Organic Syntheses

A Publication
of Reliable Methods
for the Preparation
of Organic Compounds

Working with Hazardous Chemicals

The procedures in *Organic Syntheses* are intended for use only by persons with proper training in experimental organic chemistry. All hazardous materials should be handled using the standard procedures for work with chemicals described in references such as "Prudent Practices in the Laboratory" (The National Academies Press, Washington, D.C., 2011; the full text can be accessed free of charge at http://www.nap.edu/catalog.php?record_id=12654). All chemical waste should be disposed of in accordance with local regulations. For general guidelines for the management of chemical waste, see Chapter 8 of Prudent Practices.

In some articles in *Organic Syntheses*, chemical-specific hazards are highlighted in red "Caution Notes" within a procedure. It is important to recognize that the absence of a caution note does not imply that no significant hazards are associated with the chemicals involved in that procedure. Prior to performing a reaction, a thorough risk assessment should be carried out that includes a review of the potential hazards associated with each chemical and experimental operation on the scale that is planned for the procedure. Guidelines for carrying out a risk assessment and for analyzing the hazards associated with chemicals can be found in Chapter 4 of Prudent Practices.

The procedures described in *Organic Syntheses* are provided as published and are conducted at one's own risk. *Organic Syntheses, Inc.*, its Editors, and its Board of Directors do not warrant or guarantee the safety of individuals using these procedures and hereby disclaim any liability for any injuries or damages claimed to have resulted from or related in any way to the procedures herein.

These paragraphs were added in September 2014. The statements above do not supersede any specific hazard caution notes and safety instructions included in the procedure.

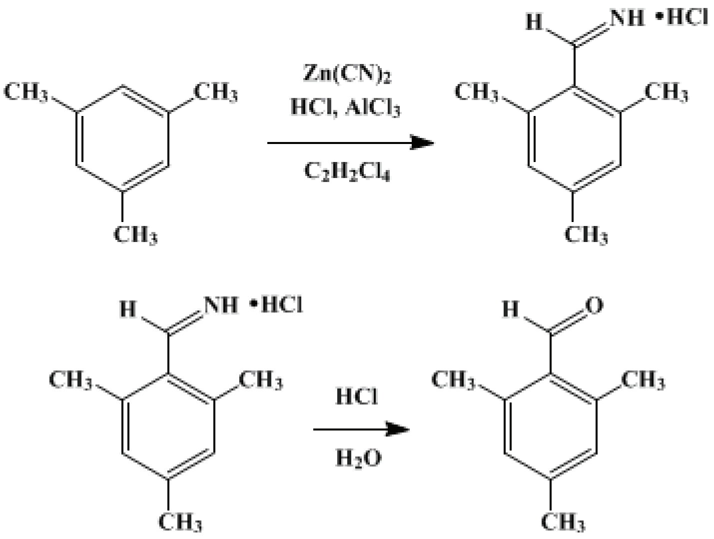
DOI:10.15227/orgsyn.023.0057

Organic Syntheses, Coll. Vol. 3, p.549 (1955); Vol. 23, p.57 (1943).

MESITALDEHYDE

[Benzaldehyde, 2,4,6-trimethyl-]

[I. METHOD A]



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

1. Procedure

In a 1-l. three-necked round-bottomed flask, fitted with an efficient stirrer, a reflux condenser, an inlet tube, and a thermometer (Note 1) and (Note 2), are placed 102 g. (118 ml., 0.85 mole) of mesitylene, 147 g. (1.25 moles) of zinc cyanide (Note 3), and 400 ml. of tetrachloroethane (Note 4). The inlet tube is connected to a source of hydrogen chloride (Note 5), and the mixture is stirred at room temperature while a rapid stream of dry hydrogen chloride is passed through it. This is continued until the zinc cyanide is decomposed; usually about 3 hours is required. The flask is then immersed in an ice bath, the inlet tube is removed, and 293 g. (2.2 moles) of finely ground anhydrous aluminum chloride is added to the mixture (Note 6) and (Note 7), with *very vigorous* stirring. The ice bath is then removed, and the passage of hydrogen chloride is resumed for the remainder of the reaction period. The heat of reaction is sufficient to warm the mixture slowly, and a temperature of about 70° is reached at the end of an hour. A temperature of 67–72° is maintained for an additional 2.5 hours. The cooled mixture is decomposed by pouring it cautiously, with stirring by hand, into a 4-l. container about half full of crushed ice, to which has been added 100 ml. of concentrated hydrochloric acid. After the mixture has stood overnight, it is transferred to a 3-l. round-bottomed flask and refluxed for 3 hours. The organic layer is then separated, and the aqueous layer is extracted once with 50 ml. of tetrachloroethane. The combined tetrachloroethane solutions are washed with 150 ml. of a 10% solution of sodium carbonate and distilled with steam. The first 800–900 ml. of distillate is set aside for recovery of the solvent (Note 8) and (Note 9), and the second portion is collected as long as oily drops are observed (Note 10). This distillate is extracted with 500 ml. of benzene, the solvent is removed on the steam bath, and the residue is distilled from a 250-ml. modified Claisen flask. After a small fore-run, the mesitaldehyde distils at 118–121°/16 mm. The yield is 95–102 g. (75–81%) (Note 11) and (Note 12).

