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.

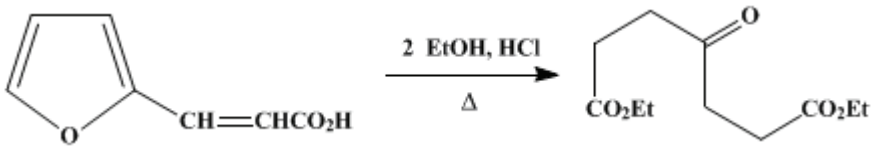
These paragraphs were added in September 2014. The statements above do not supersede any specific hazard caution notes and safety instructions included in the procedure.

DOI:10.15227/orgsyn.033.0025

Organic Syntheses, Coll. Vol. 4, p.302 (1963); Vol. 33, p.25 (1953).

DIETHYL γ-OXOPIMELATE

[Heptanedioic acid, 4-oxo-, diethyl ester]



Submitted by W. S. Emerson and R. I. Longley, Jr.[1].
Checked by William S. Johnson and I. A. David.

1. Procedure

A 3-l. three-necked flask equipped with a stirrer, reflux condenser, and gas inlet tube is charged with 476 g. (3.45 moles) of furylacrylic acid[2] and 1580 g. (about 33 moles) of 95% ethanol (Note 1). The mixture is heated to boiling, and anhydrous hydrogen chloride is introduced at such a rate that the mixture becomes saturated after 90 minutes. The gas inlet tube is replaced by a stopper, and a 2-ft. Vigreux column is substituted for the reflux condenser. About 250 ml. of solvent is removed by distillation at atmospheric pressure; then another 300 ml. is removed while the pressure is slowly reduced (water aspirator). The residue is cooled and stirred with a solution of about 260 g. of sodium carbonate in water (Note 2). The mixture is extracted with two 250-ml. portions of benzene, and the combined extracts are washed with 100 ml. of water (Note 3). Distillation of the organic portion through a 2-ft. Vigreux column yields, after a small fore-run, 579–657 g. (73–83%) of diethyl γ-oxopimelate, b.p. 116–121° /0.3 mm., n_D^{25} 1.4395–1.4400.

2. Notes

1. If absolute ethanol is used the yield is much lower.
2. A slight excess of sodium carbonate is used. The amount required depends on the amount of hydrogen chloride remaining after the distillation.
3. Sodium chloride may be added if the layers do not separate.

3. Discussion

Diethyl γ-oxopimelate has been prepared by saturating an ethanol solution of furylacrylic acid[3,4,5,6,7] or γ-oxopimelic acid dilactone with hydrogen chloride[5] or sulfuric acid.[8] It was found as a by-product in the esterification of furylacrylic acid with ethanol in the presence of *p*-toluenesulfonic acid.[9] A mechanism has been proposed for the formation of esters of γ-oxopimelic acid from furylacrylic acid.[10] The present procedure is a modification of the original Marckwald process.[3,4]

References and Notes

1. Monsanto Chemical Company, Dayton, Ohio.
2. *Org. Syntheses Coll. Vol.* **3**, 425 (1955).
3. Marckwald, *Ber.*, **20**, 2811 (1887).
4. Marckwald, *Ber.*, **21**, 1398 (1888).
5. Volhard, *Ann.*, **253**, 206 (1889).
6. Chichibabin, *Chim. & ind. (Paris)*, **27**, 563 (1932).
7. Komppa, *Ann. Acad. Sci. Fennicae*, **A51**, No. 3 (1938) [*C. A.*, **34**, 2335 (1940)].
8. Reppe et al., *Ann.*, **596**, 80 (1955).
9. Murahashi, *Bull. Inst. Phys. Chem. Research (Tokyo)*, **22**, 476 (1943) [*C. A.*, **42**, 1205 (1948)].
10. Gavat and Glineschi, *Rev. chim. (Bucharest)*, **7**, 575 (1956) [*C. A.*, **52**, 1991 (1958)].

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

γ-oxopimelic acid dilactone

ethanol (64-17-5)

sulfuric acid (7664-93-9)

hydrogen chloride (7647-01-0)

Benzene (71-43-2)

sodium chloride (7647-14-5)

sodium carbonate (497-19-8)

Furylacrylic acid (539-47-9)

DIETHYL γ-OXOPIMELATE,
Heptanedioic acid, 4-oxo-, diethyl ester (6317-49-3)

γ-oxopimelic acid (502-50-1)

p-toluenesulfonic acid (104-15-4)