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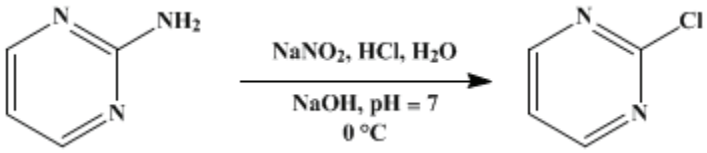
2-CHLOROPYRIMIDINE

[Pyrimidine, 2-chloro-]



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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)