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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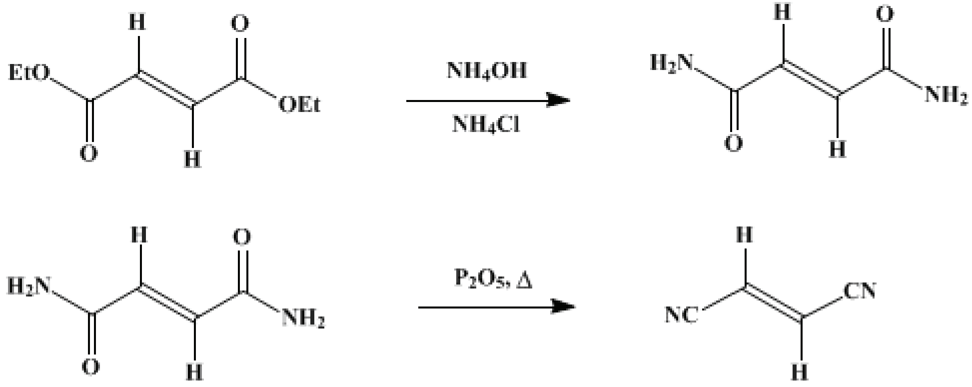
FUMARONITRILE



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1. Procedure

Caution! Fumaronitrile is both a vesicant and a lachrymator.

A. *Fumaramide.* A mixture of 516 g. (3.0 moles) of diethyl fumarate (Note 1) and (Note 2), 600 ml. of concentrated ammonium hydroxide (28%, sp. gr. 0.90, 9.0 moles), and 60 g. of ammonium chloride is placed in a 2-l. flask equipped with a stirrer and a thermometer. The reaction mixture is stirred at 25–30° with slight cooling for 7 hours (Note 3). The thick slurry of fumaramide is then filtered with suction, reslurried with 1 l. of water, filtered, and washed with about 50 ml. of ethanol. The white crystalline product is then dried in air or in an oven below 75° (Note 4). The yield is 270–300 g. (80–88%).

B. *Fumaronitrile.* The dry, finely powdered amide (Note 5) (228 g., 2.0 moles) and 613 g. (4.3 moles) of phosphorus pentoxide are placed in a 3-l. flask and thoroughly mixed by shaking. The flask is connected to a 1-l. suction flask receiver by means of a short 17-mm. i.d. 60° elbow extending about 15 cm. into the receiver. The receiver is cooled by immersion in an ice bath or by cold running water. The system is evacuated to 15–30 mm. by means of a water aspirator. The flask is then heated with one or two burners, using large soft flames. Heating should be started at the side and moved toward the bottom as the reaction progresses (Note 6). The reaction mass froths and blackens, and the product distils and sublimes into the receiver. The elbow leading to the receiver must be heated occasionally to melt condensed fumaronitrile. Heating is continued until no more fumaronitrile distils from the reaction flask (1.5 to 2 hours) (Note 7). The product, usually white and sufficiently pure (m.p. 93–95°) for most purposes, is obtained in a yield of 125–132 g. (80–85%). The product is recrystallized conveniently (in a fume hood) by dissolving it in 150 ml. of hot benzene and decanting or filtering the solution into 500 ml. of hexane or petroleum ether (Note 8) and (Note 9). The yield of long, glistening prisms, m.p. 96°, amounts to 117–125 g. (75–80%).

2. Notes

1. Diethyl fumarate liquid and vapors often cause reddening and itching of the skin, which usually disappear after a few hours.
2. Dimethyl fumarate gives equally good results but is less convenient to handle because it is a solid.
3. Additional ammonium hydroxide may be added if the slurry becomes too thick.
4. Temperatures higher than 75° often cause yellowing of the amide and excessive foaming during the dehydration with phosphorus pentoxide.
5. The amide is considered sufficiently dry if no heat is evolved when a sample is shaken vigorously in

a test tube with phosphorus pentoxide powder.

6. On somewhat smaller runs it may be more convenient to effect heating by the use of a wax or Wood's metal bath or an electric mantle. A bath or mantle temperature of 200° is sufficient for optimum yield. The reaction may froth vigorously if heated too rapidly or if the fumaramide is impure.

7. The cooled reaction flasks are easily cleaned by first soaking overnight in water and then rinsing with dilute sodium hydroxide solution.

8. *Caution!* This should be done in a hood. Fumaronitrile vapors and dust are irritating to the mucous membranes and are both vesicatory and lachrymatory. In the event of skin contact, the area should be washed promptly and thoroughly with soap and water to avoid irritation and blistering.

9. The principal impurities are a benzene-insoluble brown tar and hexane-soluble ethyl β-cyanoacrylate.

3. Discussion

The preparation described is based on the method of deWolf and van de Straete.[2] Fumaronitrile also has been prepared by the reaction of diiodoethylene with cuprous cyanide[3] and by hydrolyzing the product from the reaction of hydrogen cyanide with chloroacrylonitrile.[4] Pace claims that the yield of nitrile is improved when fumaramide is heated with phosphorus pentoxide in the presence of metal powders such as magnesium, cadmium, zinc, iron, and aluminum.[5]

References and Notes

1. Monsanto Chemical Company, Dayton, Ohio.
2. deWolf and van de Straete, *Bull. classe sci., Acad. roy. Belg.*, **21**, 216 (1935) [*C. A.*, **29**, 3985 (1935)].
3. Jennen, *Bull. classe sci., Acad. roy. Belg.*, **22**, 1169 (1936) [*C. A.*, **31**, 1010 (1937)]; Gaade, *Rec. trav. chim.*, **65**, 823 (1946).
4. Mowry and Yanko (to Monsanto Chemical Co.), U. S. pat. 2,471,767 [*C. A.*, **43**, 7498 (1949)].
5. Pace (to Wingfoot Corp.), U. S. pat. 2,438,019 [*C. A.*, **42**, 4606 (1948)].

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

petroleum ether

ethanol (64-17-5)

Benzene (71-43-2)

ammonium chloride (12125-02-9)

sodium hydroxide (1310-73-2)

magnesium (7439-95-4)

iron (7439-89-6)

hydrogen cyanide (74-90-8)

Cuprous Cyanide (544-92-3)

aluminum (7429-90-5)

zinc (7440-66-6)

ammonium hydroxide (1336-21-6)

diethyl fumarate (623-91-6)

cadmium (7440-43-9)

hexane (110-54-3)

Fumaronitrile (764-42-1)

Fumaramide (627-64-5)

Dimethyl fumarate (624-49-7)

ethyl β-cyanoacrylate

diiodoethylene

chloroacrylonitrile

phosphorus pentoxide (1314-56-3)