



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.

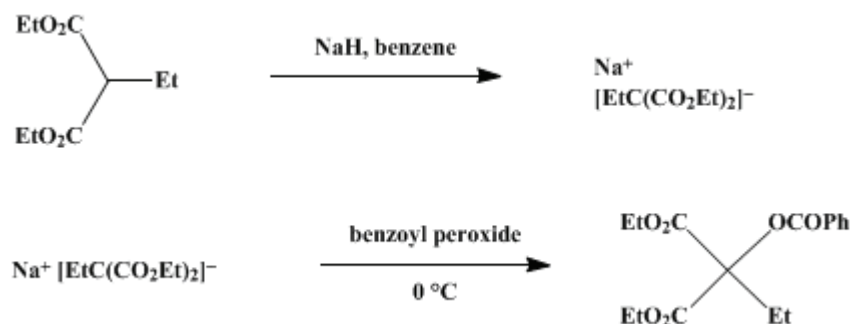
The procedures described in *Organic Syntheses* are provided as published and are conducted at one's own risk. *Organic Syntheses, Inc.*, its Editors, and its Board of Directors do not warrant or guarantee the safety of individuals using these procedures and hereby disclaim any liability for any injuries 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.

Organic Syntheses, Coll. Vol. 5, p.379 (1973); Vol. 45, p.37 (1965).

DIETHYL [O-BENZOYL]ETHYLTARTRONATE

[Malonic acid, ethylhydroxy-, diethyl ester, benzoate]



Submitted by E. H. Larsen and S.-O. Lawesson¹.

Checked by M. R. Michalewich and William D. Emmons.

1. Procedure

Caution! This reaction should be carried out behind a safety screen. The solvent removal and product distillation steps should also be carried out behind a screen to minimize trouble if the product is contaminated with undetected peroxides. Benzoyl peroxide should be handled with caution because it is impact-sensitive.

To a 1-l., three-necked, round-bottomed flask is added 7.2 g. (0.15 mole) of a 50% dispersion of sodium hydride in mineral oil (Note 1). The sodium hydride is washed several times by decantation with dry ether and is then covered with 300 ml. of dry benzene (Note 2). The flask is equipped with dropping funnel, stirrer, and reflux condenser. Diethyl ethylmalonate (28.2 g., 0.15 mole) (Note 1) is added dropwise over a 5-minute period, and the reaction mixture is stirred for 2 hours until a clear solution forms. The solution is cooled in an ice bath, and 24.2 g. (0.1 mole) of benzoyl peroxide (Note 3) in 300 ml. of dry benzene is added dropwise over a 1-hour period with continuous stirring. After another 30 minutes, a peroxide test (Note 4) is made to ensure that all the peroxide has reacted.

The porridge-like mixture is then poured into 300 ml. of water and vigorously shaken in a 1-l. separatory funnel. The benzene phase is separated, and the water phase is extracted three times with 100-ml. portions of ether. The combined extracts are washed until neutral and are dried over anhydrous sodium sulfate. The volatile solvents are evaporated at aspirator pressure, and the residue (Note 5) is distilled through a short Vigreux column. After a fore-run of diethyl ethylmalonate 23.3–24.1 g. (75–78%) of diethyl [O-benzoyl]ethyltartronate is obtained, b.p. 132° (0.1 mm.); n_D^{20} 1.4885.

2. Notes

1. The sodium hydride is obtained from Metal Hydrides Inc., Beverly, Massachusetts; the diethyl ethylmalonate from Eastman Organic Chemicals.
2. Reagent grade benzene was dried over calcium hydride prior to use.
3. The benzoyl peroxide is recrystallized from chloroform and methanol at room temperature. The checkers used the 96% purity commercial grade available from the Lucidol Division of Wallace and Tiernan without further purification.
4. A few drops of the reaction mixture are added to a dilute solution of sodium iodide in glacial acetic acid; if a brown ring is not formed, all peroxides have reacted.
5. A peroxide test on the residue is recommended before the distillation is begun.

3. Discussion

The present procedure is essentially that described by one of the submitters.²

4. Merits of the Preparation

The reaction described is of considerable general utility for the preparation of benzoyloxy derivatives of β -carbonyl compounds. Thus O-benzoyl tartronates have been prepared, from which routes to diethyl tartronates and tartronic acids have been developed.² Ethyl benzoyloxy cyanoacetates have similarly been prepared and are of potential interest in connection with the chemistry of amino acid precursors.³ Similarly the benzoyloxy group has been introduced into β -keto esters^{4,5} and β -diketones.⁶ Also a new method for the preparation of acyloins was found.⁵ An extension of the method has led to certain types of benzoyloxy γ -keto esters⁷ and benzoyloxy δ -ketonitriles.⁸ The method has been reviewed.⁹

References and Notes

1. Department of Chemistry, University of Åarhus, 8000 Åarhus C, Denmark.
 2. S.-O. Lawesson, T. Busch, and C. Berglund, *Acta Chem. Scand.*, **15**, 260 (1961).
 3. S.-O. Lawesson and C. Frisell, *Arkiv Kemi*, **17**, 393 (1961).
 4. S.-O. Lawesson, M. Andersson, and C. Berglund, *Arkiv Kemi*, **17**, 429 (1961).
 5. S.-O. Lawesson, S. Grönwall, and M. Andersson, *Arkiv Kemi*, **17**, 457 (1961).
 6. S.-O. Lawesson, P.-G. Jönsson, and J. Taipale, *Arkiv Kemi*, **17**, 441 (1961).
 7. S.-O. Lawesson, M. Dahlen, and C. Frisell, *Acta Chem. Scand.*, **16**, 1191 (1962).
 8. G. Näslund, A. Senning, and S.-O. Lawesson, *Acta Chem. Scand.*, **16**, 1324 (1962).
 9. S.-O. Lawesson, C. Frisell, D. Z. Denney, and D. B. Denney, *Tetrahedron*, **19**, 1229 (1963).
-

Appendix

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

Ethyl benzoyloxy cyanoacetates

benzoyloxy γ -keto esters

benzoyloxy δ -ketonitriles

acetic acid (64-19-7)

Benzene (71-43-2)

methanol (67-56-1)

ether (60-29-7)

chloroform (67-66-3)

sodium sulfate (7757-82-6)

sodium iodide (7681-82-5)

diethyl ethylmalonate (133-13-1)

benzoyl peroxide (94-36-0)

sodium hydride (7646-69-7)

calcium hydride (7789-78-8)

DIETHYL [O-BENZOYL]ETHYL TARTRONATE

Malonic acid, ethylhydroxy-, diethyl ester, benzoate (6259-78-5)