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.

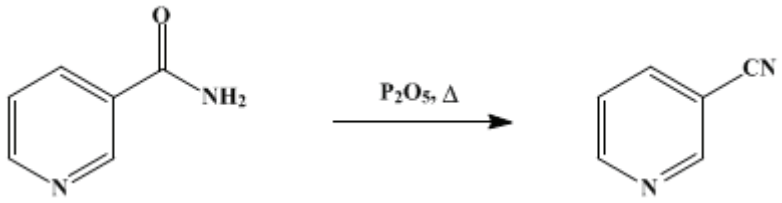
The procedures described in *Organic Syntheses* are provided as published and are conducted at one's own risk. *Organic Syntheses, Inc.*, its Editors, and its Board of Directors do not warrant or guarantee the safety of individuals using these procedures and hereby disclaim any liability for any injuries 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.033.0052

Organic Syntheses, Coll. Vol. 4, p.706 (1963); Vol. 33, p.52 (1953).

NICOTINONITRILE



Submitted by Peyton C. Teague and William A. Short[1].
Checked by Arthur C. Cope, John C. Sheehan, and Louis A. Cohen.

1. Procedure

In a dry 1-l. round-bottomed flask are placed 100 g. (0.82 mole) of powered nicotinamide and 100 g. (0.70 mole) of phosphorus pentoxide. The flask is stoppered and shaken to mix the two powders. It is then connected by means of a 10-mm. i.d. tube to an 80-cm. air condenser arranged for distillation. A 125-ml. Claisen flask immersed in an ice-salt bath is used as the receiver (Note 1). The pressure is reduced to 15–20 mm., and the mixture is heated with a large free flame of a high-temperature burner (such as a Fisher or Meker type). The flame is moved about freely to melt the material as rapidly as possible, and then the mixture is heated vigorously until nothing more comes over or until foam reaches the top of the flask (15–20 minutes). The apparatus is allowed to cool (Note 2), and the product is rinsed out of the tube and condenser with ether (Note 3). The ether solution is added to the distillate, the ether is distilled on a steam bath, and the product is distilled at atmospheric pressure using an air condenser. The yield of nicotinonitrile, boiling at 205–208° and melting at 50–51°, is 71–72 g. (83–84%).

2. Notes

1. To prevent possible clogging of the condenser by the solid nicotinonitrile, the end of the condenser should not be constricted and should not extend far into the receiver.
2. The residue left in the flask may be removed by carefully adding water, allowing the mixture to stand overnight, and then washing repeatedly with water.
3. A small amount of material insoluble in ether but soluble in water remains in the condenser. The nicotinonitrile can be washed from the condenser more easily with acetone. If acetone is used, it should be removed by distillation under reduced pressure before the product is distilled.

3. Discussion

The method described is essentially that of La Forge.[2] Nicotinonitrile has also been prepared from nicotinic acid by heating with ammonium acetate and acetic acid,[3] from 3-pyridinesulfonic acid by fusion of the sodium salt with sodium cyanide,[4] from 3-bromopyridine and cuprous cyanide,[5] from nicotinamide and benzenesulfonyl or *p*-toluenesulfonyl chloride in pyridine,[6] from nicotinic acid and ammonia in the presence of a dehydrating catalyst,[7] from β-picoline and ammonia,[8] and from heating a mixture of nicotinic acid and lead thiocyanate.[9]

References and Notes

1. University of South Carolina, Columbia, South Carolina.
2. La Forge, *J. Am. Chem. Soc.*, **50**, 2477 (1928).
3. Adkins, Wolff, Pavlic, and Hutchinson, *J. Am. Chem. Soc.*, **66**, 1293 (1944).
4. McElvain and Goese, *J. Am. Chem. Soc.*, **65**, 2233 (1943).
5. McElvain and Goese, *J. Am. Chem. Soc.*, **63**, 2283 (1941).
6. Stephens, Bianco, and Pilgrim, *J. Am. Chem. Soc.*, **77**, 1701 (1955).

7. Scudi, Maschetto, and Mayurnik (to Nepera Chemical Co., Inc.), U. S. pat. 2,680,742 [*C. A.*, **49**, 6316 (1955)].
8. Hadley and Wood, Brit. pat. 777,746 [*C. A.*, **51**, 18011 (1957); Porter, Erchak, and Cosby (to Allied Chemical and Dye Corp.), U. S. pat. 2,510,605 [*C. A.*, **45**, 187 (1951)]; Mayurnik, Moschetto, Bloch, and Scudi, *Ind. Eng. Chem.*, **44**, 1630 (1952).
9. Spasov and Golovinskii, *Compt. rend. acad. bulgare sci.*, **11**, No 4, 287 [*C. A.*, **53**, 18026 (1959)].

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

benzenesulfonyl or p-toluenesulfonyl chloride

acetic acid (64-19-7)

ammonia (7664-41-7)

ether (60-29-7)

ammonium acetate (631-61-8)

sodium cyanide (143-33-9)

Cuprous Cyanide (544-92-3)

acetone (67-64-1)

pyridine (110-86-1)

Nicotinic acid (59-67-6)

nicotinamide (98-92-0)

3-bromopyridine (626-55-1)

Nicotinonitrile (100-54-9)

β-picoline (108-99-6)

3-pyridinesulfonic acid (636-73-7)

phosphorus pentoxide (1314-56-3)

lead thiocyanate