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.

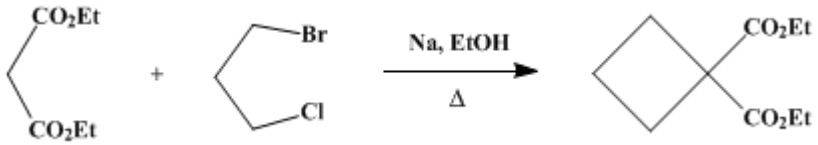
These paragraphs were added in September 2014. The statements above do not supersede any specific hazard caution notes and safety instructions included in the procedure.

DOI: 10.15227/orgsyn.033.0023

Organic Syntheses, Coll. Vol. 4, p.288 (1963); Vol. 33, p.23 (1953).

DIETHYL 1,1-CYCLOBUTANEDICARBOXYLATE

[1,1-Cyclobutanedicarboxylic acid, diethyl ester]



Submitted by Raymond P. Mariella and Richard Raube[1].
Checked by William S. Johnson, William DeAcetis, and Herbert Title.

1. Procedure

A solution of sodium ethoxide is prepared by adding 138 g. (6.0 g. atoms) of fresh-cut sodium in small pieces to 2.5 l. of absolute ethanol in a 5-l. round-bottomed flask fitted with an efficient reflux condenser capped with a calcium chloride drying tube (Note 1). In a three-necked 5-l. round-bottomed flask, equipped with a reflux condenser capped with a calcium chloride tube, a rubber-sealed mechanical stirrer, and an inlet tube for addition of the sodium ethoxide solution, are mixed 480 g. (3.0 moles) of diethyl malonate (Note 2) and 472 g. (3.0 moles) of trimethylene chlorobromide (Note 3). The mixture is heated to 80° and vigorously stirred while the sodium ethoxide solution is slowly forced into the flask by means of dry air pressure. The rate of addition is regulated so that the reaction mixture refluxes smoothly. After the addition is complete (this requires about 1.5 hours), the mixture is refluxed, with continued stirring (Note 4), for an additional 45 minutes. Upon completion of the reflux period, the alcohol is removed by distillation (Note 4), 90–95% of the alcohol being recovered. The reaction mixture is cooled, and 900 ml. of cold water is added. After the sodium halides are completely dissolved, the organic layer is separated and the aqueous layer is extracted with three 500-ml. portions of ether. The organic layer and the ether extracts are combined, shaken with 50 ml. of saturated salt solution, and dried over 100 g. of anhydrous sodium sulfate. The solution is filtered, the ether is removed by distillation on a steam bath, and the residue, which weighs 600–625 g., is distilled through a short Vigreux column. The yield of product boiling at 91–96°/4 mm. is 320–330 g. (53–55%) (Note 5).

2. Notes

1. It is important to maintain strictly anhydrous conditions throughout this reaction. The equipment should be carefully predried and the absolute ethanol freshly prepared (preferably by the magnesium ethoxide method[2]) and distilled directly into the reaction flask. If the volume of ethanol is less than 2.5 l. the sodium ethoxide may not remain in solution. It is convenient to employ a three-necked flask carrying two condensers for this operation and to add the sodium through the third neck, which is otherwise kept stoppered.
2. Material boiling at 95.2–95.8°/14 mm., n_D^{25} 1.4120, was used.
3. Trimethylene chlorobromide can be obtained commercially. Material boiling at 141–142°/755 mm., n_D^{25} 1.4843, was used.
4. The stirring must be continued during this operation; otherwise the mixture will bump badly.
5. This material, n_D^{25} 1.433–1.434, d_{20}^{25} 1.042–1.044, is of fair purity and can be hydrolyzed and decarboxylated[3,4] to give cyclobutanecarboxylic acid in more than 80% yield. In order to obtain a highly pure product it may be necessary to fractionally distil the material. For example, on slow redistillation of a product prepared as described above through a 3-ft. Vigreux column at a high reflux ratio, the checkers obtained 8.5% of forerun n_D^{25} 1.4287–1.4328, 43% of diethyl 1,1-cyclobutanedicarboxylate, n_D^{25} 1.4332–1.4335, and 2.5% of higher-boiling material n_D^{25} 1.4362–1.4427. The pure product is reported to boil at 104.6°/12 mm., 85.2°/3.5 mm. or 60.0°/0.5 mm., n_D^{25} 1.4336, d_{20}^{25} 1.0470.[5]

3. Discussion

Diethyl 1,1-cyclobutanedicarboxylate has been prepared by the alkylation of diethyl sodiomalonate with trimethylene dibromide,[3,4,6,7] trimethylene diiodide,[7] or trimethylene chlorobromide.[8,9] It is claimed that the yield of product from the latter reaction may be increased by the use of a mixture of benzene and ethanol as a solvent.[10] Diethyl 1,1-cyclobutanedicarboxylate also may be obtained by the peroxide-catalyzed addition of hydrogen bromide to diethyl allylmalonate followed by intramolecular alkylation.[11] The procedure described here is that of Mariella and Raube.[8]

This preparation is referenced from:

- Org. Syn. Coll. Vol. 6, 271

References and Notes

1. Northwestern University, Evanston, Illinois.
2. Lund and Bjerrum, *Ber.*, **64**, 210 (1931). Fieser, *Experiments in Organic Chemistry*, 3rd ed., p. 286, D. C. Heath and Company, Boston, Massachusetts, 1955.
3. *Org. Syntheses Coll. Vol.* **3**, 213 (1955).
4. Cason and Allen, *J. Org. Chem.*, **14**, 1036 (1949).
5. Perkin, *J. Chem. Soc.*, **51**, 1 (1887).
6. Rupe, *Ann.*, **327**, 183 (1903).
7. Gol'mov, *Zhur. Obshcheii Khim.*, **22**, 1944 (1952) [*C. A.*, **47**, 9268 (1953)].
8. Mariella and Raube, *Bol. col. quím. Puerto Rico*, **8**, 24 (1951) [*C. A.*, **46**, 4491*h* (1952)].
9. Kishner, *J. Russ. Phys. Chem. Soc.*, **37**, 507 (1905) [*Chem. Zentr.*, [2] **76**, 761 (1905)]; Favorskaya and Yakovlev, *Zhur. Obshcheii Khim. (J. Gen. Chem.)*, **22**, 122 (1952) [*C. A.*, **46**, 11118 (1952)]; Gol'mov and Kazanskii, *Akad. Nauk. S.S.S.R. Inst. Org. Khim. Sintezy Org. Soedinenii Sbornik*, **I**, 93 (1950) [*C.A.*, **47**, 8003 (1953)].
10. Raik and Kazanskii, *Vestnik Moskov. Univ.*, **8**, No. 3, *Ser. Fiz.-Mat. i Estestven. Nauk*, No. 2, 125 (1953) [*C. A.*, **49**, 3833 (1955)].
11. Walborsky, *J. Am. Chem. Soc.*, **71**, 2941 (1949).

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

ethanol (64-17-5)

Benzene (71-43-2)

ether (60-29-7)

hydrogen bromide (10035-10-6)

trimethylene dibromide (109-64-8)

sodium sulfate (7757-82-6)

sodium (13966-32-0)

sodium ethoxide (141-52-6)

Trimethylene chlorobromide (109-70-6)

diethyl malonate (105-53-3)

Diethyl 1,1-cyclobutanedicarboxylate,
1,1-Cyclobutanedicarboxylic acid, diethyl ester (3779-29-1)

diethyl sodiomalonate

trimethylene diiodide (627-31-6)

diethyl allylmalonate (2049-80-1)

Cyclobutanecarboxylic acid (3721-95-7)