2. Notes

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

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

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

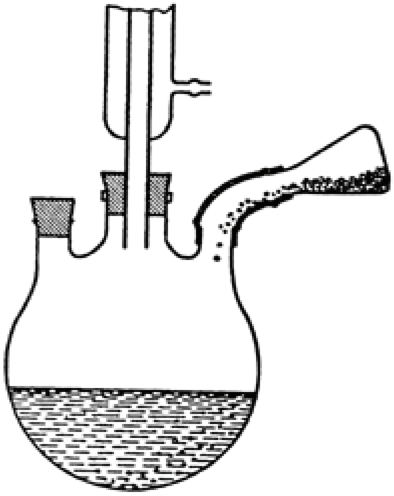
4. Tetrachloroethane is a toxic substance; it should be handled with due care.

5. Commercial cylinders of hydrogen chloride, now available, are most convenient.

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

7. The apparatus shown in Fig. 19 is most convenient. A 250-ml. Erlenmeyer flask is connected to the side neck of the flask by a 13-cm. length of 20-mm. thin-walled rubber tubing.[3]

Fig. 19.



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

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

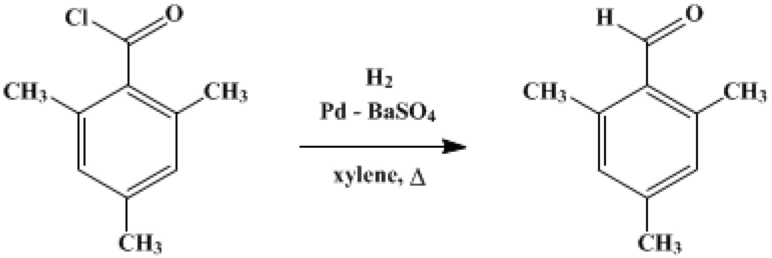
10. About 9 l. of water is obtained; the time required is about 4 hours.

11. If a smaller yield of mesitaldehyde is acceptable and time is of importance, the preparation may be carried out without a solvent, and with other changes as follows: The zinc cyanide and aluminum chloride are mixed by shaking, the mesitylene is added, and the flask is immersed in an oil bath at 100°. The stirrer is started, and a fairly rapid current of dry hydrogen chloride is passed into the mixture, below the surface of the liquid, for 4 hours; at the end of this time, the current of gas is discontinued, but stirring and heating are maintained for 2 hours longer. The reaction mixture is decomposed and processed as already described. The fraction which boils at 110–120°/9–10 mm. is taken as mesitaldehyde; the yield is 73% (private communication, D. B. Glass).

12. 2,4,6-Triethylbenzaldehyde and 2,4,6-triisopropylbenzaldehyde may be prepared in yields of 69 and 65%, respectively, by the procedure described above, with a reaction time of 8 hours and the following modifications:

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

[II. METHOD B]



Submitted by R. P. Barnes
Checked by Nathan L. Drake, Harry D. Anspon, and Ralph Mozingo.

1. Procedure

A 1-l. three-necked flask *with ground-glass joints* is fitted with a mercury-sealed stirrer (Note 1) and (Note 2), a glass tube of 6-mm. internal diameter which runs to the bottom of the flask, and a Friedrich condenser, protected by a drying tube. A solution of 90 g. (0.49 mole) of mesitoyl chloride (p. 555) in 270 g. of carefully dried xylene is placed in the flask together with 20 g. of palladium-barium sulfate (Note 3). The contents of the flask are refluxed while a stream of hydrogen (Note 4), which has been freed from oxygen by passage through Fieser's solution,[4] and dried by passage through concentrated sulfuric acid followed by a drying tube of Drierite (Note 5), is bubbled through the suspension until hydrogen chloride ceases to be evolved (Note 2). The catalyst is then removed by filtration and the xylene distilled. The residual liquid is transferred to a 125-ml. modified Claisen flask and distilled. The product boils at 96–98°/6 mm., and weighs 53–60 g. (70–80%) (Note 6).

