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.

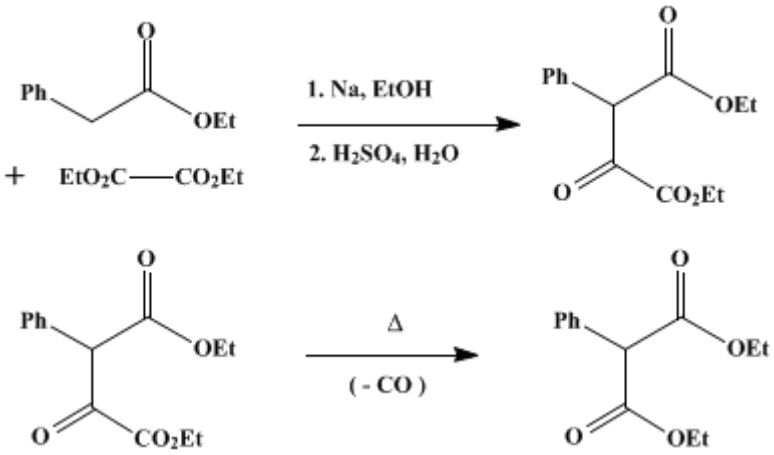
These paragraphs were added in September 2014. The statements above do not supersede any specific hazard caution notes and safety instructions included in the procedure.

DOI:10.15227/orgsyn.016.0033

Organic Syntheses, Coll. Vol. 2, p.288 (1943); Vol. 16, p.33 (1936).

ETHYL PHENYLMALONATE

[Malonic acid, phenyl-, diethyl ester]



Submitted by P. A. Levene and G. M. Meyer.
Checked by Louis F. Fieser and C. H. Fisher.

1. Procedure

In a 2-l. three-necked flask, fitted with a mercury-sealed stirrer, reflux condenser, and dropping funnel, is placed 500 cc. of absolute ethyl alcohol (Note 1), and 23 g. (1 gram atom) of cleanly cut sodium is added in portions. When the sodium has dissolved the solution is cooled to 60°, and 146 g. (1 mole) of ethyl oxalate (Note 2) is added in a rapid stream through the funnel with vigorous stirring. This is washed down with a small quantity of absolute alcohol and is followed immediately by the addition of 175 g. (1.06 moles) of ethyl phenylacetate. Stirring is discontinued at once, the reaction flask is lowered from the stirrer, and a 2-l. beaker is made ready. Within four to six minutes after the ethyl phenylacetate has been added crystallization sets in. The contents of the flask are transferred immediately to the beaker at the first sign of crystallization, which is nearly instantaneous.

The nearly solid paste of the sodium derivative is allowed to cool to room temperature and then stirred thoroughly with 800 cc. of dry ether. The solid is collected by suction and washed repeatedly with dry ether. The phenyloxaloacetic ester is liberated from the sodium salt with dilute sulfuric acid (29 cc. of concentrated sulfuric acid in 500 cc. of water). The almost colorless oil is separated, and the aqueous layer is extracted with three 100-cc. portions of ether, which are combined with the oil. The ethereal solution is dried over anhydrous sodium sulfate, and the ether is distilled. The residual oil, contained in a modified Claisen flask having a fractionating side arm, is heated under a pressure of about 15 mm. in a bath of Wood's metal. The temperature of the bath is brought gradually to 175° and kept there until the evolution of carbon monoxide is complete. During this process the heating is momentarily discontinued in the event of a temporary increase in pressure. At the end of the reaction (five to six hours) the oil which has distilled is returned to the flask, and the ethyl phenylmalonate is distilled at reduced pressure. The fraction boiling at 158–162°/10 mm. weighs 189–201 g. (80–85 per cent of the theoretical amount).

2. Notes

1. A high grade of absolute alcohol is essential. Ordinary "absolute" alcohol may be treated with about 5 per cent of its weight of sodium and distilled directly into the reaction flask.
2. To ensure absolutely dry and neutral reagents the ethyl oxalate (Org. Syn. Coll. Vol. I, **1941**, 261) and ethyl phenylacetate (Org. Syn. Coll. Vol. I, **1941**, 270) were shaken with anhydrous potassium carbonate and distilled carefully under reduced pressure, after a preliminary heating under atmospheric

pressure until their boiling points were reached.

3. Discussion

The procedure is based upon the standard method of Wislicenus.[1] Ethyl phenylmalonate has also been obtained from benzyl cyanide and ethyl carbonate.[2] Phenylmalonic acid has been prepared by carbonation of the enolate of phenylacetic acid.[3]

References and Notes

1. Wislicenus, Ber. **27**, 1091 (1894); Ruhemann, J. Chem. Soc. **81**, 1214 (1902); Pickard and Yates, ibid. **95**, 1015 (1909); Forster and Müller, ibid. **97**, 135 (1910); Baker and Ingold, ibid. **1927**, 835; Blum-Bergmann, Ber. **65**, 115 (1932).
2. Nelson and Cretcher, J. Am. Chem. Soc. **50**, 2760 (1928).
3. Ivanoff and Spassoff, Bull. soc. chim. (4) **49**, 20 (1931).

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

phenyloxaloacetic ester

ethyl alcohol,
alcohol (64-17-5)

potassium carbonate (584-08-7)

sulfuric acid (7664-93-9)

ether (60-29-7)

carbon monoxide (630-08-0)

sodium sulfate (7757-82-6)

sodium (13966-32-0)

Benzyl cyanide (140-29-4)

Phenylacetic acid (103-82-2)

Ethyl oxalate

Ethyl phenylacetate (101-97-3)

ethyl carbonate

Ethyl phenylmalonate (83-13-6)

Malonic acid, phenyl-, diethyl ester (83-13-6)

Phenylmalonic acid (2613-89-0)