



A Publication
of Reliable Methods
for the Preparation
of Organic Compounds

Working with Hazardous Chemicals

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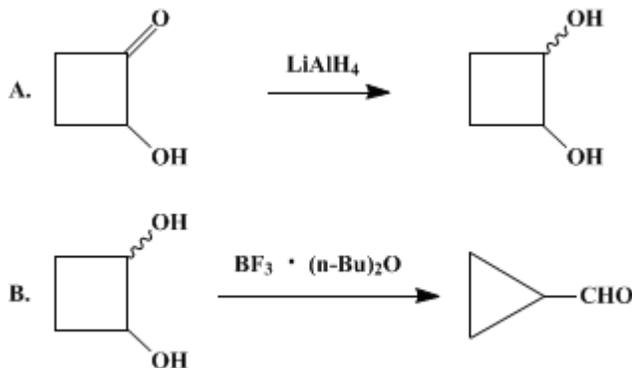
In some articles in *Organic Syntheses*, chemical-specific hazards are highlighted in red "Caution Notes" within a procedure. It is important to recognize that the absence of a caution note does not imply that no significant hazards are associated with the chemicals involved in that procedure. Prior 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.

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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. 7, p.129 (1990); Vol. 60, p.25 (1981).

CYCLOPROPANECARBOXALDEHYDE



Submitted by J. P. Barnier, J. Champion, and J. M. Conia¹.
Checked by Robert V. Stevens and Steven R. Angle.

1. Procedure

A. *1,2-Cyclobutanediol*. A 2-L, three-necked, round-bottomed flask fitted with a 200-mL dropping funnel, a mechanical stirrer, a nitrogen-inlet tube, and a reflux condenser equipped with a calcium chloride drying tube is charged with 6.2 g (0.16 mol) of lithium aluminum hydride (Note 1) and (Note 2) and 200 mL of anhydrous diethyl ether (Note 3). The dropping funnel is charged with 42 g (0.48 mol) of 2-hydroxycyclobutanone (Note 4) and 150 mL of anhydrous diethyl ether. While the suspension of lithium aluminum hydride is gently stirred under a nitrogen atmosphere, the solution of 2-hydroxycyclobutanone is added dropwise at a rate maintaining a gentle reflux. When the addition is complete, the mixture is heated at reflux for 1 hr. After the mixture has returned to room temperature, 200 mL of anhydrous diethyl ether is added. The gray reaction mixture is hydrolyzed by addition, in small parts, of a sufficient amount of wet sodium sulfate (Note 5). The reaction mixture is filtered through a sintered-glass funnel (porosity 3). The organic layer is decanted and dried over sodium sulfate. The solid is extracted with anhydrous tetrahydrofuran (Note 6) by means of a Soxhlet apparatus over a period of 24 hr. The combined organic layers are concentrated by distillation of the solvent with a rotary evaporator. The yield of crude *cis*- and *trans*-1,2-cyclobutanediol (ca. 50:50) is 34–40 g (80–95%) (Note 7).

B. *Cyclopropanecarboxaldehyde*. A 50-mL distilling flask equipped with a receiver cooled to -20°C with a dry ice–methanol bath is charged with 34 g (0.39 mol) of a crude mixture of both *cis*- and *trans*-1,2-cyclobutanediol and 10 μL of boron trifluoride butyl etherate (Note 8). The mixture is heated to 230°C with a metal bath. Drops of liquid appear on the condenser, and the aldehyde and water distill into the receiver. The temperature of the distillate oscillates between 50 and 100°C . Each time the distillation stops, 5–10 μL of boron trifluoride butyl etherate is added to the distilling flask (Note 9). The distillate is transferred into a separatory funnel and sodium chloride is added. The organic layer is decanted and the aqueous layer is extracted three times with 25-mL portions of methylene chloride. The combined organic solution is dried over sodium sulfate, and the solvent is removed by distillation through a 15-cm, helix-packed, vacuum-insulated column. The residue consists of practically pure cyclopropanecarboxaldehyde, 17.5–21.6 g (65–80%) (Note 10).

