



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.

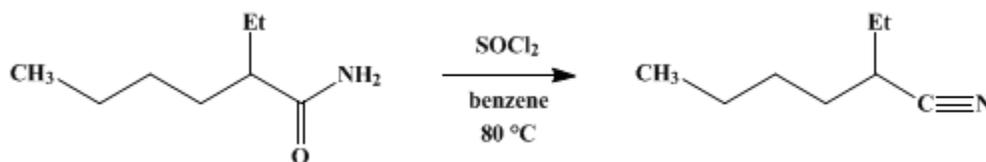
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These paragraphs were added in September 2014. The statements above do not supersede any specific hazard caution notes and safety instructions included in the procedure.

Organic Syntheses, Coll. Vol. 4, p.436 (1963); Vol. 32, p.65 (1952).

2-ETHYLHEXANONITRILE

[Hexanenitrile, 2-ethyl-]



Submitted by John A. Krynitsky and Homer W. Carhart¹.
Checked by H. R. Snyder and Richard S. Colgrove.

1. Procedure

In a 1-l. round-bottomed flask, bearing an efficient reflux condenser (Note 1), are placed 286 g. (2 moles) of 2-ethylhexanamide (Note 2), 300 ml. of dry benzene (Note 3), and 357 g. (218 ml., 3 moles) of thionyl chloride (Note 4). The flask is placed in a water bath, which is heated quickly to 75–80° and maintained at that temperature for 4.5 hours (Note 5). The reaction mixture is transferred to a 1.5-l. beaker and cooled in an ice bath. A mixture of 100 g. of crushed ice and 100 ml. of water is added to decompose the excess thionyl chloride. Cold 50% potassium hydroxide solution is added in small portions, with stirring, until the mixture is alkaline to litmus (Note 6). The mixture is transferred to a separatory funnel, and the layers are separated. The aqueous portion is extracted with 100 ml. of benzene. The benzene solutions are combined and washed once with 150 ml. of 1% sodium carbonate solution and twice with 150-ml. portions of water (Note 7). The mixture is distilled from a modified Claisen flask, the bulk of the solvent being removed at atmospheric pressure. The yield of nitrile is 215–236 g. (86–94%); b.p. 118–120°/100 mm. (Note 8), (Note 9), and (Note 10).

2. Notes

1. Unless the temperature of the water supplied to the condenser is below 20°, a larger amount of thionyl chloride may be required. The condenser should be attached to a gas trap.
2. The 2-ethylhexanamide was prepared in 86–88% yield from technical 2-ethylhexanoic acid (Carbide and Carbon Chemicals Corporation) by a method similar to that described previously,² except that the crude amide was filtered directly from the reaction mixture, washed well with water, and dried. The resulting product, which melted at 99–101°, was used without further purification. If the pure amide is desired, this product may be recrystallized (with 83–90% recovery) from 50% ethanol. For 100 g. of amide, 2 l. of 50% ethanol is used, and the hot solution is decolorized with charcoal. The product thus obtained is in the form of white needles which melt at 102–103°.
3. Benzene dried over sodium was used.
4. The submitters used Eastman Kodak Company white label grade thionyl chloride. The checkers purified commercial thionyl chloride (Hooker Electrochemical Company, refined grade) by the method of Cottle.³
5. It is advisable to carry out the reaction in a hood, as hydrogen chloride and sulfur dioxide are evolved. The evolution of gases stops just before the end of the specified heating period.
6. Approximately 150–200 ml. of the potassium hydroxide solution is required.
7. Drying of the solution is unnecessary, since the water present is removed in the next step by azeotropic distillation with benzene.
8. The checkers collected the product at 70.5–72°/10 mm.; n_D^{25} 1.4145.
9. Benzonitrile also can be prepared by this method in comparable yields, but a longer reaction time (7 hours) is required. The method was found to be unsatisfactory for the preparation of the nitriles of azelaic and phthalic acids from the corresponding diamides.
10. The submitters prepared palmitonitrile in more than 90% yield by heating the amide with a benzene solution of thionyl chloride for 6 hours followed directly by distillation. The nitrile so obtained was contaminated with a product having a strong sulfurous odor which could be removed by washing with

aqueous [mercuric acetate](#). By the described procedure, [palmitonitrile](#) free from objectionable odor was prepared in 80% yield. Troublesome emulsions were formed during the neutralization and washing steps; the addition of a small amount of [ethanol](#) aided in breaking the emulsions.

3. Discussion

Racemic 2-ethylhexanonitrile has been obtained only by the action of [phosphorus pentachloride](#) on [2-ethylhexanaldoxime](#);⁴ the levorotatory form has been prepared from the active amide by the method described.⁵ Other amides have been converted to nitriles by dehydration with [thionyl chloride](#).^{5,6}

References and Notes

1. Naval Research Laboratory, Washington, D. C.
 2. *Org. Syntheses Coll. Vol.* **3**, 490 (1955).
 3. Cottle, *J. Am. Chem. Soc.*, **68**, 1380 (1946).
 4. von Braun and Manz, *Ber.*, **67**, 1696 (1934).
 5. Levene and Kuna, *J. Biol. Chem.*, **140**, 263 (1941).
 6. Michaelis and Siebert, *Ann.*, **274**, 312 (1893).
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Appendix Chemical Abstracts Nomenclature (Collective Index Number); (Registry Number)

Racemic 2-ethylhexanonitrile

[ethanol](#) (64-17-5)

[hydrogen chloride](#) (7647-01-0)

[Benzene](#) (71-43-2)

[benzonitrile](#) (100-47-0)

[phosphorus pentachloride](#) (10026-13-8)

[thionyl chloride](#) (7719-09-7)

[sodium carbonate](#) (497-19-8)

[sulfur dioxide](#) (7446-09-5)

[mercuric acetate](#) (1600-27-7)

[potassium hydroxide](#) (1310-58-3)

[sodium](#) (13966-32-0)

[2-ETHYLHEXANONITRILE](#),
[Hexanenitrile, 2-ethyl-](#) (4528-39-6)

2-ethylhexanamide (4164-92-5)

2-ethylhexanoic acid (149-57-5)

palmitonitrile (629-79-8)

2-ethylhexanaldoxime