2. Notes

1. The stirrer is not essential, but without it the time required for the reduction is increased about threefold.
2. The course of the reaction may be followed conveniently by passing the exit gases into water and titrating with approximately 1 *N* sodium hydroxide. The time for complete reduction is about 6–7 hours with stirring, and about 18 hours with no stirrer.
3. The palladium-barium sulfate is prepared by the method described by Houben.[5] The barium sulfate should be freshly precipitated material.
4. The checkers found that electrolytic hydrogen directly from the cylinder without purification gives only a slightly decreased yield.
5. Dehydrite or Anhydrone should not be used because of the danger of sulfuric acid spraying into it. Drierite is much more efficient than calcium chloride.
6. This preparation illustrates Rosenmund's method of synthesizing aldehydes without use of a poisoned catalyst. See p. 629 for the more general form of the method.

3. Discussion

Mesitaldehyde has been prepared from mesitylglyoxylic acid;[6,7] from mesitylmagnesium bromide and ethoxymethyleneaniline,[8] ethyl orthoformate,[8] or N-methylformanilide;[9] from mesitylene, hydrogen cyanide, and hydrogen chloride[10] or mesitylene, carbon monoxide, and hydrogen chloride[11] in the presence of aluminum and cuprous chlorides; and from mesitylene, zinc cyanide, and hydrogen chloride in the presence of aluminum chloride.[12,13,14]

The procedures described here are based on the method applied to the preparation of other aldehydes by Rosenmund and Zetzsche;[15] and by Nencki, as adapted for mesitaldehyde.[12,13,14]

This preparation is referenced from:

- Org. Syn. Coll. Vol. 3, 771
- Org. Syn. Coll. Vol. 3, 841

- Org. Syn. Coll. Vol. 4, 649
- Org. Syn. Coll. Vol. 5, 49
- Org. Syn. Coll. Vol. 5, 959

References and Notes

1. Adams and Levine, *J. Am. Chem. Soc.*, **45**, 2375 (1923).
2. Arnold and Sprung, *J. Am. Chem. Soc.*, **60**, 1699 (1938).
3. Fieser, *Experiments in Organic Chemistry*, p. 311, New York, 1941. Reprinted by special permission of D. C. Heath and Company.
4. Fieser, *J. Am. Chem. Soc.*, **46**, 2639 (1924).
5. Houben, *Die Methoden der organischen Chemie*, 3rd ed., Vol. II, p. 500, Verlag Georg Thieme, Leipzig, 1930; Schmidt, *Ber.*, **52**, 409 (1919).
6. Bouveault, *Compt. rend.*, **124**, 156 (1897).
7. Feith, *Ber.*, **24**, 3542 (1891).
8. Smith and Nichols, *J. Org. Chem.*, **6**, 489 (1941).
9. Smith and Bayliss, *J. Org. Chem.*, **6**, 437 (1941).
10. German pat. 99,568 [*Chem. Zentr.*, **70**, I, 461 (1899)].
11. German pat. 98,706 [*Chem. Zentr.*, **69**, II, 952 (1898)].
12. Fuson, Horning, Ward, Rowland, and Marsh, *J. Am. Chem. Soc.*, **64**, 30 (1942).
13. Hinkel, Ayling, and Morgan, *J. Chem. Soc.*, **1932**, 2793.
14. Hinkel, Ayling, and Beynon, *J. Chem. Soc.*, **1936**, 339.
15. Rosenmund, *Ber.*, **51**, 585 (1918); Rosenmund and Zetzsche, *Ber.*, **54**, 425 (1921).

Appendix
Chemical Abstracts Nomenclature (Collective Index Number);
(Registry Number)

Drierite

Dehydrite

Anhydrone

aluminum and cuprous chlorides

calcium chloride (10043-52-4)

sulfuric acid (7664-93-9)

hydrogen chloride,
hydrochloric acid (7647-01-0)

Benzene (71-43-2)

hydrogen (1333-74-0)

sodium hydroxide (1310-73-2)

carbon monoxide (630-08-0)

hydrogen cyanide (74-90-8)

sodium carbonate (497-19-8)

oxygen (7782-44-7)

barium sulfate (7727-43-7)

aluminum chloride (3495-54-3)

xylene (106-42-3)

Mesitylene (108-67-8)

Ethyl orthoformate

tetrachloroethane (630-20-6)

ethoxymethyleneaniline (6780-49-0)

N-methylformanilide (93-61-8)

Mesitaldehyde,
Benzaldehyde, 2,4,6-trimethyl- (487-68-3)

zinc cyanide (557-21-1)

2,4,6-Triethylbenzaldehyde

2,4,6-triisopropylbenzaldehyde

Mesitoyl chloride (938-18-1)

palladium-barium sulfate

mesitylglyoxylic acid (3112-46-7)

mesitylmagnesium bromide

Triethylbenzaldehyde

Triisopropylbenzaldehyde