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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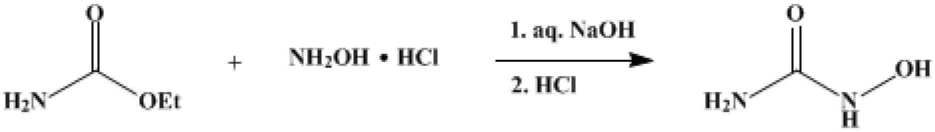
HYDROXYUREA

[Urea, hydroxy-]



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1. Procedure

To a solution of 20.8 g. (0.3 mole) of hydroxylamine hydrochloride and 20.6 g. (0.5 mole) of sodium hydroxide (98%) in 100 ml. of water is added 22.26 g. (0.25 mole) of ethyl carbamate. After 3 days at room temperature the solution is cooled in an ice bath and carefully neutralized with concentrated hydrochloric acid (Note 1). If necessary (Note 2), the solution is filtered and then extracted with ether; the aqueous phase is evaporated on a water bath under reduced pressure as rapidly as possible at a temperature not above 50–60°.

The dry residue is extracted by boiling with 100 ml. of absolute ethanol, and the solution is filtered through a heated funnel. On cooling, a first crop (6–8 g.) of hydroxyurea crystallizes.

The saline residue on the filter is extracted once again with 50 ml. of boiling absolute ethanol. On concentrating the filtrate from the second extraction and the mother liquor from the first crystallizate to a small volume, a second crop (4–6 g.) of product is obtained. The yield of the hydroxyurea is 10–14 g. (53–73%) of white crystals, m.p. 137–141° (dec.).

The product may be purified by recrystallization of 10 g. from 150 ml. of absolute ethanol. The rate of solution is slow (15–30 minutes is required), and the yield of hydroxyurea, m.p. 139–141° (dec.), is about 8 g. (Note 3).

2. Notes

1. Neutralization to phenolphthalein is satisfactory, but a glass electrode might give better results. Hydroxyurea is decomposed very rapidly in aqueous acidic medium, whereas its metallic salts (sodium or the copper complex salts) are stable.
2. Insoluble matter is sometimes present if a commercial grade of reactants is employed.
3. It is preferable to store the crystals in a cool, dry place. Some decomposition may occur after a few weeks.

3. Discussion

The improved method herein described is adapted from the procedure of Runti and Deghenghi.[2] Hydroxyurea has been prepared from potassium cyanate and hydroxylamine hydrochloride.[3,4,5] A lower melting isomeric substance, m.p. 71°, has been described.[4,5,6] The structure $NH_2CO_2NH_2$ has been proposed[5,6] for this low-melting substance.

References and Notes

1. Department of Medical Research, University of Western Ontario, Ontario, Canada.
2. C. Runti and R. Deghenghi, *Ann. Triest. Cura Univ. Trieste, sez.* **2**, 22, 185 (1953); *C.A.*, **49**, 1568 (1955).

3. W. F. C. Fresler and R. Stein, *Ann.*, **150**, 242 (1869).
4. L. Francesconi and A. Parrozzani, *Gazz. Chim. Ital*, **31 II**, 334 (1901).
5. H. Kofod, *Acta Chem. Scand.*, **7**, 274, 938 (1953).
6. O. Exner, *Chem. Lisly*, **50**, 2025 (1956).

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

ethanol (64-17-5)

hydrochloric acid (7647-01-0)

ether (60-29-7)

sodium hydroxide (1310-73-2)

Hydroxylamine hydrochloride (5470-11-1)

phenolphthalein (77-09-8)

potassium cyanate (590-28-3)

ethyl carbamate (51-79-6)

Hydroxyurea,
Urea, hydroxy- (127-07-1)