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.

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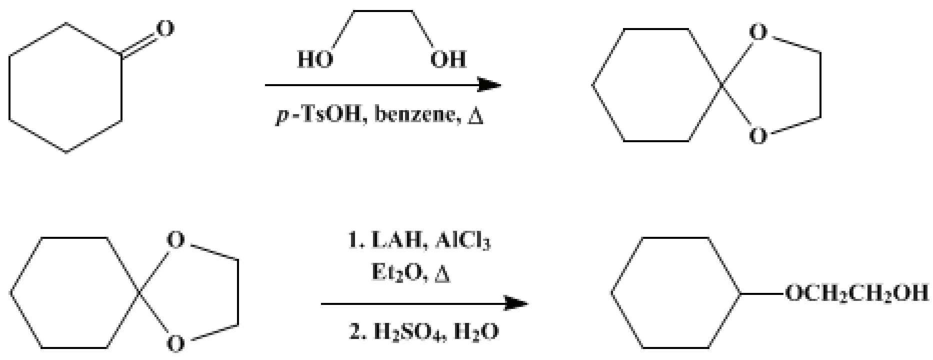
These paragraphs were added in September 2014. The statements above do not supersede any specific hazard caution notes and safety instructions included in the procedure.

DOI:10.15227/orgsyn.047.0037

Organic Syntheses, Coll. Vol. 5, p.303 (1973); Vol. 47, p.37 (1967).

2-CYCLOHEXYLOXYETHANOL

[Ethanol, 2-(cyclohexyloxy)-]



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1. Procedure

A. *1,4-Dioxaspiro[4.5]decane*. A 1-l. round-bottomed flask is charged with 118 g. (1.20 moles) of cyclohexanone, 82 g. (1.32 moles) of 1,2-ethanediol, 250 ml. of reagent grade benzene, and 0.05 g. of *p*-toluenesulfonic acid monohydrate. The flask is attached to a water separator[2] under a reflux condenser fitted with a drying tube. A heating mantle is placed under the flask, and the reaction mixture is refluxed until close to the theoretical amount of water (21.6 ml.) has collected in the trap; this requires about 6 hours. The reaction mixture is cooled to room temperature, extracted successively with 200 ml. of 10% sodium hydroxide solution and five 100-ml. portions of water, dried over anhydrous potassium carbonate, and distilled through a 20-cm. Vigreux column. 1,4-Dioxaspiro[4.5]decane is obtained as a colorless liquid, b.p. 65–67° (13 mm.), weight 128–145 g. (75–85%), n^{25}D 1.4565–1.4575.

B. *2-Cyclohexyloxyethanol*. A well-dried, 3-l. three-necked, round-bottomed flask is equipped with a stirrer, a pressure-equalizing dropping funnel, and a condenser to whose top is attached a calcium chloride drying tube. The flask is charged with 242 g. (1.81 moles) of anhydrous aluminum chloride powder and is immersed in an ice-salt bath. Anhydrous ether (25–50 ml.) is added dropwise through the dropping funnel, stirring is begun as soon as possible, and an additional 450–475 ml. of ether is added rapidly (total volume of ether added: 500 ml.). The mixture is stirred for approximately 30 minutes and becomes a light gray solution. During this period a mixture of 16.7 g. (0.44 mole) of lithium aluminum hydride and 500 ml. of anhydrous ether is vigorously stirred in a 1-l. round-bottomed flask under a nitrogen atmosphere (Note 1). The resulting suspension is added to the ethereal aluminum chloride solution through the dropping funnel. The resulting mixture, a gray slurry, is stirred for at least 30 minutes.

