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.

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.

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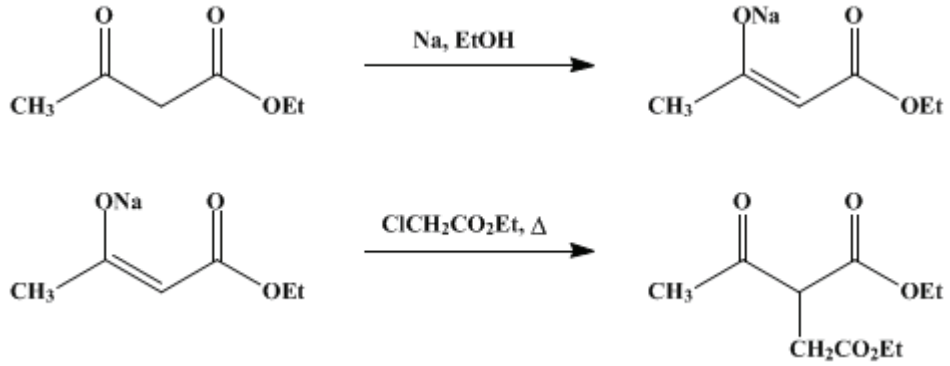
Organic Syntheses, Coll. Vol. 2, p.262 (1943); Vol. 14, p.38 (1934).

ETHYL ACETOSUCCINATE

[Succinic acid, acetyl-, diethyl ester]



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1. Procedure

In a 3-l. three-necked, round-bottomed flask, fitted with a mechanical stirrer, reflux condenser, and separatory funnel, is placed 400 cc. of absolute alcohol (Note 1). Through the condenser tube is added slowly 23 g. (1 gram atom) of clean sodium cut into thin slices. The completion of the reaction is hastened by heating the flask on a steam bath. When the sodium has dissolved completely, 143 g. (1.1 moles) of ethyl acetoacetate (Org. Syn. Coll. Vol. I, **1941**, 235) is introduced slowly. After the mechanical stirrer is started, 123 g. (1 mole) of ethyl chloroacetate (Note 2) is added slowly over a period of an hour, and the reaction mixture is refluxed for five to six hours. At this point the reaction mixture should no longer give an alkaline reaction with moist litmus.

After cooling, the precipitated sodium chloride is removed by filtering with suction and is washed with two 50-cc. portions of absolute alcohol. The alcohol is removed by distilling through a short column from a steam bath. The residue is filtered and transferred to a round-bottomed flask and is fractionated under reduced pressure through a Widmer column containing an 8-cm. spiral (Note 3). The fraction boiling at 121–124°/5 mm. is collected. The yield is 121–134 g. (56–62 per cent of the theoretical amount) (Note 4).

2. Notes

1. A good grade of absolute alcohol is required. For this purpose ordinary absolute alcohol may be dried by treating with a little sodium, adding a few cubic centimeters of ethyl succinate, and distilling directly into the reaction flask (see Note 1, p. 155, and Org. Syn. Coll. Vol. I, **1941**, 259).
2. Ethyl chloroacetate boiling at 142–145° was used. This ester can be prepared readily by refluxing for six hours a mixture of 200 g. of chloroacetic acid, 120 g. ofabsolute alcohol, and 25 g. of concentrated sulfuric acid.[1] The product is purified in the conventional way, and the yield is 185 g. (70 per cent of the theoretical amount).
3. It is advantageous to use an electrically heated column for this fractionation. The principal by-product of the reaction is ethyl β-acetotricarballylate[2] (b.p. 190°/16 mm.), formed by further action of ethyl chloroacetate upon the initial product.
4. Ethyl α-acetoglutarate may be prepared in a similar way by using 181 g. (1 mole) of ethyl β-bromopropionate (Org. Syn. Coll. Vol. I, **1941**, 246) instead of ethyl chloroacetate. The product is collected at 132–134°/4 mm. and weighs 120 g. (52 per cent of the theoretical amount).

3. Discussion

Ethyl acetosuccinate has been prepared by the interaction of ethyl sodioacetoacetate and ethyl chloroacetate[1] or bromoacetate.[2] The method given above is a modification[3] of that given by Conrad.[1]

This preparation is referenced from:

- Org. Syn. Coll. Vol. 2, 85

References and Notes

1. Conrad, Ann. **188**, 218 (1877).
2. Emery, Ber. **23**, 3755 (1890); Fichter and Pfister, ibid. **37**, 1997 (1904).
3. Isbell, Wojcik, and Adkins, J. Am. Chem. Soc. **54**, 3685 (1932).

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

alcohol (64-17-5)

sulfuric acid (7664-93-9)

ethyl succinate

sodium chloride (7647-14-5)

chloroacetic acid (79-11-8)

sodium (13966-32-0)

Ethyl chloroacetate (105-39-5)

Ethyl acetoacetate (141-97-9)

Ethyl β-bromopropionate (539-74-2)

Ethyl acetosuccinate

Succinic acid, acetyl-, diethyl ester (1115-30-6)

ethyl β-acetotricarballylate

Ethyl α-acetoglutarate

ethyl sodioacetoacetate

bromoacetate (79-08-3)