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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September 2014: The paragraphs above replace the section "Handling and Disposal of Hazardous Chemicals" in the originally published version of this article. The statements above do not supersede any specific hazard caution notes and safety instructions included in the procedure.

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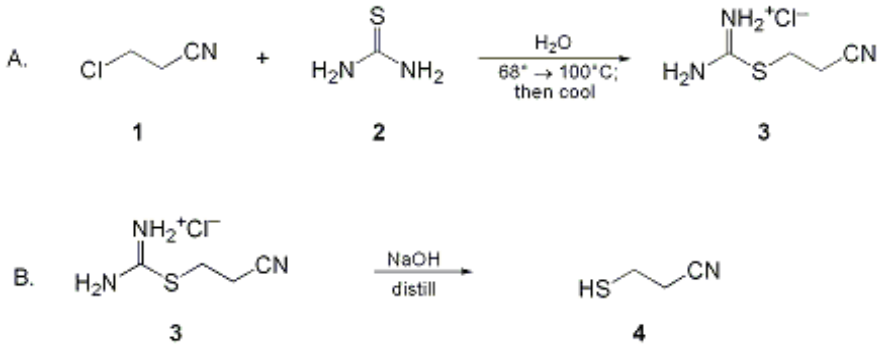
β-MERCAPTOPROPIONITRILE (2-CYANOETHANETHIOL)

[Propanenitrile, 3-mercapto-]



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1. Procedure

Caution: The procedure should be carried out in a well-ventilated hood because of the extreme stench of the mercaptan products. All glassware used in the procedure should be soaked in a bleach solution prior to removal from the hood.

A. 2-Cyanoethylthiouronium hydrochloride **(3)**. To a 5-L, flanged-top, spherical Morton flask equipped with a supporting clamp (Note 1) are added water (380 mL), thiourea (575 g, 7.53 mol), and 3-chloropropionitrile (500 g, 5.58 mol) (Note 2). The flask is equipped with a three-necked (with thermometer inlet) flanged-top, mechanical stirring rod (600 mm) with Teflon paddle (110 mm), temperature probe, reflux condenser, gas bubbler, and 5-L heating mantle. The reaction mixture is slowly heated to 68°C over a 30-min period under nitrogen and maintained at 68-70°C for 1 hr (Note 3). After 1 hr, the temperature of the reaction mixture is increased over a 15-min period to 100°C and maintained at 100-101°C for 2 hr (Note 4). After 2 hr, the heating mantle is replaced with a large ice-salt bath, and the reaction mixture is cooled with stirring to 45°C. When the internal temperature of the reaction mixture reaches 45°C, stirring is stopped, the cooling process is continued, and the product is allowed to crystallize (Note 5). Cold acetone (2 L) is added and the solid is broken up with a spatula and homogenized (Note 6). The solid is collected using a 160 × 160-mm medium-fritted funnel and washed with 4 L of cold acetone , stirring with the spatula during the filtration process. The solid is then washed with 2 L of ether and air dried. Final drying in a vacuum oven at room temperature affords 693.7 g (75.0%) of the title compound as a white solid, mp 161.5-162.5°C (Note 7) and (Note 8). The filtrate is placed in a freezer (4°C) for two days. The crystallized product is collected by vacuum filtration, washed with ether (2 × 1 L), air dried, and then dried under vacuum to afford an additional 75.8 g (8.2%) of the title compound, mp 162.5-163.5°C (Note 9).

B. 2-Cyanoethanethiol **(4)**. To a 3-L, three-necked, round-bottomed flask equipped with a supporting clamp are added thiouronium salt **3** (369.8 g, 2.23 mol) and water (470 mL) (Note 10). The flask is equipped with a mechanical stirring rod (600 mm) with Teflon paddle (110 mm), temperature probe, gas bubbler, a Teflon tube that extends into the reaction mixture for bubbling nitrogen gas, and a 3-L heating mantle. The reaction mixture is purged with nitrogen by rapidly bubbling nitrogen into the reaction mixture with stirring for 15 min. The Teflon tube is removed, replaced with a 500-mL addition funnel, and then a concentrated solution of sodium hydroxide (NaOH, 11.25 M, 4.24 mol) is slowly added under a nitrogen atmosphere, keeping the internal temperature below 25°C (Note 11). After the addition is complete, the reaction mixture is heated to 45°C over a 10-min period and held at 45-47°C

for 45 min (Note 12). The heating mantle is removed and replaced with a large ice-salt bath. After the reaction mixture has cooled to 20°C, a 6 M solution of H_2SO_4 is slowly added under nitrogen, keeping the internal reaction temperature between 20-25°C, until the pH of the reaction mixture is 6 (Note 13). With rapid bubbling of nitrogen to maintain a nitrogen atmosphere, the addition funnel is removed and commercial anhydrous ether (500 mL) is added to the reaction mixture. The flask is equipped with a one-hole rubber septum into which a Teflon tube (1 m × 4-mm id) is inserted. The mixture is stirred for 1 min, and the layers are allowed to separate. The temperature probe is removed and replaced with a rubber septum. Positive