



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](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.

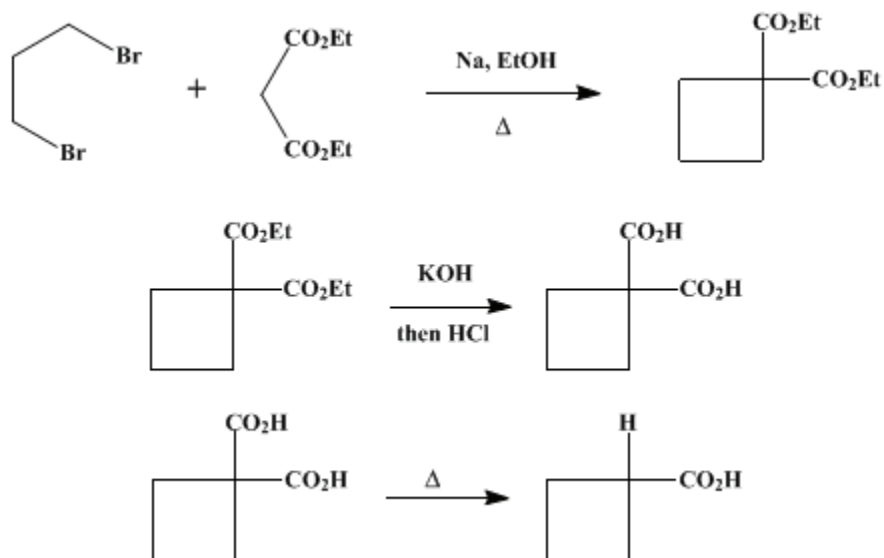
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*These paragraphs were added in September 2014. The statements above do not supersede any specific hazard caution notes and safety instructions included in the procedure.*

*Organic Syntheses, Coll. Vol. 3, p.213 (1955); Vol. 23, p.16 (1943).*

## 1,1-CYCLOBUTANEDICARBOXYLIC ACID AND CYCLOBUTANECARBOXYLIC ACID



Submitted by G. B. Heisig and F. H. Stodola.

Checked by F. C. Whitmore, T. S. Oakwood, and D. L. Green.

### 1. Procedure

A. *1,1-Cyclobutanedicarboxylic acid.* In a 3-l. three-necked round-bottomed flask, carrying a separatory funnel, a mechanical stirrer, a reflux condenser fitted with a calcium chloride tube, and a thermometer, are placed 160 g. (1 mole) of ethyl malonate and 212 g. (1.05 moles) of trimethylene bromide. The thermometer is adjusted so that the bulb is immersed in the liquid in the flask; the stirrer is started, and a solution of 46 g. (2 gram atoms) of sodium in 800 ml. of absolute ethanol is added through the separatory funnel while the temperature of the reaction mixture is kept at 60–65° (Note 1). During the addition of the first quarter of the ethoxide solution (20 minutes) it is necessary to cool the reaction mixture occasionally in order to maintain the proper temperature, but after this point the remainder of the ethoxide solution is added just rapidly enough to keep the reaction mixture at 60–65°; this part of the addition requires about 30 minutes.

The reaction mixture is allowed to stand until the temperature drops to 50–55°, after which it is heated on a steam bath until a sample added to water is neutral to phenolphthalein (about 2 hours). Water is added to dissolve the precipitate of sodium bromide, and the ethanol is removed by distillation. The flask is now arranged for steam distillation, and the ethyl 1,1-cyclobutanedicarboxylate and unchanged malonic ester are removed by steam distillation (Note 2); about 4 l. of distillate is collected. The ester layer in the distillate is separated, and the aqueous layer is extracted once with 1 l. of ether. The extract and the ester layer are combined, and the ether is removed on the steam bath (Note 3).

The esters are hydrolyzed by refluxing them for 2 hours with a solution of 112 g. of potassium hydroxide in 200 ml. of ethanol. Most of the ethanol is removed by distillation, and the mixture is then evaporated to dryness on a steam bath. The residue is dissolved in the minimum amount of hot water (100 to 125 ml.), and concentrated hydrochloric acid (about 90–95 ml.) is added until the solution is slightly acid (Note 4). After the solution has been boiled for a few minutes to remove carbon dioxide, it is made slightly alkaline with ammonia. To the boiling solution there is added a slight excess of barium chloride. The hot solution is filtered to remove barium malonate, the filtrate is cooled, and to it is added 100 ml. of 12 N hydrochloric acid. The solution is then extracted with four 250-ml. portions of ether. The extracts are combined and dried over calcium chloride, and the ether is removed by

distillation on a steam bath. The residual pasty mass (about 38 g.) is pressed on a porous plate to remove adherent oil and then dissolved in 30–50 ml. of hot [ethyl acetate](#). The solution, when cooled in an ice-salt bath, deposits the pure dicarboxylic acid. This is filtered; the filtrate, when evaporated, yields a pasty mass of acid which, in turn, is crystallized from [ethyl acetate](#). The yield of pure [1,1-cyclobutanedicarboxylic acid](#) melting at 156–158° is 30–34 g. (21–23%).

B. [Cyclobutanecarboxylic acid](#). The above dibasic acid is placed in a 75-ml. distilling flask carrying a thermometer and attached to a 75-ml. Claisen flask as a receiver. The receiver is cooled with running water while the flask containing the dibasic acid is heated in a metal or oil bath (bath temperature, 160–170°) until no more [carbon dioxide](#) is evolved. Then the temperature of the bath is raised to 210–220°, and the material that boils at 189–195° is collected. The crude [cyclobutanecarboxylic acid](#) (19–22 g.) is redistilled from the Claisen flask in which it was collected. The pure acid boils at 191.5–193.5°/740 mm. (Note 5) and weighs 18–21 g. (18–21% based on malonic ester). There is a small higher-boiling fraction, which comes over at 193.5–196°/740 mm.

