



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.

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.

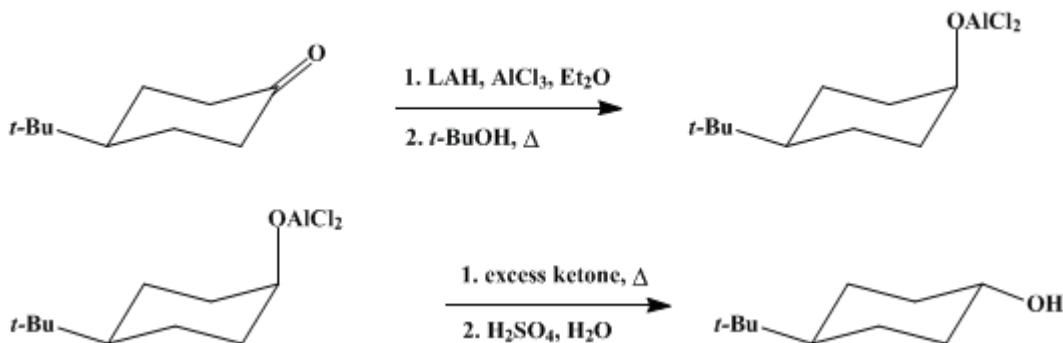
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*These paragraphs were added in September 2014. The statements above do not supersede any specific hazard caution notes and safety instructions included in the procedure.*

*Organic Syntheses, Coll. Vol. 5, p.175 (1973); Vol. 47, p.16 (1967).*

## ***trans*-4-*t*-BUTYLCYCLOHEXANOL**

[Cyclohexanol, 4-*t*-butyl, *trans*-]



Submitted by E. L. Eliel, R. J. L. Martin, and D. Nasipuri<sup>1</sup>.

Checked by E. J. Corey and Barbara Kaski.

### 1. Procedure

In a 3-l. three-necked flask, equipped with a mercury-sealed Hershberg stirrer, a dropping funnel, and a reflux condenser protected with a calcium chloride tube, is placed 67 g. (0.5 mole) of powdered anhydrous aluminum chloride. The flask is cooled in an ice bath, 500 ml. of dry ether is slowly added from the dropping funnel, and the mixture is stirred for a few minutes. Meanwhile 5.5 g. of powdered lithium aluminum hydride (Note 1) is placed in a 1-l. flask fitted with a condenser, and 140 ml. of dry ether is added slowly from the top of the condenser with caution while the flask is kept cooled in ice. The mixture is gently refluxed for 30 minutes to effect, as far as possible, solution of the hydride. It is then cooled, and the resulting slurry (which consists of a suspension of lithium aluminum hydride in its solution) is transferred to the dropping funnel of the previous setup and is added to the ethereal solution of aluminum chloride with stirring within 10 minutes. After the addition is complete, the reaction mixture is stirred for an additional 30 minutes without cooling to complete the formation of the "mixed hydride."

A solution of 77.2 g. (0.5 mole) of 4-*t*-butylcyclohexanone (Note 2) in 500 ml. of dry ether is then placed in the dropping funnel and slowly added to the "mixed hydride" solution without much cooling so that gentle refluxing is maintained (Note 3) After addition of the ketone over a period of 45–60 minutes the reaction mixture is refluxed for 2 hours more to complete the reduction. The excess hydride is destroyed by the addition of 10 ml. of dry *t*-butanol, and the mixture is refluxed for an additional 30 minutes. 4-*t*-Butylcyclohexanone (3 g.) in 20 ml. of dry ether is then added to the reaction mixture, which is refluxed for 4 hours more and allowed to stand overnight (Note 4), (Note 5). The reaction mixture is cooled in an ice bath and decomposed by successive additions of 100 ml. of water and 250 ml. of 10% aqueous sulfuric acid. The ethereal layer is separated and the aqueous layer extracted once with 150 ml. of ether. The combined ether extracts are washed once with water and dried over anhydrous magnesium sulfate. The extract is filtered from magnesium sulfate and the ether removed by distillation on a steam bath. The residue, weighing 85–87 g., solidifies in the flask and on gas chromatographic analysis (see Note 5) is found to contain 96% *trans* alcohol, 0.8% *cis* alcohol, and 3.2% ketone.

The crude white product is dissolved in 150 ml. of hot petroleum ether (b.p. 60–70°). On cooling, it forms a solid cake which is transferred to a Buchner funnel and rinsed with small portions of cooled petroleum ether. The yield of product, m.p. 75–78° (Note 6), is 57–61 g. (73–78%). It has an approximate composition of 99.3% *trans* alcohol, 0.3% *cis* alcohol, and 0.4% ketone. A further crop of 12 g. is obtained by concentration of the mother liquor. It contains less than 1% of the *cis* alcohol and the ketone and is sufficiently pure for most preparative purposes (Note 7).

