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.

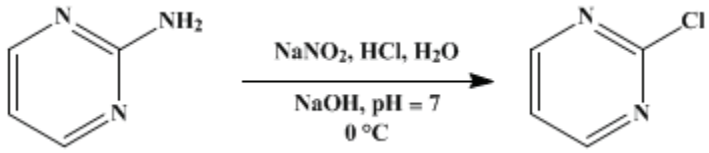
These paragraphs were added in September 2014. The statements above do not supersede any specific hazard caution notes and safety instructions included in the procedure.

DOI:10.15227/orgsyn.035.0034

Organic Syntheses, Coll. Vol. 4, p.182 (1963); Vol. 35, p.34 (1955).

2-CHLOROPYRIMIDINE

[Pyrimidine, 2-chloro-]



Submitted by Irving C. Kogon, Ronald Minin, and C. G. Overberger[1].
Checked by Charles C. Price and T. L. V. Ulbricht.

1. Procedure

Caution! This procedure should be carried out in a good hood.

In a 3-l. three-necked round-bottomed flask fitted with a stirrer and a low-temperature thermometer is placed 500 ml. of concentrated hydrochloric acid (6.0 moles), and the solution is cooled to 0°. To the cooled solution, 142 g. (1.5 moles) of 2-aminopyrimidine (Note 1) is added portionwise with stirring until a homogeneous solution is obtained. The solution is cooled to −15° (Note 2), and a 500-ml. dropping funnel is fitted to the flask. A cold solution of 207 g. (3.0 moles) of sodium nitrite in 375 ml. of water is then added dropwise with stirring over a period of 55 minutes, the reaction temperature being maintained at −15° to −10° (Note 3). The solution is stirred an additional hour, and the temperature is allowed to rise to −5°. The mixture is then carefully neutralized to about pH 7 with a 30% solution of sodium hydroxide (about 3.0 moles), care being taken not to allow the temperature to rise above 0° (Note 4). The solid which forms, consisting of 2-chloropyrimidine and sodium chloride, is collected by filtration and washed thoroughly with ether to dissolve all the 2-chloropyrimidine. The cold solution is extracted with four 75-ml. portions of ether (Note 5). The combined extracts are dried over anhydrous sodium sulfate, the solvent is removed, and the residue is recrystallized from isopentane to give white crystals of 2-chloropyrimidine. The yield is 44–46 g. (26–27%), m.p. 64.5–65.5°.

2. Notes

1. Purchased from the Matheson, Coleman and Bell Company, Norwood, Ohio.
2. Cooling below −15° causes the mixture to solidify.
3. Care should be exercised since at this point nitrogen oxides are being evolved. Addition should be started cautiously, as there tends to be a rapid initial rise in temperature.
4. Yields are appreciably reduced if the temperature is allowed to rise above 0°.
5. Filtration and extraction should be performed immediately or extensive decomposition occurs.

3. Discussion

2-Chloropyrimidine has been prepared by Howard[2] and by Sperber, Papa, Schwenk, Sherlock, and Fricano[3] by a similar procedure. The compound also has been obtained from 2-hydroxypyrimidine hydrochloride by treatment with a mixture of phosphorus pentachloride and phosphorus oxychloride[4] or by treatment with phosphorus oxychloride alone.[5] The present procedure has been published.[6]

This preparation is referenced from:

- Org. Syn. Coll. Vol. 4, 336

References and Notes

1. Polytechnic Institute of Brooklyn, Brooklyn 2, New York.
2. Howard, U. S. pat. 2,477,409 [*C. A.*, **43**, 8105 (1949)].
3. Sperber, Papa, Schwenk, Sherlock, and Fricano, *J. Am. Chem. Soc.*, **73**, 5752 (1951).
4. Matsukawa and Ohta, *J. Pharm. Soc. Japan*, **69**, 491 (1949) [*C. A.*, **44**, 3456 (1950)].
5. Copenhaver and Kleinschmidt, Brit. pat. 663,302 [*C. A.*, **46**, 10212 (1952)].
6. Overberger and Kogon, *J. Am. Chem. Soc.*, **76**, 1065 (1954).

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

nitrogen oxides

hydrochloric acid (7647-01-0)

ether (60-29-7)

sodium hydroxide (1310-73-2)

phosphorus pentachloride (10026-13-8)

sodium chloride (7647-14-5)

sodium sulfate (7757-82-6)

sodium nitrite (7632-00-0)

Phosphorus Oxychloride (21295-50-1)

isopentane (78-78-4)

2-Chloropyrimidine,
Pyrimidine, 2-chloro- (1722-12-9)

2-aminopyrimidine (109-12-6)

2-hydroxypyrimidine hydrochloride (38353-09-2)