopropyl Carbinol (12, 48):

Produced along with other higher alcohols by the hydrogenation of carbon monoxide under high pressure. GRAVES, Ind. Eng. Chem. **23**, 1381 (1931).

Propionaldehyde (12, 64):

Formed along with acetone by passing propylene oxide over an alkaline earth halide at elevated temperature. Brit. pat. 354,388 [C. A. **26**, 5310 (1932)].

Formed in 76 per cent yield by the catalytic oxidation of *n*-propyl alcohol. DAY and EISNER, J. Phys. Chem. **36**, 1912 (1932)

p-Tolualdehyde (12, 80):

p-Tolyl dithiocarboxylic acid prepared from *p*-tolylmagnesium bromide and carbon bisulfide is converted by treatment with semicarbazine into *p*-tolualdehyde semicarbazone, which is hydrolyzed to *p*-tolualdehyde. WUYTS, BERMAN and LACOURT, Bull. Soc. chim. Belg. **40**, 665 (1931) [C. A. **26**, 2723 (1932)].

Triethyl Carbinol (11, 98):

By the action of ethylmagnesium bromide on ethyl propionate. BÖESEKEN and WILDSCHUT, Rec. trav. chim. **51**, 168 (1932).

Trimethylacetic Acid (*Coll. Vol.* 1, 510):

The yield of *ter.*-butylmagnesium chloride is increased to 85 per cent of the theoretical by slight changes in the manner of adding the *ter.*-butyl chloride. WHITMORE and HOUK, J. Am. Chem. Soc. **54**, 3716 (1932).

1,3,5-Trinitrobenzene (*Coll. Vol.* 1, 526):

By the action of alcoholic ammonia on trinitrobenzaldehyde. SECAREANU, Bull. soc. chim. **51**, 596 (1932).

ADDITIONS AND CORRECTIONS FOR PRECEDING VOLUMES

(The numbers in parentheses following the name of the compound refer to the volume and page of Organic Syntheses.)

Adipic Acid (*Coll. Vol.* 1, 18):

The yield is reported to be improved by the following modification of the method described. In a 3-l. three-necked flask provided with a stirrer, reflux condenser, and dropping funnel, set in asbestos-sodium silicate stoppers (5, 9), are placed 1900 cc. of 50 per cent nitric acid (1262 cc. of nitric acid, sp. gr. 1.42, diluted to 1900 cc.) and 1 g. of ammonium vanadate. The flask is surrounded by a water bath heated to 50–60°, and, while the mixture is stirred, 357 g. (3.5 moles) of commercial cyclohexanol is added very slowly so that the temperature of the bath is maintained at 50–60°. This requires about six to eight hours. The reaction is completed by heating the water bath to boiling until the evolution of nitrogen oxides has ceased (about one hour). The hot reaction mixture is siphoned off and allowed to cool. The yield of crude adipic acid is 372 g. (72 per cent of the theoretical amount).

DUNCAN G. FOSTER, private communication.

Cyclopentanone (*Coll. Vol.* 1, 187):

In salting out the product from the distillate it is reported that potassium carbonate is more satisfactory than calcium chloride; traces of adipic acid are removed, and the loss which attends washing with alkali is avoided.

WAGNER, J. Chem. Education 10, 115 (1933).

2-Furancarboxylic Acid and 2-Furylcarbinol (*Coll. Vol.* 1, 270):

It is reported that the necessity of extracting the carbinol with ether after completion of the Cannizzaro reaction can be avoided and the yields are improved if the excess alkali is neutralized with furoic acid or ammonium sulfate or if a slight deficiency of alkali is used in the first place. HURD, GARRETT and OSBORNE, J. Am. Chem. Soc. 55, 1083 (1933).

Itaconic Acid (11, 70):

The following method is a great improvement on that described. Nine 120-g. portions of citric acid are distilled rapidly (four to six minutes), using 300-cc. Kjeldahl flasks, and all the distillates are collected in the same receiver. The distillate, which generally does not consist of two layers, is placed in an evaporating dish, 50 cc. of water is added, and the mixture is allowed to stand on a steam bath for three hours. On cooling it sets to a semi-solid mass; this is filtered and washed with 150 cc. of water. The residue consists of 138 g. of perfectly white crystals melting at 165°. By concentrating the filtrate an additional 42 g. of product melting at 157–165° is obtained. The total yield is 26–27 per cent of the theoretical amount.

C. V. WILSON and C. F. H. ALLEN, private communication.

Perbenzoic Acid (*Coll. Vol* 1, 422):

The procedure described in the present volume (p. 86) represents a considerable improvement over that described in the Collective Volume. The latter also contains two errors: The amount of sodium specified (23 g.) is twice the correct amount, and the percentage yield stated as 90 is actually only 65.

Pinacol Hydrate (*Coll. Vol.* 1, 449):

The product obtained by this method is reported to contain volatile compounds of mercury. These toxic impurities can be destroyed by distilling with steam. BACKER and BOTTEMA, Rec. trav. chim. 51, 295 (1932).

Thiophosgene (*Coll. Vol.* 1, 493):

No reference was made to HELFRICH and REID, J. Am. Chem. Soc. **43**, 591 (1921), who describe what appears to be a simpler method for preparing the intermediate thiocarbonyl perchloride. AUTENRIETH and HEFNER, Ber. **58**, 2151 (1925), have also studied and made improvements in the preparation of thiophosgene.

SUBJECT INDEX

(This Index Comprises Material from Volumes X to XIII of this Series)

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

ORGANIC SYNTHESES

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

VOL. XIII

PREFACE TO VOLUME XIII

THIS is the first volume of *Organic Syntheses* to be published since the appearance of the first Collective Volume. The latter contains in revised form all the material originally presented in the first nine annual volumes. The index of the present volume therefore includes those of Volumes X, XI, and XII but not those of earlier volumes; and in the text, citations are made only to Org. Syn. **10**, **11**, and **12** and to Coll. Vol. **1**.

TABLE OF CONTENTS