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.

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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.

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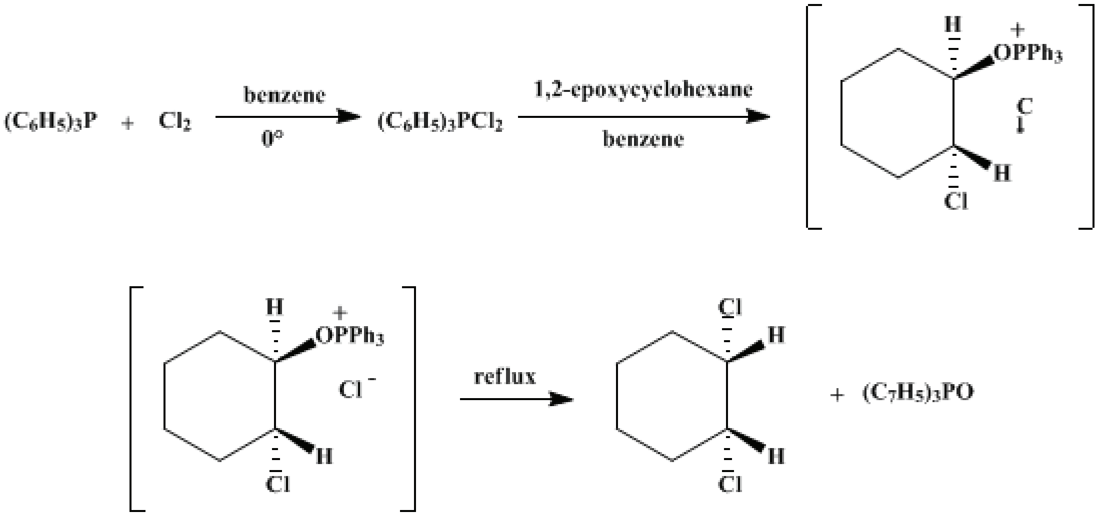
cis-DICHLOROALKANES FROM EPOXIDES: *cis*-1,2-DICHLOROCYCLOHEXANE

[Cyclohexane, 1,2-dichloro-, *cis*-]



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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 hood should be employed for the chlorination.

A 1-l., three-necked flask is charged with 95 g. (0.36 mole) of triphenylphosphine (Note 1) and 500 ml. of anhydrous benzene, and fitted with a gas-inlet (Note 2), a mechanical stirrer, and a condenser with attached drying tube. The flask is cooled in an ice bath, stirring is begun, and chlorine is introduced through the gas-inlet. Dichlorotriphenylphosphorane separates as a white solid or as a milky oil; the flow of chlorine is discontinued when the mixture develops a strong lemon-yellow color (Note 3). The gas inlet is quickly replaced by an addition funnel, and a solution of 10 g. of triphenylphosphine in 60 ml. of benzene is added dropwise fairly rapidly (Note 4). A solution of 24.5 g. (0.250 mole) of 1,2-epoxycyclohexane (Note 5) in 50 ml. of benzene is then added dropwise over *ca.* 20 minutes. The ice bath is replaced by a heating mantle, and the mixture, which consists of two liquid phases, is stirred and refluxed for 4 hours. It is then cooled, and excess dichlorotriphenylphosphorane is destroyed by the slow addition of 10 ml. of methanol (Note 6). The mixture is concentrated on a rotary evaporator at *ca.* 100 mm., and the residue, which may be a white solid or a viscous oil, is triturated with 300 ml. of petroleum ether (30–60°). The solid triphenylphosphine oxide that separates is collected by suction filtration. The cake is thoroughly broken up with a spatula and washed with three 100-ml. portions of petroleum ether. The combined filtrates, from which a little more triphenylphosphine oxide precipitates, are refiltered, then washed with 250-ml. portions of aqueous 5% sodium bisulfite (Note 7) and with water. The organic phase is dried over magnesium sulfate, filtered, concentrated on a rotary evaporator at *ca.* 100 mm., and distilled through a 20-cm. Vigreux column. There is very little forerun before 27–28 g. (71–73%) of *cis*-1,2-dichlorocyclohexane is collected at 105–110° (33 mm.), n_D^{25} 1.4977 (Note 8).

