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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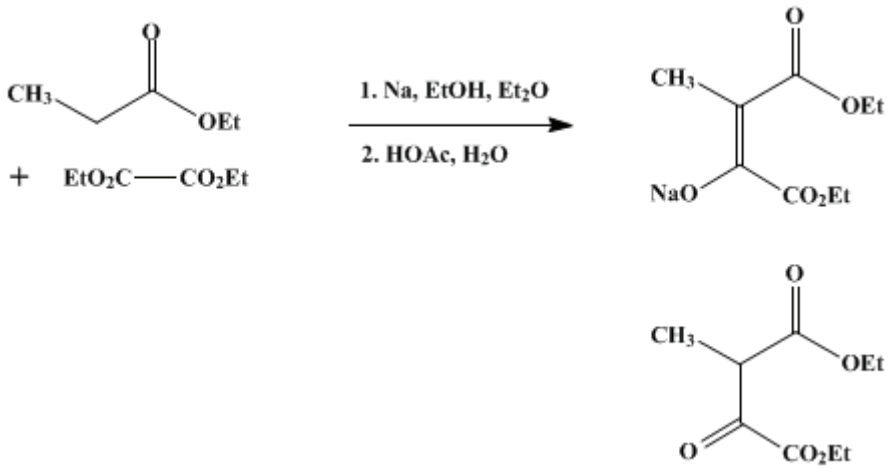
Organic Syntheses, Coll. Vol. 2, p.272 (1943); Vol. 17, p.54 (1937).

ETHYL ETHOXALYLPROPIONATE

[Oxalacetic acid, methyl-, diethyl ester]



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1. Procedure

Sixty-nine grams (3 gram atoms) of sodium is powdered under xylene in a 3-l. three-necked flask. The mixture is cooled, the xylene is decanted, and the sodium is washed twice with small portions of dry ether. One liter of absolute ether is then added to the powdered sodium. The flask is fitted with a mercury-sealed stirrer, an efficient reflux condenser, and a dropping funnel, the condenser and the funnel being protected from moisture with calcium chloride tubes. One hundred and thirty-eight grams (175 cc., 3 moles) of absolute ethyl alcohol is added drop by drop through the funnel (Note 1). After the alcohol has been added and there is no unchanged sodium (as evidenced by cessation of boiling) the flask is immersed in an ice-water bath, and a mixture of 306 g. (3 moles) of ethyl propionate and 438 g. (3 moles) of ethyl oxalate (Org. Syn. Coll. Vol. I, **1941**, 261) is added slowly through the dropping funnel (Note 2).

After the ester mixture has been added, the stirrer is removed and the condenser set for downward distillation. The ether and the alcohol formed in the reaction are removed by heating on a water bath (Note 3). The residue, which usually solidifies upon cooling, is treated with 600 cc. of cold, 33 per cent acetic acid solution. The mixture is allowed to stand for several hours with occasional shaking in order to decompose the sodium derivative completely, and the product is extracted with four 500-cc. portions of ether. The ether solution is washed with 1 l. of water, with two 500-cc. portions of 10 per cent sodium bicarbonate solution, and finally with 1 l. of water. The ether is then removed by distillation, using a steam bath. The residue is fractionated through an efficient column (Note 4). The portion boiling at 114–116°/10 mm. is collected. The yield is 363–425 g. (60–70 per cent of the theoretical amount).

2. Notes

1. The addition of the alcohol takes from four to six hours, depending on the efficiency of the condenser and stirrer.
2. The addition of the ester mixture should be slow enough so that the ether does not reflux. This addition takes two to three hours.
3. When most of the alcohol has distilled, a yellow scum forms on the surface of the red, viscous liquid. The distillation is stopped at this point. When the solution is cooled, the sodium derivative crystallizes with considerable expansion in volume.

4. No appreciable decomposition of the ethoxalyl ester into ethyl methylmalonate takes place when the distillation is carried out at 10 mm. To prevent overheating, the use of an oil bath and a heated column is recommended.

3. Discussion

Ethyl ethoxalylpropionate has been prepared by the Claisen condensation of ethyl oxalate with ethyl propionate[1] as above, and by the alkylation of ethyl ethoxalylacetate.[1]

This preparation is referenced from:

- Org. Syn. Coll. Vol. 2, 279

References and Notes

1. Wislicenus and Arnold, Ann. **246**, 329, 336 (1888).

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

ETHYL ETHOXALYLPROPIONATE

ethyl ethoxalylacetate

ethyl alcohol (64-17-5)

acetic acid (64-19-7)

ether (60-29-7)

sodium bicarbonate (144-55-8)

sodium (13966-32-0)

xylene (106-42-3)

Ethyl oxalate

Oxalacetic acid, methyl-, diethyl ester

ethyl propionate (105-37-3)

Ethyl methylmalonate