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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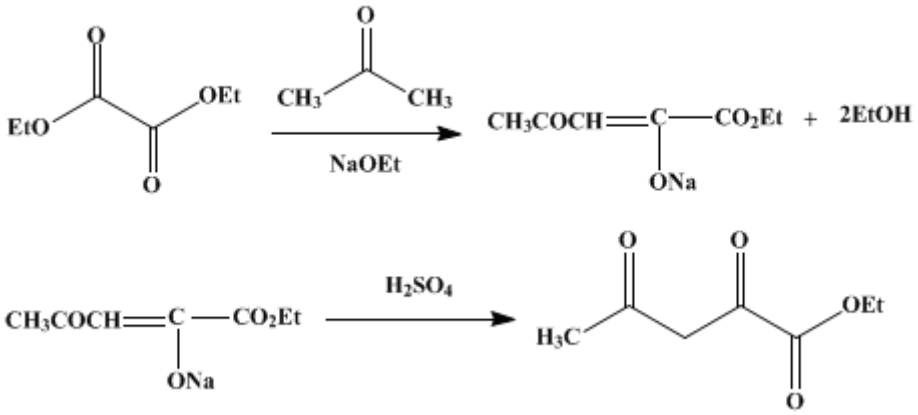
Organic Syntheses, Coll. Vol. 1, p.238 (1941); Vol. 6, p.40 (1926).

ETHYL ACETOPYRUVATE

[Valeric acid, α,γ-dioxo-, ethyl ester]



Submitted by C. S. Marvel and E. E. Dreger.
Checked by Frank C. Whitmore and Gladys E. Woodward.

1. Procedure

In a 5-l. round-bottomed flask fitted with a reflux condenser, a mechanical stirrer (Note 1) and a 1-l. separatory funnel, is placed 2800 cc. of absolute ethyl alcohol (Note 2), and to this is added 125 g. (5.4 atoms) of sodium over a period of one to two hours. The stirrer is started and the mixture allowed to cool to room temperature (Note 3), and a mixture of 730 g. (673 cc., 5 moles) of ethyl oxalate (Note 4) and 290 g. (366 cc., 5 moles) of acetone (Note 5) is added slowly over a period of two to three hours. At first a white precipitate forms; this is followed by a yellow precipitate that darkens as the reaction proceeds and later turns yellow again. The temperature rises to about 40°. Toward the end the mixture becomes so thick that stirring is difficult. Stirring is continued for one hour after the addition of the oxalate and acetone mixture. The yellow sodium salt is filtered by suction on two 20-cm. Büchner funnels (Note 6). The reaction flask is rinsed with 200 cc. of absolute ethyl alcohol, which is then used to wash the salt. The filtrate is turbid as a rule, but there is not enough sodium salt in suspension or solution to warrant recovery.

When the sodium salt has been sucked dry, it is returned to the 5-l. flask and treated with 1.5 l. of water and 1 kg. of cracked ice. The stirrer is started and there is added rapidly a cold sulfuric acid solution made by adding enough ice to 200 cc. of concentrated sulfuric acid (sp. gr. 1.84) (Note 7) so that some of the ice is not melted. The stirring is continued for five or ten minutes or until the yellow lumps of the sodium salt disappear. The mixture is then extracted with three 600-cc. portions of benzene (Note 8). The benzene is distilled (Note 9) from the extracts on a water bath and the residue is transferred to a special 2-l. Claisen flask (p. 130) and distilled under diminished pressure. The product boils at 130–132°/37 mm. or 117–119°/29 mm. A small high-boiling fraction is redistilled to yield 20–30 g. more of the ethyl acetopyruvate. The total yield is 480–520 g. (61–66 per cent of the theoretical amount) (Note 10).

2. Notes

1. The stirrer used is a bent glass rod which nearly scrapes the sides of the flask. A simple paddle stirrer is not efficient enough to stir the semi-solid mass.
2. The quality of the absolute alcohol (p. 249) influences the yields decidedly. The amount of alcohol indicated is the smallest which can be used effectively.
3. No better yields were obtained at lower temperatures.
4. The ethyl oxalate used (p. 261) was dried over calcium chloride for a week.

5. The acetone used was commercial acetone dried over calcium chloride for a week and then distilled. Some acetone is lost in this operation as it combines chemically with the calcium chloride.[1] See, Org. Syn. **20**, 7.
6. The filtration is likely to be slow and may take as much as two or three hours. When a 40-cm. Büchner funnel was used, it was complete in less than one hour.
7. This is sufficient acid to turn Congo red paper distinctly blue. If less acid is used, a troublesome emulsion is likely to form. If such an emulsion forms it can be broken by pouring into it a small amount of sulfuric acid cooled by the addition of ice.
8. If less than 600-cc. portions of benzene are used, the danger of emulsion formation is greater.
9. About 1 l. of benzene is recovered.
10. Care should be exercised in storing ethyl acetopyruvate because spontaneous decomposition, accompanied by gas evolution, may shatter the container.

3. Discussion

Ethyl acetopyruvate can be prepared by the condensation of ethyl oxalate and acetone in the presence of sodium ethoxide.[2] The procedure described is based on that of Claisen and Stylos.[2] It is reported that the condensation of ethyl oxalate and acetone by means of sodium methoxide furnishes methyl acetopyruvate in excellent yields and that the reaction requires less care than when the ethoxide is used.[3]

This preparation is referenced from:

- Org. Syn. Coll. Vol. 1, 459

References and Notes

1. Bagster, J. Chem. Soc. **111**, 494 (1917).
2. Claisen and Stylos, Ber. **20**, 2189 (1887); Meister, Lucius and Brüning, Ger. pat. 43,847 [Winther, I, 98 (1877–1905)]; Ger. pat. Anmeldung, F. 3,299 [Frdl. **1**, 218 (1877-87)]; Clark, J. Phys. Chem. **12**, 4 (1908); Meldrum and Perkin, J. Chem. Soc. **95**, 1896 (1909).
3. Freri, Gazz. chim. ital. **68**, 616 (1938).

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

ethyl alcohol,
alcohol (64-17-5)

calcium chloride (10043-52-4)

sulfuric acid (7664-93-9)

Benzene (71-43-2)

acetone (67-64-1)

sodium methoxide (124-41-4)

sodium (13966-32-0)

sodium ethoxide (141-52-6)

Ethyl acetopyruvate,
Valeric acid, α,γ-dioxo-, ethyl ester (615-79-2)

Ethyl oxalate

methyl acetopyruvate (20577-61-1)