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.

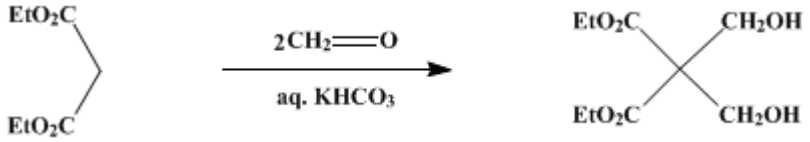
These paragraphs were added in September 2014. The statements above do not supersede any specific hazard caution notes and safety instructions included in the procedure.

DOI:10.15227/orgsyn.040.0027

Organic Syntheses, Coll. Vol. 5, p.381 (1973); Vol. 40, p.27 (1960).

DIETHYL BIS(HYDROXYMETHYL)MALONATE

[Malonic acid, bis(hydroxymethyl)-, diethyl ester]



Submitted by Paul Block, Jr.[1]
Checked by Melvin S. Newman and Reinhardt Stein.

1. Procedure

Formaldehyde solution equivalent to 60 g. of formaldehyde (2 moles) (Note 1) and 8 g. of potassium bicarbonate (small crystals) are placed in an 800-ml. beaker standing in a water bath at 20° in a hood. Mechanical stirring is started and 160 g. (1 mole) of diethyl malonate (Note 2) is added dropwise during about 40–50 min., at such a rate that the temperature of the reaction mixture is held at 25–30°. Stirring is continued for 1 hour. The reaction mixture is transferred to a separatory funnel. A saturated solution of ammonium sulfate (320 ml.) (Note 3) is added and the mixture is extracted with 320 ml. of ether. The ethereal extract, dried for 1 hour with anhydrous sodium sulfate (20 g.), is filtered into a 1-l., three-necked flask through a fluted filter paper. The sodium sulfate and paper are washed with 50 ml. of anhydrous ether. The flask (fitted with a thermometer reaching to the bottom, a condenser set for downward distillation; third neck closed) is placed in a suitable heating bath (Note 4). Boiling chips are introduced and the ether is distilled until the temperature of the liquid has risen to 45–50°. The heating bath is then removed and the distillation assembly is replaced by a glass tube (about 4 mm. I.D.) reaching to the bottom of the flask and closed by a piece of rubber tubing and a screw clamp. An aspirator is now connected to the third neck of the flask. Vacuum is applied and volatile material is removed until the pressure falls to 20–30 mm. The temperature of the contents of the flask is brought to 40° and maintained there until crystallization begins and for an additional 30 minutes (Note 5). Isopropyl ether (500 ml.) (Note 6) is added. The mixture is warmed to 50° and swirled until the product (crystalline and oily) dissolves. The solution is transferred to an Erlenmeyer flask, and cooled in ice water with stirring until a thick suspension of crystals results. The suspension is refrigerated for 1 hour, filtered with suction (rubber dam), and the crystals are dried overnight at room temperature, and then in a vacuum desiccator over sulfuric acid. The yield of colorless crystals, m.p. 48–50°, is 158–166 g. (72–75%). This product may be recrystallized from isopropyl ether (3.5 volumes) with an 85% recovery to yield material with m.p. 50–52°. Melting points of 52–53° and 52° are reported.[2,3]

2. Notes

1. Exactly 3 ml. of formaldehyde solution is assayed by the method of U.S.P. XIII, and the result calculated to grams of formaldehyde per milliliter of solution.
2. The diethyl malonate used boiled over a 2° range.
3. Ammonium sulfate (175 g.) is added to 235 ml. of water, warmed until it is dissolved, and cooled.
4. A heating mantle or liquid bath may be used.
5. The screw clamp may be adjusted so that there will be a spattering on the upper, cool part of the flask, while the pressure is still maintained below 30 mm. Under these conditions, the initiation of crystallization is speeded.
6. A practical grade is adequate, but is should be peroxide-free.

3. Discussion

The only reported method of preparation of diethyl bis(hydroxymethyl)malonate is by the reaction described here.[2,3]

4. Use of Diethyl Bis(hydroxymethyl)malonate_

Diethyl bis(hydroxymethyl)malonate is a useful intermediate for preparing substituted malonic esters, acrylic esters, and isobutyric esters.[2,4]

This preparation is referenced from:

- Org. Syn. Coll. Vol. 7, 210
- Org. Syn. Coll. Vol. 7, 319
- Org. Syn. Coll. Vol. 8, 265

References and Notes

1. Department of Chemistry, University of Toledo, Toledo, Ohio.
2. K. N. Welch, *J. Chem. Soc.*, 257 (1930).
3. H. Gault and A. Roesch, *Bull. Soc. Chim. France*, **5 (4)**, 1410 (1937).
4. A. F. Ferris, *J. Org. Chem.*, **20**, 780 (1955).

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

sulfuric acid (7664-93-9)

ether (60-29-7)

formaldehyde (50-00-0)

sodium sulfate (7757-82-6)

diethyl malonate (105-53-3)

ammonium sulfate (7783-20-2)

isopropyl ether (108-20-3)

potassium bicarbonate (298-14-6)

Diethyl bis(hydroxymethyl)malonate,
Malonic acid, bis(hydroxymethyl)-, diethyl ester (20605-01-0)