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.

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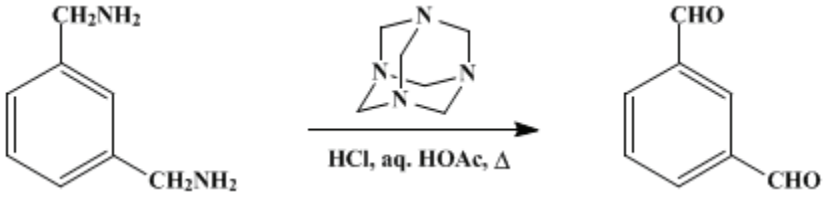
ISOPHTHALALDEHYDE



Submitted by J. H. Ackerman and A. R. Surrey[1].
Checked by Kenneth H. Brown, Wayland E. Noland, and William E. Parham.

1. Procedure

A solution of 272 g. (261 ml., 2.00 moles) of α,α'-diamino-*m*-xylene (Note 1), 1.00 kg. (7.1 moles) of hexamethylenetetramine, 480 ml. of concentrated hydrochloric acid, and 3.2 l. of 50% aqueous acetic acid in a 12-l. flask is stirred and heated at the reflux temperature for 2.5 hours. The hot amber reaction mixture is then poured into a large battery jar in a well-ventilated hood, and a solution prepared from 298 g. of sodium hydroxide and 3.85 l. of water is added slowly with stirring (Note 2). The mixture is covered and allowed to stand overnight at about 5°. The product, which separates as long needles, is collected, washed on a Buchner funnel with 100 ml. of cold water, and then dried to constant weight under vacuum (Note 3) over calcium chloride. There is obtained 158–166 g. (59–62%) of almost colorless needles of isophthalaldehyde, m.p. 88–90° (Note 4).

2. Notes

1. α,α'-Diamino-*m*-xylene was obtained from California Chemical Company and Aldrich Chemical Company.
2. The sodium hydroxide solution is added to neutralize most of the acetic acid present. Better yields are obtained using this neutralization procedure than by merely cooling the reaction mixture.
3. The checkers observed that house vacuum removed only 50% of the water after 48 hours.
4. One lot of α,α'-diamino-*m*-xylene from Aldrich Chemical Company gave the isophthalaldehyde as pale pink, long needles, m.p. 88–90°. When 12.0 g. of this material was recrystallized from 500 ml. of water, there was obtained 10.9 g. (91%) of pale cream, long needles, m.p. 89–91°.

3. Discussion

The procedure described is a modification of the general procedure of Angyal[2] for the preparation of aldehydes from benzylamines by the Sommelet reaction. Isophthalaldehyde has been prepared from *m*-xylene by preparation of the tetrachloro derivative and hydrolysis,[3] from isophthaloyl chloride by the Rosenmund reaction,[4] from α,α'-dibromo-*m*-xylene by the Sommelet reaction,[5] and from isophthaloyl chloride by reduction with lithium tri-*t*-butoxyaluminumhydride.[6]

4. Merits of the Preparation

Isophthalaldehyde is a valuable intermediate. Although the yields obtained by some of the other reported methods of preparation are better than the yield obtained here, the availability of starting material and the simplicity of reaction make this method attractive.

This appears to be the first reported case of the Sommelet reaction starting with a diamine.

References and Notes

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

2. S. J. Angyal, *Org. Reactions*, **8**, 197 (1954).
3. A. Colson and H. Gautier, *Bull. Soc. Chim. France*, **45**, 509 (1886).
4. K. W. Rosenmund F. Zetzsche, and C. Flütsch, *Ber.*, **54**, 2888 (1921).
5. K. F. Jennings, *J. Chem. Soc.*, 1172 (1957).
6. H. C. Brown and B. C. Subba Rao, *J. Am. Chem. Soc.*, **80**, 5377 (1958).

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

calcium chloride (10043-52-4)

hydrochloric acid (7647-01-0)

acetic acid (64-19-7)

sodium hydroxide (1310-73-2)

hexamethylenetetramine (100-97-0)

Isophthalaldehyde (626-19-7)

isophthaloyl chloride (99-63-8)

lithium tri-t-butoxyaluminumhydride

m-xylene (108-38-3)

α,α'-diamino-m-xylene

α,α'-dibromo-m-xylene