2. Notes

1. Lithium aluminum hydride is available from Prolabo—France or Alfa Products, Morton Thiokol, Inc.
2. On one occasion the checkers found it necessary to add more lithium aluminum hydride (0.3 g) for complete reaction.
3. The checkers used diethyl ether distilled from sodium–benzophenone.
4. The checkers prepared 2-hydroxycyclobutanone by the Bloomfield procedure.² The submitters

prepared it by their aqueous hydrolysis procedure.³ This procedure was checked also and proceeds in quantitative yield as described.³

5. Sodium sulfate is mixed with water to form a thick slurry. It is added to the reaction mixture with vigorous stirring to obtain a good dispersion of the slurry in the medium. The added amount of wet sodium sulfate is sufficient when the reaction effervescence ceases and the gray color of the mixture turns to yellow–white.

6. Tetrahydrofuran is purified by distillation from lithium aluminum hydride after 48-hr refluxing over potassium hydroxide (see *Org. Synth. Coll. Vol. V* **1973**, 976 for hazard warning).

7. The crude 1,2-cyclobutanediol is dried by azeotropic distillation with anhydrous benzene. The product is a mixture of *cis* and *trans* isomers (ca. 50:50) readily separable by gas chromatography on a 12-ft column containing 20% silicone SE 30 on Chromosorb W at 140°C. *cis*-1,2-Cyclobutanediol (mp 12–13°C): IR (CCl₄) cm⁻¹: hydroxyl absorption at 3625 and 3580; ¹H NMR (CCl₄) δ: multiplet at 1.98, multiplet at 4.20, and a singlet at 4.51 in a ratio 4:2:2, respectively. *trans*-1,2-Cyclobutanediol (mp 72°C): IR (CCl₄) cm⁻¹: hydroxyl absorption at 3620; ¹H NMR (CD₃COCD₃) δ: multiplet between 0.9 and 2.2, multiplet between 3.6 and 4.0, and singlet at 3.6 in a ratio of 4:2:2, respectively.

8. Boron trifluoride butyl etherate, purchased from Fluka AG, is chosen for its convenient boiling point.

9. In a typical run 10 μL of boron trifluoride butyl etherate is added every 10–15 min over a period of 3–4 hr.

10. The crude product is more than 99% pure as shown by gas chromatography; IR (CCl₄) cm⁻¹: carbonyl absorption at 1730; ¹H NMR (CCl₄) δ: doublet at 8.93, multiplet between 1.5 and 2.2, and a multiplet between 1.02 and 1.75 in the ratio 1:1:4, respectively. The product has bp 95–98°C (760 mm).

3. Discussion

This method of preparation of cyclopropanecarboxaldehyde is an adaptation of that given by J. M. Conia and J. P. Barnier.³ The various methods so far reported, which involve in the last step oxidation,⁴ reduction,⁵ or hydrolysis⁶ of a suitable cyclopropane derivative, are tedious or require expensive starting materials. The other routes involve the direct ring contraction of cyclobutane derivatives into cyclopropanecarboxaldehyde starting from cyclobutene oxide⁷ or from 2-bromo- or 2-tosyloxycyclobutanol.⁸ The present procedure uses a particularly easy ring contraction, that of 1,2-cyclobutanediol, and it involves cheap, easily available starting materials. This method can be applied to symmetrical dialkylcyclobutane-1,2-diols, but it gives a mixture of two cyclopropyl carbonyl compounds from unsymmetrical diols.

References and Notes

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

boron trifluoride butyl etherate

2-bromo- or 2-tosyloxycyclobutanol

Benzene (71-43-2)

diethyl ether (60-29-7)

sodium chloride (7647-14-5)

sodium sulfate (7757-82-6)

potassium hydroxide (1310-58-3)

Benzophenone (119-61-9)

sodium (13966-32-0)

methylene chloride (75-09-2)

cyclopropane (75-19-4)

Tetrahydrofuran (109-99-9)

lithium aluminum hydride (16853-85-3)

2-Hydroxycyclobutanone (17082-63-2)

Cyclopropanecarboxaldehyde (1489-69-6)

1,2-Cyclobutanediol,
cis- and trans-1,2-cyclobutanediol (35358-34-0)

cyclobutene oxide

cis-1,2-Cyclobutanediol (35358-33-9)

trans-1,2-cyclobutanediol