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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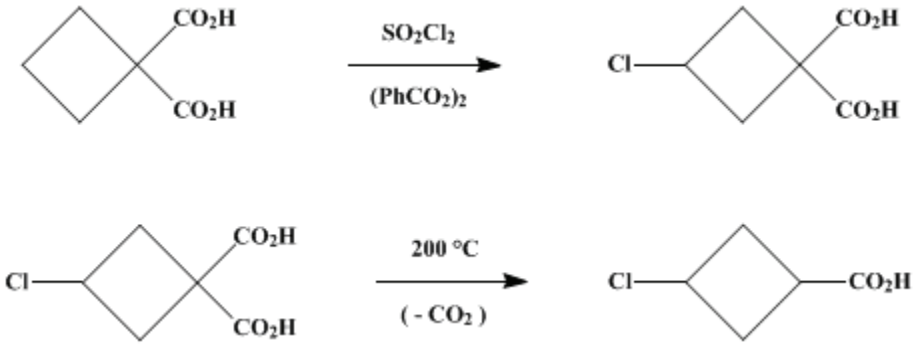
Organic Syntheses, Coll. Vol. 6, p.271 (1988); Vol. 51, p.73 (1971).

3-CHLOROCYCLOBUTANECARBOXYLIC ACID

[Cyclobutanecarboxylic acid, 3-chloro-]



Submitted by Gary M. Lampman and James C. Aumiller[1].
Checked by G. Nelson and K. B. Wiberg.

1. Procedure

Caution! Benzene has been identified as a carcinogen; OSHA has issued emergency standards on its use. All procedures involving benzene should be carried out in a well-ventilated hood, and glove protection is required.

A 2-l., three-necked, round-bottomed flask equipped with a Trubore stirrer and paddle is charged with 172.8 g. (1.200 moles) of 1,1-cyclobutanedicarboxylic acid (Note 1) and 1500 ml. of benzene. The mixture is stirred and heated at reflux, and 200 ml. of benzene and benzene-water azeotrope is removed by distillation to ensure anhydrous conditions. The flask is then fitted with an addition funnel and a reflux condenser attached to a drying tube. Stirring and heating are continued, and over a 40-minute period, 170 g. (102 ml., 1.26 moles) of sulfuryl chloride (Note 2) is added from the funnel, while 4.0 g. of benzoyl peroxide (Note 3) is added simultaneously in small portions through the top of the condenser. After a short induction period, hydrogen chloride and sulfur dioxide are evolved. After the addition is complete, heating at reflux is maintained for 22 hours. The solid is dissolved after 1 hour, leaving a light brown solution. After the heating period is complete, the benzene is removed by distillation, and the residue is heated to 190–210° for 45 minutes to effect decarboxylation. The black residue is transferred to a small flask and distilled under vacuum through a 6-cm. Vigreux column. After a forerun of about 25–30 g. (Note 4), 65–79 g. (40–49%) of *cis*- and *trans*-3-chlorocyclobutanecarboxylic acid is collected as a light yellow liquid, b.p. 131–137° (15 mm.) n_D^{24} 1.4790 (Note 5). A black residue remains in the distillation flask.

2. Notes

1. Diethyl 1,1-cyclobutanedicarboxylate is prepared by the method in *Org. Synth.*, **Coll. Vol. 4**, 288 (1963). The diester is isolated in 55% yield, b.p. 111–114° (16 mm.). The diester can be saponified by the method in *Org. Synth.*, **Coll. Vol. 3**, 213 (1955), but omitting the barium chloride step, to give the diacid. This material upon recrystallization from ethyl acetate gives the diacid in high purity. The diacid may also be purchased from Aldrich Chemical Company, Inc.
2. Eastman Organic Chemicals or Matheson, Coleman and Bell practical grade material was distilled before use. Since hydrogen chloride and sulfur dioxide are evolved, the preparation should be carried out in an efficient hood.
3. Eastman Organic Chemicals white label material was used.
4. The forerun contains cyclobutanecarboxylic acid and 3-chlorocyclobutanecarboxylic acid, b.p. 100–130° (15 mm.) n_D^{24} 1.4623. The presence of cyclobutanecarboxylic acid indicates that some of the

diacid was not chlorinated. Attempts were made to reduce the amount of unchlorinated product by increasing the amount of sulfuryl chloride. Instead, this increased the amount of a dichlorinated impurity which is difficult to separate from the desired product.
5. The product is analyzed by GC at 190° on a Beckman GC-2 chromatograph equipped with a 180 cm. × 6 mm. column (Beckman 17449) containing 42/60 Johns-Manville C-22 firebrick coated with Dow-Corning 550 silicone oil. The retention times are 8 and 9 minutes for the *trans*- and *cis*- compounds, respectively.

3. Discussion

3-Chlorocyclobutanecarboxylic acid has been prepared from the rather inaccessible 3-hydroxy-1,1-cyclobutanedicarboxylic acid.[2] The related 3-bromocyclobutanecarboxylic acid has also been prepared by an eight-step synthetic scheme.[3] The present method, based upon the procedure of Nevill, Frank, and Trepka,[4] affords the 3-chloro acid in high yield in one step. Thus this method provides a compound which cannot be easily made by other methods.

The use of sulfuryl chloride for free radical chlorination of aliphatic carboxylic acids gives mixtures of positional isomers;[5] however, with the cyclobutane ring, the attack is much more selective. The present method provides a procedure for free radical halogenation of a cyclobutane ring.

The conversion of 3-chlorocyclobutanecarboxylic acid to 1-bromo-3-chlorocyclobutane is described in *Organic Syntheses*.[6]

This preparation is referenced from:

- Org. Syn. Coll. Vol. 6, 179

References and Notes

1. Department of Chemistry, Western Washington University, Bellingham, Washington 98225.
2. R. C. Jones, Ph.D. Thesis, Harvard University, 1941.
3. K. B. Wiberg and G. M. Lampman, *J. Am. Chem. Soc.*, **88**, 4429 (1966).
4. W. A. Nevill, D. S. Frank, and R. D. Trepka, *J. Org. Chem.*, **27**, 422 (1962).
5. M. S. Kharasch and H. C. Brown, *J. Am. Chem. Soc.*, **62**, 925 (1940).
6. G. M. Lampman and J. C. Aumiller, *Org. Synth.*, **Coll. Vol. 6**, 179 (1988).

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

hydrogen chloride (7647-01-0)

Benzene (71-43-2)

ethyl acetate (141-78-6)

sulfur dioxide (7446-09-5)

barium chloride (10361-37-2)

sulfuryl chloride (7791-25-5)

Diethyl 1,1-cyclobutanedicarboxylate (3779-29-1)

benzoyl peroxide (94-36-0)

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

Cyclobutanecarboxylic acid (3721-95-7)

cyclobutane (287-23-0)

1-Bromo-3-chlorocyclobutane (4935-03-9)

3-Chlorocyclobutanecarboxylic acid,
Cyclobutanecarboxylic acid, 3-chloro-,
cis- and trans-3-chlorocyclobutanecarboxylic acid (35207-71-7)

3-bromocyclobutanecarboxylic acid

3-hydroxy-1,1-cyclobutanedicarboxylic acid