



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.

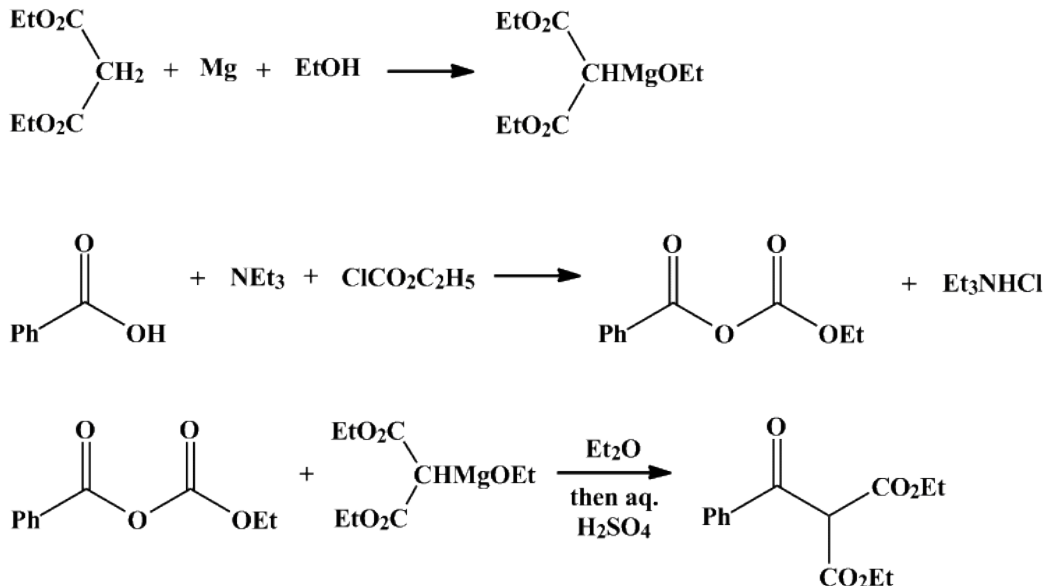
The procedures described in *Organic Syntheses* are provided as published and are conducted at one's own risk. *Organic Syntheses, Inc.*, its Editors, and its Board of Directors do not warrant or guarantee the safety of individuals using these procedures and hereby disclaim any liability for any injuries 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. 4, p.285 (1963); Vol. 37, p.20 (1957).

DIETHYL BENZOYLMALONATE

[Malonic acid, benzoyl-, diethyl ester]



Submitted by John A. Price and D. S. Tarbell¹.

Checked by T. L. Cairns and C. L. Dickinson.

1. Procedure

A. *Ethoxymagnesiummalonic ester* (Note 1). In a 250-ml. three-necked flask equipped with a dropping funnel and an efficient reflux condenser fitted with a calcium chloride drying tube are placed 5.0 g. (0.2 g. atom) of **magnesium turnings** (Grignard), 5 ml. of absolute **alcohol** (Note 2), 0.2 ml. of **carbon tetrachloride**, and 6 ml. of a mixture of 32.0 g. (30.2 ml., 0.2 mole) of **diethyl malonate** (Note 3) and 16 ml. of absolute alcohol. The reaction will proceed in a few minutes and may require occasional cooling before the addition of the remainder of the **diethyl malonate** solution. The addition should be controlled so that the reaction goes at a fairly vigorous rate. When the reaction mixture has cooled to room temperature, 60 ml. of **ether** dried over **sodium wire** is cautiously (Note 4) added. When the reaction again appears to subside, gentle heating by means of a steam bath is begun and continued until nearly all the **magnesium** has disappeared (Note 5). The alcohol and **ether** are removed by distillation, first at atmospheric pressure and then at reduced pressure secured with a water pump. To the partially crystalline product is added 60 ml. of dry **benzene**, and the solvent is again removed by distillation at atmospheric and then reduced pressure (Note 6). The residue is dissolved in 60 ml. of dry **ether** to await the completion of the mixed carbonic-carboxylic anhydride preparation.

B. *Mixed benzoic-carbonic anhydride* (Note 7). In a 500-ml. three-necked flask, equipped with a low-temperature thermometer, an efficient sealed stirrer, and an adaptive joint carrying a drying tube and a dropping funnel, is placed a solution of 24.4 g. (0.2 mole) of **benzoic acid** (Note 8) and 20.2 g. (0.2 mole) of **triethylamine** (Note 9) in 200 ml. of dry **toluene**. The solution is cooled below 0° by means of an ice-salt mixture, and 21.7 g. (0.2 mole) of **ethyl chlorocarbonate** (Note 10) is added at such a rate that the temperature does not rise above 0° (approximate time for addition is 25–30 minutes). **Triethylamine hydrochloride** precipitates both during the addition and while the mixture is stirred for 15–25 minutes thereafter.