## 2. Notes

1. The lithium aluminum hydride was obtained from Metal Hydrides Incorporated and was more than 95% pure. For calculation of the quantity of hydride required it was assumed that the purity was 95%.
2. 4-*t*-Butylcyclohexanone was supplied by the Dow Chemical Company.
3. The continuance of gentle refluxing as the last portion of the ketone is added assures that there is an excess of "mixed hydride" present.
4. It is not necessary to allow the reaction mixture to stand overnight, and it may be decomposed at this stage without any loss in purity.
5. At this stage the attainment of equilibrium can be checked by removing a 5-ml. aliquot from the reaction product and working it up in the same way as described in the preparation. The product is then analyzed by gas-liquid chromatography using a 20% Carbowax 20M on firebrick column at 150°. The features to note in the chromatogram are almost complete absence (less than 1%) of the *cis* isomer (second peak, disregarding initial solvent and *t*-butanol peaks) and the presence of some 4-*t*-butylcyclohexanone (first peak). The *trans* isomer constitutes the third peak with longest retention time.
6. The melting point of a highly purified sample<sup>2</sup> of *trans* alcohol is 82.5–83°.
7. Since the alcohol has a relatively high solubility in petroleum ether, the yield from the crystallization depends on the volume of solvent used. However, by concentrating the mother liquor the overall yield from the first and second crops of crystals varies from 74% to 94%.

## 3. Discussion

4-*t*-Butylcyclohexanol has been prepared from *p*-*t*-butylphenol by reduction under a variety of conditions.<sup>3,4</sup> Winstein and Holness<sup>5</sup> prepared the pure *trans* alcohol from the commercial alcohol by repeated crystallization of the acid phthalate followed by saponification of the pure *trans* ester. Eliel and Ro<sup>6</sup> obtained 4-*t*-butylcyclohexanol containing 91% of the *trans* isomer by lithium aluminum hydride reduction of the ketone. Hüchel and Kurz<sup>7</sup> reduced *p*-*t*-butylphenol with platinum oxide in acetic acid and then separated the isomers by column chromatography.

## 4. Merits of the Preparation

The procedure employs a readily available starting material and produces the pure *trans* isomer in high yield. The method described is an improvement on that used by Eliel and Rerick<sup>2</sup> in that it is not necessary to use a clear solution of lithium aluminum hydride in ether for the preparation of the "mixed hydride." It is not necessary to know the precise amount of lithium aluminum hydride used so long as a slight excess is present. The excess hydride is destroyed by adding *t*-butanol; the excess *t*-butanol has no effect on the subsequent equilibration and purification. The equilibration of the 4-*t*-butylcyclohexanol is effected by adding a small amount of 4-*t*-butylcyclohexanone.

The method is useful in the preparation of other equatorial alcohols.<sup>2,8</sup>

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## References and Notes

1. Department of Chemistry, University of Notre Dame, Notre Dame, Indiana.
  2. E. L. Eliel and M. N. Rerick, *J. Am. Chem. Soc.*, **82**, 1367 (1960).
  3. G. Vavon and M. Barbier, *Bull. Soc. Chim. France*, [4] **49**, 567 (1931).
  4. H. Pines and V. Ipatieff, *J. Am. Chem. Soc.*, **61**, 2728 (1939).
  5. S. Winstein and N. J. Holness, *J. Am. Chem. Soc.*, **77**, 5562 (1955).
  6. E. L. Eliel and R. S. Ro, *J. Am. Chem. Soc.*, **79**, 5992 (1957).
  7. W. Hüchel and J. Kurz, *Ann.*, **645**, 194 (1961).
  8. E. L. Eliel, *Record Chem. Progr. (Kresge-Hooker Sci. Lib.)*, **22**, 129 (1961); M. N. Rerick, in R. L. Augustine, "Reduction," Marcel Dekker, Inc., New York, 1968, pp. 32–34.
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**Appendix**  
**Chemical Abstracts Nomenclature (Collective Index Number);**  
**(Registry Number)**

petroleum ether

sulfuric acid (7664-93-9)

acetic acid (64-19-7)

ether (60-29-7)

platinum oxide

aluminum chloride (3495-54-3)

magnesium sulfate (7487-88-9)

lithium aluminum hydride (16853-85-3)

t-butanol (75-65-0)

4-t-butylcyclohexanone (98-53-3)

trans-4-t-BUTYLCYCLOHEXANOL,  
Cyclohexanol, 4-t-butyl, trans- (21862-63-5)

4-t-Butylcyclohexanol (98-52-2)

p-t-butylphenol (98-54-4)