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.

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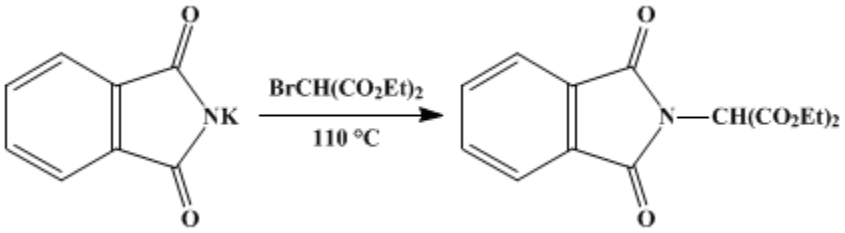
ETHYL PHTHALIMIDOMALONATE

[Malonic acid, phthalimido-, diethyl ester]



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1. Procedure

In a 600-cc. beaker 210 g. (0.88 mole) of ethyl bromomalonate (p. 245) (Note 1) and 165 g. (0.89 mole) of potassium phthalimide (p. 119) are intimately stirred together. The mixture is stirred approximately every ten minutes. If no spontaneous reaction starts within one-half hour (Note 1), it is necessary to initiate the reaction by heating to 110–120°. The mixture then becomes liquid and can be stirred easily. It turns to a light brown color, especially near the top where it comes in contact with the air. When the temperature begins to drop, the mixture is heated in an oil bath at 110° for one hour to insure completion of the reaction.

The mixture is then poured into a mortar where it solidifies to a solid mass (Note 2). When cold, the mixture is ground up with water to remove most of the potassium bromide and filtered. The precipitate is then reground with water and refiltered, finally being washed well with water. The solid material on the filter consists of some potassium bromide, some phthalimide, and the ethyl phthalimidomalonate. Without drying, it is put into a 1-l. flask with 400 cc. of benzene and heated to boiling. After cooling, the insoluble bromide and phthalimide are removed by filtration. The filtrate contains some water, which is removed by means of a separatory funnel.

The benzene solution is dried with 20 g. of calcium chloride and the benzene removed by distillation under diminished pressure on a water bath. The residue is poured into a mortar where it solidifies. The crystalline mass is then ground with small amounts of ether (200 cc. in all), filtered, and washed with ether (about 100 cc.) until pure white. The yield of ethyl phthalimidomalonate melting at 73–74° is 155–162 g. From the ether filtrate after distilling the ether, there may be recovered a further amount by washing with a small amount of ether to remove the brown color. The total weight of ester obtained in the two crops is 180–190 g. (67–71 per cent of the theoretical amount).

2. Notes

1. When freshly prepared ethyl bromomalonate is used, the temperature of the mixture may rise spontaneously to 140°. In such event no heat should be applied until the temperature falls again.
2. If the solidification does not take place as soon as the mixture is cold, about 100 cc. of water should be added. This accelerates the solidification.

3. Discussion

The procedure described is adapted from that of Sörensen.[1]

This preparation is referenced from:

- Org. Syn. Coll. Vol. 2, 384

References and Notes

1. Sörensen, Compt. rend. trav. lab. Carlsberg **6**, 1 (1903) [Chem. Zentr. II, 33 (1903)].

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

ester

calcium chloride (10043-52-4)

Benzene (71-43-2)

ether (60-29-7)

Potassium Phthalimide (1074-82-4)

Phthalimide (85-41-6)

potassium bromide (7758-02-3)

Ethyl bromomalonate

Ethyl phthalimidomalonate,
Malonic acid, phthalimido-, diethyl ester (5680-61-5)