C. *Diethyl benzoylmalonate*. The dropping funnel used for the chlorocarbonate addition is replaced

by another into which the ethereal solution of the ethoxymagnesium compound has been transferred. Approximately 30 ml. of dry ether is used to rinse the flask, and this is also added to the dropping funnel. The ether solution is added to the mixed anhydride with stirring, as the temperature is held at -5° to 0° . After the mixture has been allowed to stand overnight and to come to room temperature during this time, it is treated cautiously with 400 ml. of 5% sulfuric acid; then the aqueous solution is separated and extracted once with ether. The two organic layers are combined, washed once with dilute sulfuric acid and then with a concentrated sodium bicarbonate solution until no further benzoic acid is obtained from acidification of the bicarbonate extracts (Note 11). The organic layer is washed with water and dried over anhydrous sodium sulfate. After removal of the sodium sulfate by filtration, the solvent is removed at water-pump pressure from a water bath held at about 50° . The resulting product is purified by distillation through a 30-cm. Vigreux column, and the fraction boiling at $144-149^{\circ}/0.8$ mm. is collected (Note 12). The yield is 35.8–39.4 g. (68–75%), n_D^{25} 1.5063–1.5066.

2. Notes

1. The described procedure is essentially the same as that reported by Lund and Voigt.² A similar preparation has been described by Reynolds and Hauser (p. 708).
2. A commercial grade is satisfactory for this preparation.
3. Commercial malonic ester was redistilled at reduced pressure to give material with n_D^{20} 1.4047.
4. The ether dissolves the crystalline cake which has formed on cooling. This releases unreacted material and vigorous reaction again sets in.
5. From 6 to 8 hours is required for this operation.
6. The benzene removes any residual alcohol which may interfere with the subsequent acylation.³
7. The mixed carbonic anhydride procedure^{4,5,6} has been useful in the preparation of amide linkages and thiol esters. Mixed carbonic anhydrides have successfully acylated, under very mild conditions, the carbanions derived from diethyl ethylmalonate and diethylcadmium.⁷ The latter gives as a product the corresponding ketone. Mixed anhydrides derived from acetic and acetylsalicylic acids give results similar to those described here.⁷
8. A good reagent grade of benzoic acid is satisfactory.
9. Redistillation of a commercial grade gave material boiling at $87.0-87.2^{\circ}$.
10. Redistillation of a commercial grade gave material boiling at $90.8-92.0^{\circ}$.
11. If the benzoic acid is not all removed at this stage, it is troublesome during the final distillation.
12. The fore-run, if giving a positive test with ferric chloride reagent, may be redistilled to give increased yields.

3. Discussion

Diethyl benzoylmalonate has been prepared by treatment of the copper derivative of ethyl benzoylacetate with ethyl chlorocarbonate.⁸ It has also been obtained by the action of benzoyl chloride on the magnesium derivative of diethyl malonate,⁹ and on a mixture of malonic ester and sodium methoxide^{10,11} or sodium.^{12,13} This compound has been found to be obtainable in higher yield by the reaction of benzoyl chloride and the ethoxymagnesium derivative.¹⁴ The present method has been described in a previous communication and is of interest as an illustration of the use of mixed carbonic anhydrides as acylating agents.⁷

This preparation is referenced from:

- *Org. Syn. Coll. Vol. 8, 247*

References and Notes

1. University of Rochester, Rochester, New York.
2. *Org. Syntheses Coll. Vol. 2, 594* (1943).
3. Riegel and Lilienfeld, *J. Am. Chem. Soc.*, **67**, 1273 (1945).
4. Vaughan, *J. Am. Chem. Soc.*, **73**, 3547 (1951).

5. Boissonnas, *Helv. Chim. Acta*, **34**, 874 (1951).
 6. Wieland and Bernhard, *Ann.*, **572**, 190 (1951).
 7. Tarbell and Price, *J. Org. Chem.*, **21**, 144 (1956); **22**, 245 (1957).
 8. Bernhard, *Ann.*, **282**, 165 (1894).
 9. Gagnon, Boivin, and Laflamme, *Can. J. Chem.*, **34**, 530 (1956).
 10. Claisen and Falk, *Ann.*, **291**, 72 (1896).
 11. Bülow and Hailer, *Ber.*, **35**, 934 (1902).
 12. King, King, and Thompson, *J. Chem. Soc.*, **1948**, 552.
 13. Borsche and Wannagat, *Ber.*, **85**, 193 (1952).
 14. Lund, *Ber.*, **67**, 935 (1934).
-

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

Ethoxymagnesiummalonic ester

benzoic-carbonic anhydride

copper derivative of ethyl benzoylacetate

magnesium derivative of diethyl malonate

alcohol (64-17-5)

sulfuric acid (7664-93-9)

Benzene (71-43-2)

ether (60-29-7)

sodium bicarbonate (144-55-8)

magnesium,
magnesium turnings (7439-95-4)

sodium sulfate (7757-82-6)

carbon tetrachloride (56-23-5)

Benzoic acid (65-85-0)

sodium methoxide (124-41-4)

benzoyl chloride (98-88-4)

toluene (108-88-3)

sodium,
sodium wire (13966-32-0)

ferric chloride (7705-08-0)

diethyl malonate (105-53-3)

Diethyl benzoylmalonate,
Malonic acid, benzoyl-, diethyl ester (1087-97-4)

Triethylamine hydrochloride (554-68-7)

diethyl ethylmalonate (133-13-1)

diethylcadmium

ethyl chlorocarbonate (541-41-3)

triethylamine (121-44-8)