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.

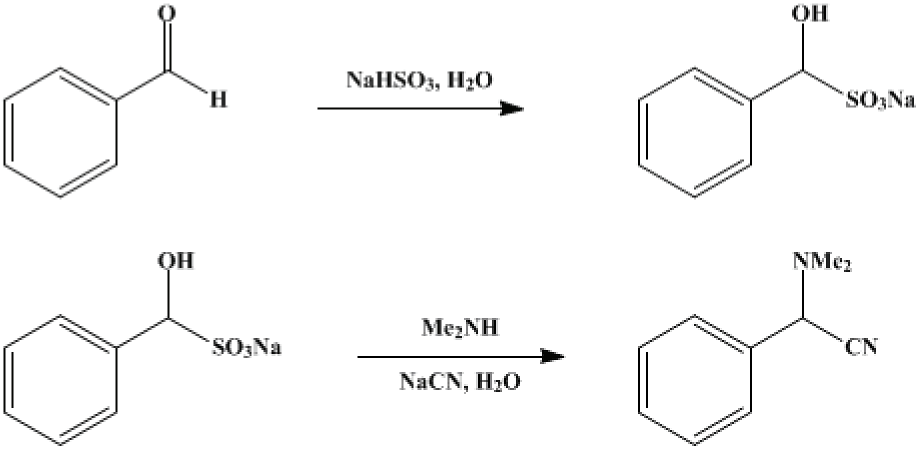
These paragraphs were added in September 2014. The statements above do not supersede any specific hazard caution notes and safety instructions included in the procedure.

DOI:10.15227/orgsyn.043.0025

Organic Syntheses, Coll. Vol. 5, p.437 (1973); Vol. 43, p.25 (1963).

α-(N,N-DIMETHYLAMINO)PHENYLACETONITRILE

[Glycinonitrile, N,N-dimethyl-2-phenyl-]



Submitted by Harold M. Taylor and Charles R. Hauser[1].
Checked by W. Bruce Kover and John D. Roberts.

1. Procedure

A mixture of 1.5 l. of water and 624 g. (6.00 moles) of sodium bisulfite in a 5-l. beaker equipped with a mechanical stirrer is stirred until solution is complete. Benzaldehyde (Note 1) (636 g., 6.00 moles) is added and the mixture is stirred for 20 minutes, during which time a slurry of the benzaldehyde-bisulfite addition product is formed. A 25% aqueous solution of dimethylamine (1100 g.) containing 275 g. (6.13 moles) of the amine is run in, and stirring is continued as most of the addition compound dissolves. The beaker is immersed in an ice bath, and 294 g. (6.00 moles) of sodium cyanide *(Caution! Toxic)* is added over a period of 20–25 minutes.

The ice bath is removed after addition of the sodium cyanide, and the mixture is stirred for 4 hours. The organic layer is separated, and the aqueous layer is extracted with three 500-ml. portions of ether. The combined ethereal extracts and organic layer are washed with two 100-ml. portions of cold water and dried over anhydrous magnesium sulfate. The ethereal solution is filtered, and the ether is removed at atmospheric pressure. The residue is transferred to a vacuum distillation system and distilled under reduced pressure *(Caution! See (Note 2))*. The yield of α-(N,N-dimethylamino)phenylacetonitrile boiling at 88–90°/1.9–2.1 mm. is 842–844 g. (87–88%) (Note 3) and (Note 4).

2. Notes

1. Eastman Kodak benzaldehyde (white label grade) was used without further purification.
2. Occasionally the odor of hydrogen cyanide can be detected during the distillation, even when a trap filled with sodium hydroxide pellets precedes the usual trap cooled in dry ice and acetone to protect the pump. For safety, the vacuum pump should be placed in a hood, or provision should be made for the pump exhaust to be vented into a hood or out-of-doors during the distillation.
3. Anhydrous dimethylamine has been used by the submitters in a slightly different procedure to give yields up to 95% of the theory.
4. The checkers carried out the preparation with one-half of the specified quantities without any decrease in the yield.

3. Discussion

The procedure described above is a modification of that of Hauser, Taylor, and Ledford[2] and of

Luten[3] which avoids use of anhydrous dimethylamine. It is related to the procedure of Goodson and Christopher[4] that employs benzaldehyde, aqueous dimethylamine hydrochloride, and potassium cyanide.

The product can also be prepared from benzaldehyde, dimethylamine, and potassium cyanide in cold acetic acid and aqueous ethanol.[5]

4. Merits of the Preparation

The method can be used to prepare a number of α-aminonitriles from aliphatic or aromatic aldehydes and ketones and secondary aliphatic amines.[6]

The nitrile group of α-(N,N-dimethylamino)phenylacetonitrile can generally be replaced by an alkyl or aryl group of a Grignard reagent to form the corresponding tertiary amines.[4,7] The α-hydrogen of the aminonitrile can be alkylated,[2,7] and the resulting alkylation product can be converted to enamines[2] or to ketones.[7]

References and Notes

1. Department of Chemistry, Duke University, Durham, North Carolina.
2. C. R. Hauser, H. M. Taylor, and T. G. Ledford, *J. Am. Chem. Soc.*, **82**, 1786 (1960).
3. D. B. Luten, *Jr., J. Org. Chem.*, **3**, 588 (1939).
4. L. H. Goodson and H. Christopher, *J. Am. Chem. Soc.*, **72**, 358 (1950).
5. T. S. Stevens, J. M. Cowan, and J. MacKinnon, *J. Chem. Soc.*, 2568 (1931).
6. V. Migrdichian, "The Chemistry of Organic Cyanogen Compounds," Reinhold Publishing Company, New York, 1947, pp. 198–217.
7. H. M. Taylor and C. R. Hauser, *J. Am. Chem. Soc.*, **82**, 1960 (1960).

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

ethanol (64-17-5)

acetic acid (64-19-7)

ether (60-29-7)

sodium hydroxide (1310-73-2)

sodium cyanide (143-33-9)

hydrogen cyanide (74-90-8)

potassium cyanide (151-50-8)

sodium bisulfite (7631-90-5)

benzaldehyde (100-52-7)

acetone (67-64-1)

dimethylamine (124-40-3)

dimethylamine hydrochloride (506-59-2)

magnesium sulfate (7487-88-9)

Glycinonitrile, N,N-dimethyl-2-phenyl-,
α-(N,N-DIMETHYLAMINO)PHENYLACETONITRILE (30123-97-8)