2. Notes

1. Triphenylphosphine was purchased from Aldrich Chemical Company, Inc. Use of a considerable excess of triphenylphosphine ensures complete reaction and obviates the need for rigorously dried glassware and reagents. Hydrochloric acid, generated by the reaction of dichlorotriphenylphosphorane and water, can react with the epoxide to produce a *trans*-chlorohydrin, which is, however, converted to a *cis*-dichloride by dichlorotriphenylphosphorane under the conditions of the reaction.
2. A glass tube of 7-mm. diameter is recommended. If chlorine is introduced through a fritted-glass tube, the dichlorotriphenylphosphorane collects on the frit as a sticky gum.
3. A sharp endpoint is not observed. A simple test for complete chlorination is as follows: the flow of chlorine and the stirrer are stopped, and the mixture is allowed to settle. Chlorine is then admitted without stirring. If unreacted triphenylphosphine is present, a visible clouding (formation of dichlorotriphenylphosphorane) will occur at the gas–liquid interface.
4. Although a slight excess of chlorine does not appear to be deleterious, a substantial excess is avoided by adding the last portion of triphenylphosphine at this point.
5. Commercial 1,2-epoxycyclohexane, supplied by Columbia Organic Chemicals Company, Inc., was used.
6. The reaction mixture may be allowed to stand overnight before addition of methanol.
7. The distilled *cis*-dichlorocyclohexane tends to become colored if the solution is not washed with a reducing agent.
8. The checkers, using a 10-cm. Vigreux column, found that it was necessary to take a wider boiling range fraction (105–115°, 33 mm.) to obtain similar yields. The product is virtually free of *trans*-1,2-dichlorocyclohexane (the isomeric 1,2-dichlorocyclohexanes are readily separated by GC on Carbowax 20M or on diethylene glycol succinate columns).

3. Discussion

This procedure is general for the conversion of epoxides to dichlorides with inversion of configuration at each of the two carbons and, in effect, provides a method for the *cis*-addition of chlorine to a double bond.[3] *cis*-1,2-Dichlorocyclohexane has also been prepared from 1,2-epoxycyclohexane and sulfuryl chloride,[4] but the stereospecificity of the reaction appears to be extremely sensitive to reaction conditions, and the yield is lower than that obtained by the method described here. Other methods give *cis*-1,2-dichlorocyclohexane contaminated with considerable amounts of the *trans*-isomer. This method has been used to convert *cis*- and *trans*-4,5-epoxyoctanes to *meso*- and *d,l*-4,5-dichloroöctanes, respectively, and *trans*-7,8-epoxyoctadecane to *threo*-7,8-dichloroöctadecane. These conversions were carried out on smaller amounts of material, and the products were purified by column chromatography on silica gel. Yields were 51–63%.

Halogenations with dihalotriphenylphosphoranes have been reviewed briefly by Fieser and Fieser.[5] Dibromotriphenylphosphorane appears to have been studied somewhat more than the dichloro compound, but both reagents effectively convert alcohols to alkyl halides, carboxylic acids and esters to acid halides, etc. The reaction of 1,2-epoxycyclohexane with dibromotriphenylphosphorane under conditions similar to those described here gives a mixture of *cis*- and *trans*-1,2-dibromocyclohexanes. A reagent prepared from triphenylphosphine and carbon tetrachloride has been used for similar transformations.[6]

References and Notes

1. Agricultural Research, Northeastern Region, Pesticide Degradation Laboratory, Agricultural Environmental Quality Institute, Beltsville Agricultural Research Center, USDA, Beltsville, Maryland 20705. Mention of a proprietary product or company does not imply endorsement by the United States Department of Agriculture (USDA).
2. Present address: Agricultural Research, Southern Region, Insect Attractants, Behavior and Basic Biology Research Laboratory, United States Department of Agriculture, 1700 SW 23rd Drive, P.O. Box 14565, Gainesville, Florida 32604.
3. P. E. Sonnet and J. E. Oliver, *J. Org. Chem.*, **41**, 3279 (1976).
4. J. R. Campbell, J. K. N. Jones, and S. Wolfe, *Can. J. Chem.*, **44**, 2339 (1966).
5. L. F. Fieser and M. Fieser, "Reagents for Organic Synthesis," Vol. I, Wiley, New York, 1968, p.

1247.
6. J. G. Calzada and J. Hooz, *Org. Synth.*, **Coll. Vol. 6**, 634 (1988).

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

petroleum ether

threo-7,8-dichlorooctadecane

hydrochloric acid (7647-01-0)

Benzene (71-43-2)

methanol (67-56-1)

carbon tetrachloride (56-23-5)

sodium bisulfite (7631-90-5)

sulfuryl chloride (7791-25-5)

chlorine (7782-50-5)

1,2-epoxycyclohexane (286-20-4)

magnesium sulfate (7487-88-9)

triphenylphosphine (603-35-0)

triphenylphosphine oxide (791-28-6)

Dichlorotriphenylphosphorane (2526-64-9)

Dibromotriphenylphosphorane (1034-39-5)

cis-1,2-Dichlorocyclohexane,
Cyclohexane, 1,2-dichloro-, cis- (10498-35-8)

cis-dichlorocyclohexane (2108-92-1)

trans-1,2-dichlorocyclohexane (822-86-6)

trans-7,8-epoxyoctadecane