



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.

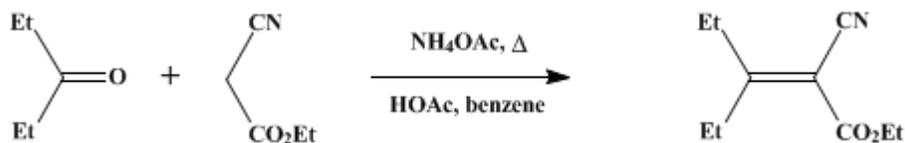
The procedures described in *Organic Syntheses* are provided as published and are conducted at one's own risk. *Organic Syntheses, Inc.*, its Editors, and its Board of Directors do not warrant or guarantee the safety of individuals using these procedures and hereby disclaim any liability for any injuries or damages claimed to have resulted from or related in any way to the procedures herein.

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. 3, p.399 (1955); Vol. 25, p.46 (1945).

ETHYL (1-ETHYLPROPYLIDENE)CYANOACETATE

[2-Pentenoic acid, 2-cyano-3-ethyl-, ethyl ester]



Submitted by Arthur C. Cope and Evelyn M. Hancock.

Checked by H. R. Snyder and J. H. Saunders.

1. Procedure

In a 500-ml. round-bottomed flask attached to a modified Dean and Stark constant water separator¹ (Note 1) which is connected to a reflux condenser are placed 67.8 g. (0.60 mole) of ethyl cyanoacetate (Note 2), 56.8 g. (0.66 mole) of diethyl ketone (Note 3), 9.2 g. (0.12 mole) of ammonium acetate, 30 g. (0.48 mole) of glacial acetic acid, and 100 ml. of benzene. The flask is heated in an oil bath at 160–165°, and the water that distils out of the mixture with the refluxing benzene is removed from the separator at intervals. Refluxing is continued for 24 hours (several hours after the separation of water has ceased) (Note 4).

The solution is cooled and washed with three 25-ml. portions of 10% sodium chloride solution, after which the benzene is removed by distillation under reduced pressure. The residue is transferred to a 1-l. bottle, a solution of 78 g. (0.75 mole) of commercial sodium bisulfite in 310 ml. of water is added, and the mixture is shaken on a mechanical shaker for 2 hours. The turbid solution is diluted with 500 ml. of water and extracted with three 50-ml. portions of benzene. The extracts are discarded (Note 5). The bisulfite solution is then cooled in an ice bath, and an ice-cold solution of 32 g. (0.8 mole) of sodium hydroxide in 130 ml. of water is added dropwise with mechanical stirring. The ester which separates is extracted at once with four 25-ml. portions of benzene (Note 6). The benzene solution is washed with 50 ml. of 1% hydrochloric acid, dried for a short time over 20 g. of anhydrous sodium sulfate, filtered into a 250-ml. modified Claisen flask, and distilled under reduced pressure. The yield of ester boiling at 123–125°/12 mm. (Note 7) is 65.4–75 g. (60.5–68%) (Note 8), (Note 9), and (Note 10).

2. Notes

1. Any continuous water separator that will return the benzene to the reaction mixture may be used.
2. Commercial ethyl cyanoacetate (Dow Chemical Company) was redistilled before use; b.p. 93–94°/12 mm.
3. Diethyl ketone was either purchased from the Eastman Kodak Company and redistilled, or prepared by passing propionic acid slowly over a mixture of manganous oxide and clay plate chips in a tube furnace at 420–440°;² the apparatus was similar to one described in *Organic Syntheses*.³ When prepared by this method the ketone was distilled, dried over potassium carbonate, and redistilled; b.p. 100–101°.
4. The water layer (20–25 ml.) contains some acetic acid and acetamide, the acetamide being formed from the ammonium acetate catalyst.
5. Extraction of the aqueous solution removes ethyl cyanoacetate from the aqueous solution of the sodium bisulfite addition product of ethyl (1-ethylpropylidene)cyanoacetate.
6. The unsaturated ester is regenerated when the bisulfite is neutralized with sodium hydroxide. The solution is kept cold during neutralization and extraction, and but little excess sodium hydroxide is used in order to prevent hydrolytic cleavage of the ester to diethyl ketone and ethyl cyanoacetate.
7. Other boiling points are 135–137°/25 mm. and 88–89°/1 mm.
8. A number of ketones have been condensed with ethyl cyanoacetate by this procedure. Reactive ketones such as aliphatic methyl ketones and cyclohexanone condense with ethyl cyanoacetate much more rapidly and give better yields of alkylidene esters. It is advantageous with such ketones to use a

lower ratio of [ammonium acetate-acetic acid](#) catalyst.¹

9. The [sodium bisulfite](#) purification step may be omitted, and the alkylidene ester purified directly by distillation. Care must be taken to separate the product from [ethyl cyanoacetate](#) by fractionation through a moderately efficient column. Purification through the bisulfite addition compound is recommended for alkylidene cyanoacetic esters derived from ketones containing four and five [carbon](#) atoms, but not for the higher homologs. The checkers obtained a slightly higher yield by the method employing fractional distillation (64% vs. 60.5%) but the quality of the product appeared to be slightly inferior (n_D^{25} 1.4645 vs. 1.4649).

10. A trace of a water-soluble white solid may cause the distillate to be slightly turbid. It may be removed by washing the product with water and redistilling.

3. Discussion

The above procedure is a very slight modification of a general method¹ for condensing ketones with [ethyl cyanoacetate](#). [Ethyl \(1-ethylpropylidene\)cyanoacetate](#) also has been prepared by condensing [diethyl ketone](#) with [ethyl cyanoacetate](#) in the presence of [piperidine](#) or [acetic anhydride](#) and [zinc chloride](#),⁴ or [piperidine](#) and anhydrous [sodium sulfate](#) in a pressure bottle at 100°.⁵

This preparation is referenced from:

- [Org. Syn. Coll. Vol. 3, 397](#)
- [Org. Syn. Coll. Vol. 4, 234](#)

References and Notes

1. Cope, Hofmann, Wyckoff, and Hardenbergh, *J. Am. Chem. Soc.*, **63**, 3452 (1941).
 2. Sabatier and Mailhe, *Compt. rend.*, **158**, 831 (1914).
 3. *Org. Syntheses Coll. Vol. 2*, 389 (1943).
 4. Birch and Kon, *J. Chem. Soc.*, **1923**, 2448.
 5. Cowan and Vogel, *J. Chem. Soc.*, **1940**, 1528.
-

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

METHYL KETONES

[potassium carbonate](#) (584-08-7)

[hydrochloric acid](#) (7647-01-0)

[Acetamide](#) (60-35-5)

[acetic acid](#) (64-19-7)

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

[ammonium acetate](#) (631-61-8)

[acetic anhydride](#) (108-24-7)

sodium hydroxide (1310-73-2)

Cyclohexanone (108-94-1)

sodium chloride (7647-14-5)

propionic acid (79-09-4)

sodium sulfate (7757-82-6)

sodium bisulfite (7631-90-5)

carbon (7782-42-5)

piperidine (110-89-4)

zinc chloride (7646-85-7)

Ethyl cyanoacetate (105-56-6)

manganous oxide

diethyl ketone (96-22-0)

Ethyl (1-ethylpropylidene)cyanoacetate,
2-Pentenoic acid, 2-cyano-3-ethyl-, ethyl ester (868-04-2)

ammonium acetate-acetic acid