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.

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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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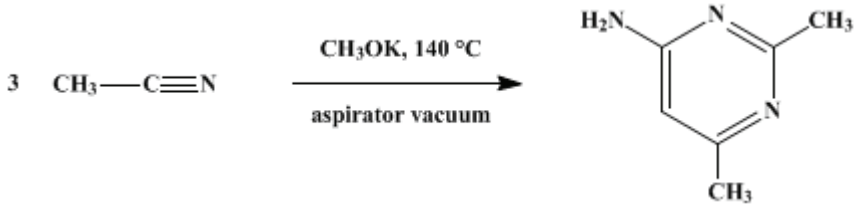
4-AMINO-2,6-DIMETHYLPYRIMIDINE

[Pyrimidine, 4-amino-2,6-dimethyl-]



Submitted by Anthony R. Ronzio and William B. Cook.
Checked by C. G. Stuckwisch and Henry Gilman.

1. Procedure

Seventy grams (1 mole) of freshly prepared potassium methoxide (Note 1) and 41 g. (1 mole) of freshly purified acetonitrile (Note 2) are placed in a 500-ml. distilling flask. A cold-finger condenser which extends into the bulb of the flask is inserted through a rubber stopper in the neck of the flask, and a short piece of rubber tubing carrying a Hofmann clamp is connected to the side arm of the flask. The tubing is connected to an aspirator, and suction is applied until the acetonitrile begins to boil, whereupon the tubing is closed by means of the clamp and the flask is heated for 5 hours in an oil bath maintained at 140°.

At the end of the heating period the contents of the flask will have solidified. To the cold mixture 40 ml. of water is added to hydrolyze the potassium methoxide and precipitate the pyrimidine; the fine crystals are filtered and dried. The crude product is placed in a 500-ml. distilling flask with 250 ml. of purified kerosene (Note 3). On distilling the kerosene, the pyrimidine codistils and solidifies in the receiving flask to a snow-white mass of crystals. These are filtered, washed well with petroleum ether, and dried in an oven at 100°. The yield of pure material, melting at 182–183°, is 27.5–28.7 g. (67–70%) (Note 4).

2. Notes

1. To prepare the potassium methoxide 39 g. (1 gram atom) of metallic potassium, cut *under toluene* (*Caution!*) in 1-cm. cubes, is placed in a 1-l. three-necked flask which has been swept with nitrogen. The flask, fitted with a reflux condenser, mechanical stirrer, and dropping funnel, is immersed in a cooling bath at −30°, and absolute methanol is added through the funnel until all the potassium has dissolved. The excess methanol is removed by heating on the steam bath, finally under reduced pressure, and the potassium methoxide is dried overnight in a vacuum desiccator over sulfuric acid.
2. Commercial acetonitrile is treated with solid sodium carbonate until no more carbon dioxide is evolved. The nitrile is then distilled over phosphorus pentoxide and stored in tightly stoppered bottles. Before use, the nitrile is redistilled over phosphorus pentoxide.
3. Kerosene is purified by shaking for 24 hours with concentrated sulfuric acid. The kerosene is separated from the acid, washed several times with dilute sodium hydroxide then with water, and finally dried over calcium chloride and distilled using an air condenser. Purified kerosene is a water-white, sweet-smelling liquid.
4. The percentage yield decreases when larger or smaller quantities of material are used.

3. Discussion

4-Amino-2,6-dimethylpyrimidine has been prepared by heating the reaction product obtained from acetic anhydride and acetamidine;[1] by treating 4-chloro-2,6-dimethylpyrimidine with ammonia;[2] and by heating acetonitrile either with sodium ethoxide in a sealed tube[3] or with sodium.[4,5]

It has been reported that this trimerization may be carried out with equally good results through the use of a small amount of sodium methoxide in place of a large amount of potassium methoxide.[6]

References and Notes

1. Pinner, *Ber.*, **22**, 1600 (1889).
2. Schmidt, *Ber.*, **35**, 1577 (1902).
3. Schwarze, *J. prakt. Chem.*, (2) **42**, 3 (1890).
4. Keller, *J. prakt. Chem.*, (2) **31**, 365 (1885).
5. von Meyer, *J. prakt. Chem.*, (2) **27**, 153 (1883).
6. Cairns, Larchar, and McKusick, *J. Am. Chem. Soc.*, **74**, 5633 (1952).

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

petroleum ether

kerosene

metallic potassium

calcium chloride (10043-52-4)

sulfuric acid (7664-93-9)

ammonia (7664-41-7)

methanol (67-56-1)

acetic anhydride (108-24-7)

acetonitrile (75-05-8)

sodium hydroxide (1310-73-2)

sodium carbonate (497-19-8)

nitrogen (7727-37-9)

carbon dioxide (124-38-9)

sodium methoxide (124-41-4)

toluene (108-88-3)

sodium (13966-32-0)

sodium ethoxide (141-52-6)

potassium (7440-09-7)

pyrimidine (289-95-2)

4-Amino-2,6-dimethylpyrimidine,
Pyrimidine, 4-amino-2,6-dimethyl- (461-98-3)

potassium methoxide (865-33-8)

acetamidine (143-37-3)

4-chloro-2,6-dimethylpyrimidine

phosphorus pentoxide (1314-56-3)