## 2. Notes

1. The submitters and the checkers prepared the [sodium ethoxide](#) in the conventional manner. However, [sodium ethoxide](#) and [sodium methoxide](#) are very conveniently prepared by the "inverse" procedure, as described by Tishler in Fieser, *Experiments in Organic Chemistry*, 2nd ed., 1941, D. C. Heath and Company, Boston, p. 385 (bottom). The metal is placed in the flask, and the alcohol is added through the condenser at such a rate that rapid refluxing is maintained. It is necessary, as a precautionary measure, to clamp the flask and not to trust to the friction between a rubber stopper and the flask to hold the flask in place. When this precaution is taken, a cooling bath may be used with safety. It is necessary to cool the flask; the metal must not be allowed to melt, as this will result in the formation of one large mass with a greatly decreased metallic surface. (Private communication, C. F. H. Allen.)
2. The steam distillation separates [ethyl malonate](#) and [ethyl 1,1-cyclobutanedicarboxylate](#) from [ethyl pentane-1,1,5,5-tetracarboxylate](#), formed in a side reaction between malonic ester (2 moles) and [trimethylene bromide](#) (1 mole). The tetraethyl ester remains in the residue from the steam distillation. In several test experiments, in which about two-thirds of the amounts specified above were used, the yield of tetraethyl ester was 30–40% of the theoretical amount, based upon the [sodium ethoxide](#) used.
3. If this extraction with [ether](#) is omitted the yield of [1,1-cyclobutanedicarboxylic acid](#) is 3–4 g. less.
4. The submitters used 55 ml. of [hydrochloric acid](#) at this point; the checkers stated that this amount was insufficient to neutralize the mixture. The purpose of acidification at this point is not to liberate the [cyclobutanedicarboxylic acid](#), but merely to remove carbonates and excess [potassium hydroxide](#). After the [carbon dioxide](#) has been expelled, the solution is made alkaline with [ammonia](#); hence a great excess of [hydrochloric acid](#) should be avoided. The submitters used only enough [hydrochloric acid](#) to make the solution acid to litmus. After the solution has been made basic with [ammonia](#), [barium chloride](#) solution is added until there is no further precipitation of [barium malonate](#).
5. This acid is quite pure. The checkers distilled 52.5 g. of it through an analytical column; except for a fore-run of 1.5–2.0 g., all the material had a constant boiling point and index of refraction.

## 3. Discussion

[1,1-Cyclobutanedicarboxylic acid](#) has been prepared by hydrolysis of the ethyl ester,<sup>1</sup> or of the half nitrile, [1-cyano-1-carboxycyclobutane](#).<sup>2</sup> The ethyl ester has been prepared by condensation of [ethyl malonate](#) with [trimethylene bromide](#)<sup>1,3</sup> or chlorobromide,<sup>4</sup> and by the action of [sodium ethoxide](#) on [diethyl  \$\gamma\$ -bromopropylmalonate](#).<sup>5</sup> The half nitrile has been prepared by condensation of [trimethylene bromide](#) with [ethyl cyanoacetate](#) followed by hydrolysis of the ester to the acid.<sup>2</sup>

[Cyclobutanecarboxylic acid](#) has been prepared by decarboxylation of the 1,1-dibasic acid,<sup>1,6</sup> and by decarboxylation of [1-cyano-1-carboxycyclobutane](#) followed by hydrolysis of the cyano group.<sup>2</sup>

This preparation is referenced from:

- [Org. Syn. Coll. Vol. 3, 733](#)
- [Org. Syn. Coll. Vol. 4, 288](#)

- Org. Syn. Coll. Vol. 5, 273
- Org. Syn. Coll. Vol. 5, 909
- Org. Syn. Coll. Vol. 6, 271
- Org. Syn. Coll. Vol. 6, 312
- Org. Syn. Coll. Vol. 7, 117

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## References and Notes

1. Perkin, *J. Chem. Soc.*, **51**, 1 (1887); Rupe, *Ann.*, **327**, 183 (1903).
  2. Carpenter and Perkin, *J. Chem. Soc.*, **75**, 930 (1899).
  3. Cason and Allen, *J. Org. Chem.*, **14**, 1036 (1949).
  4. Kishner, *J. Russ. Phys. Chem. Soc.*, **37**, 507 (1905) (*Chem. Zentr.*, **1905**, II, 761).
  5. Walborsky, *J. Am. Chem. Soc.*, **71**, 2941 (1949).
  6. Perkin and Sinclair, *J. Chem. Soc.*, **61**, 40 (1892).
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## Appendix

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

chlorobromide

ethanol (64-17-5)

calcium chloride (10043-52-4)

hydrochloric acid (7647-01-0)

ammonia (7664-41-7)

ethyl acetate (141-78-6)

ether (60-29-7)

sodium bromide (7647-15-6)

Trimethylene bromide (109-64-8)

carbon dioxide (124-38-9)

barium chloride (10361-37-2)

sodium methoxide (124-41-4)

potassium hydroxide (1310-58-3)

sodium (13966-32-0)

sodium ethoxide (141-52-6)

Ethyl cyanoacetate (105-56-6)

ethyl malonate (1071-46-1)

phenolphthalein (77-09-8)

1,1-Cyclobutanedicarboxylic acid,  
cyclobutanedicarboxylic acid (5445-51-2)

Cyclobutanecarboxylic acid (3721-95-7)

ethyl 1,1-cyclobutanedicarboxylate

barium malonate

ethyl pentane-1,1,5,5-tetracarboxylate

diethyl  $\gamma$ -bromopropylmalonate

1-cyano-1-carboxycyclobutane