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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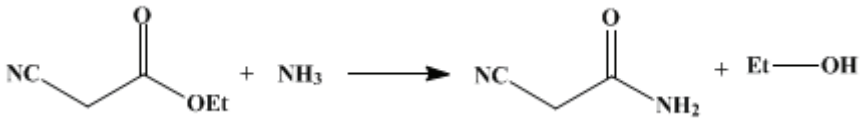
Organic Syntheses, Coll. Vol. 1, p.179 (1941); Vol. 9, p.36 (1929).

CYANOACETAMIDE



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Checked by C. S. Marvel and L. H. Bock.

1. Procedure

Four hundred grams (3.5 moles) of ethyl cyanoacetate (p. 254) is poured into 300 cc. (4.5 moles) of concentrated aqueous ammonia (sp. gr. 0.90) (Note 1) contained in a 1-l. wide-mouthed Erlenmeyer flask. The mixture, which is cloudy at first, is shaken; it then warms up a little and becomes clear in about three minutes. The flask is allowed to stand one hour in an ice-salt mixture. The product is then filtered by suction (Note 2) and the solid washed with two 50-cc. portions of ice-cold ethyl alcohol (Note 3). After drying in the air, the slightly yellowish, crystalline amide weighs 205–225 g. A snow-white product is easily obtained by crystallizing from hot alcohol (Note 4) and (Note 5). For this purpose 200 g. of amide is dissolved in 350 cc. (Note 6) of hot 95 per cent alcohol and the solution cooled; pure amide is deposited with practically no loss.

An additional yield of amide is obtained by evaporating (Note 7) the original mother liquor to dryness under reduced pressure while heating the flask in a boiling water bath. The damp, brownish residue in the flask is dissolved in 100 cc. of hot alcohol. The hot solution is shaken a few minutes with decolorizing charcoal, filtered by suction while still hot, and then cooled in ice. Forty-six to fifty-eight grams of yellowish amide is deposited. One more crystallization with charcoal yields 44–56 g. of pure product.

The total yield is 255–261 g. (86–88 per cent of the theoretical amount). The product melts at 119–120°.

2. Notes

1. Gaseous ammonia was tried with poor success, the ammonia being passed into the ester (both cold and at room temperature) and also into an alcoholic solution of the ester.
2. The product must be filtered rapidly while the mother liquor is cold because of the solubility of the amide.
3. Cyanoacetamide may be washed with ice water but cold alcohol is preferable because of its lower solubility in the latter.
4. The solubility of cyanoacetamide in 100 cc. of 95 per cent alcohol follows:

1.3 g. at 0°	9.5 g. at 52°
1.7 g. at 12°	14.0 g. at 62°
3.1 g. at 26°	16.3 g. at 66°
5.0 g. at 38°	18.7 g. at 69°
7.0 g. at 44°	21.5 g. at 71°

5. The alcoholic mother liquor from the crystallization usually contains a small amount of malonamide which melts at 170–171°.
6. If the treatment with decolorizing charcoal is necessary, about 450 cc. of alcohol should be used in order to avoid crystallization during the filtration.
7. A few cubic centimeters of an oil, presumably unchanged ethyl cyanoacetate, comes over with the water.
8. This work was done with the aid of a grant to the submitters from the Cyrus M. Warren Fund of the American Academy of Arts and Sciences.

3. Discussion

Cyanoacetamide can be prepared by the action of aqueous[1] or alcoholic[2] ammonia on cyanoacetic ester.

This preparation is referenced from:

- Org. Syn. Coll. Vol. 2, 379
- Org. Syn. Coll. Vol. 4, 210

References and Notes

1. Van't Hoff, Ber. **7**, 1383 (1874); Henry, Bull. soc. chim. (2) **48**, 656 (1887); Hesse, Am. Chem. J. **18**, 724 (1896); Thole and Thorpe, J. Chem. Soc. **99**, 429 (1911).
2. Hesse, Am. Chem. J. **18**, 724 (1896); Ott and Löpmann, Ber. **55**, 1258 (1922).

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

ester

cyanoacetic ester

ethyl alcohol,
alcohol (64-17-5)

ammonia (7664-41-7)

CYANOACETAMIDE (107-91-5)

Ethyl cyanoacetate (105-56-6)

malonamide (108-13-4)

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