A solution of 125 g. (0.88 mole) of 1,4-dioxaspiro[4.5]decane in 200 ml. of anhydrous ether is added at a rate to cause gentle refluxing. The ice-salt bath is replaced by a steam bath, and the reaction mixture is refluxed for 3 hours. The calcium chloride drying tube is removed, and the steam bath is replaced by an ice bath. The excess hydride is carefully destroyed by adding water dropwise until hydrogen is no longer evolved; about 12 ml. of water is needed. This is followed by the more rapid addition of 1 l. of 10% sulfuric acid and then 400 ml. of water. This combination dissolves all the inorganic salts formed and results in the formation of two clear layers. The ether layer is separated in a 3-l. separatory funnel, and the aqueous layer is extracted with three 200-ml. portions of ether. The combined ethereal extracts are washed successively with 200 ml. of saturated sodium bicarbonate solution and 200 ml. of saturated brine. The ethereal solution is dried overnight over anhydrous potassium carbonate, filtered through a fluted filter paper, and concentrated by distillation on a steam bath. The residue, a pale yellow liquid weighing about 130 g., is distilled through a 20-cm. Vigreux column under reduced pressure. 2-Cyclohexyloxyethanol is obtained as a colorless liquid, b.p. 96–98° (13 mm.), weight 105–119 g. (83–94%), n^{25}D 1.4600–1.4610.

2. Notes

1. Most of the lithium aluminum hydride is in solution, but some is in suspension. When the humidity is below 35%, lithium aluminum hydride can be weighed in air; otherwise the weighing should be done in a dry box. Although some workers pulverize lithium aluminum hydride before dissolving or suspending it in a liquid, *the checkers recommend that this not be done because it has led to several explosions in their laboratory*. The present procedure gives a fine suspension that generally passes through the stopcock of the dropping funnel without plugging it. A wooden stick or copper wire should be in readiness to clear the stopcock if it plugs up.

Twice the theoretical amount of lithium aluminum hydride is used, but this is necessary for the best yields.

3. Discussion

The method of preparing 1,4-dioxaspiro[4.5]decane is that of Salmi.[3] The methods used by Lorette and Howard[4] to prepare ketals are convenient for preparing 1,4-dioxaspiro[4.5]decane.

The present method of preparing 2-cyclohexyloxyethanol has been described before,[5] but on a smaller scale. Other β-hydroxy ethers[5] and β-hydroxy thio ethers[6] can be prepared by the same method. Hydrogenolysis of the C-O bond in acetals has also been reported[7] with diisobutylaluminum hydride; for example, 2-cyclohexyloxyethanol was obtained in 91% yield in this manner.

2-Cyclohexyloxyethanol has also been prepared by reduction of cyclohexyloxyacetic acid with lithium aluminum hydride[8] and by decomposition of cyclohexanone methanesulfonylhydrazone with sodium in ethylene glycol.[9]

4. Merits of the Preparation

The method described is more convenient than earlier methods of preparing 2-cyclohexyloxyethanol. It may be adapted to the preparation of other β-hydroxyethyl and γ-hydroxypropyl ethers[5] and the corresponding thio ethers.[6,10] Although ketals are resistant to reduction by lithium aluminum hydride alone, the presence of a Lewis acid facilitates C-O cleavage, presumably via an oxocarbonium ion,[11] as the procedure demonstrates.

References and Notes

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

brine

potassium carbonate (584-08-7)

sulfuric acid (7664-93-9)

Benzene (71-43-2)

ether (60-29-7)

hydrogen (1333-74-0)

sodium hydroxide (1310-73-2)

sodium bicarbonate (144-55-8)

Cyclohexanone (108-94-1)

nitrogen (7727-37-9)

copper (7440-50-8)

aluminum chloride,
aluminum chloride powder (3495-54-3)

sodium (13966-32-0)

ethylene glycol,
1,2-ethanediol (107-21-1)

lithium aluminum hydride (16853-85-3)

diisobutylaluminum hydride (1191-15-7)

2-Cyclohexyloxyethanol,
Ethanol, 2-(cyclohexyloxy)- (1817-88-5)

1,4-Dioxaspiro[4.5]decane (177-10-6)

cyclohexyloxyacetic acid

cyclohexanone methanesulfonylhydrazone

p-toluenesulfonic acid monohydrate (6192-52-5)