Reaction of Diborane in Tetrahydrofuran with Styrene Oxide and Related Epoxides in the Presence of Boron Trifluoride. A Convenient Anti-Markovnikov Reductive Opening of Such Epoxides

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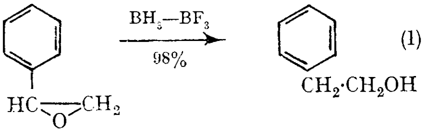
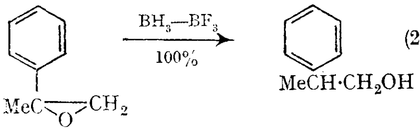
IN contrast to the complex hydrides, which are essentially nucleophilic reagents, diborane is a reducing agent with strong electrophilic or "acidic" properties.[1] In the course of a systematic examination of organic reductions we have observed that styrene oxide and similar aryl epoxides undergo a fast, simple anti-Markovnikov reductive opening at 0° when reduced by diborane in the presence of boron trifluoride.



(1)



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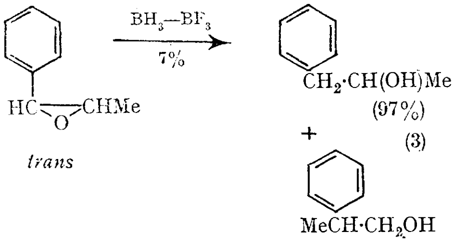

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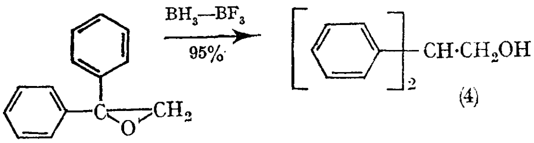
Typical reductions are shown in [(1)—(5)].



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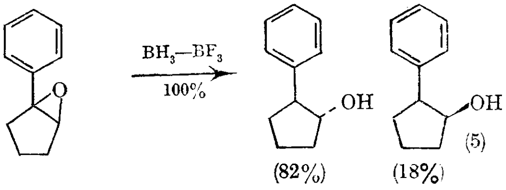

(5)

The presence of boron trifluoride is essential. Diborane alone (in tetrahydrofuran) reacts fairly fast with styrene oxide at 0°: the styrene oxide disappears and 2·13 equivalents of "hydride" per mole of epoxide are used in 6 hr. However, g.l.c. analysis of the hydrolyzed reaction mixture reveals the presence of only 28% of the expected 2-phenylethanol.† Similarly, 1-phenylcyclopentene oxide reveals an uptake of 2·37 equivalents of "hydride" in 3 hr. at 0° without giving any of the expected reduction products. Since the reduction of epoxide to the corresponding alcohol requires one equivalent of "hydride" per mole of epoxide, this high "hydride" consumption† strongly suggests involvement of the aromatic ring in the reaction. This conclusion is supported by the ^{1}H n.m.r. examination of the reaction mixture where a major decrease in the aromatic proton resonance is evident.

These difficulties are circumvented by the presence of boron trifluoride.‡ Thus, in the presence of this Lewis acid, the uptake of hydride rapidly rises to 1·0 in less than 0·5 hr. and then remains constant. G.l.c. examination of the hydrolyzed reaction mixture reveals the presence of a 98% yield of 2-phenylethanol (Reaction 1). Only traces of the corresponding secondary alcohol were indicated.

The presence of boron trifluoride likewise converted the complex reaction previously observed for 1-phenylcyclopentene oxide to a quantitative anti-Markovnikov reductive opening (Reaction 2). The product contains (82%) *trans*- and (18%) *cis*-2-phenylcyclopentanol. Reduction of 2-phenylcyclopentanone by borane–boron trifluoride under the same conditions gave (82·4%) *trans*- and (17·6%) *cis*-2-phenylcyclopentanol. Consequently, it is probable that the reaction involves a rearrangement of the epoxide under the influence of the boron trifluoride, followed by a rapid reduction of the carbonyl derivative formed during the isomerization.

The following procedure is representative. To a reaction flask, oven-dried and cooled under nitrogen, was added tetrahydrofuran (THF) (23 ml.), 1·74M-borane (5·8 ml., 10 mmole) solution in THF, and boron trifluoride etherate (1·26 ml., 10 mmole). The flask and contents were cooled to 0°, and styrene oxide (10 mmole) in THF (10 ml.) at 0° was added. The hydride uptake was 1·00 in 0·5 hr. and showed no further change with time. The reaction mixture was hydrolyzed with water to destroy the excess of hydride and to hydrolyze the borate esters. The aqueous phase was saturated with potassium carbonate. G.l.c. analysis of the clear supernatant THF solution revealed 2-phenylethanol (98%) and only a trace of 1-phenylethanol. Although we have generally used equimolar amounts of boron trifluoride and borane, we have observed that as little as 10 mole per cent. of boron trifluoride is adequate to achieve this reduction.

The anti-Markovnikov reductive opening of epoxides has previously been achieved with "mixed hydride", $LiAlH_4 + 4AlCl_3$.[2] However, the procedure recommended requires 4 mole of aluminium chloride per mole of lithium aluminium hydride and two hours of heating under reflux in ethyl ether. This reaction gave a 71% yield of 2-phenylethanol (containing 2—5% of the isomeric alcohol) from styrene oxide which contrasts with the essentially quantitative yield of isomerically pure 2-phenylethanol realized in 0·5 hr. at 0°.

Attention should be called to an additional major advantage of the present procedure. Almost no known substituents will resist the action of $LiAlH_4,4AlCl_3$ under the recommended reaction conditions, whereas diborane is a much milder reducing agent[1] and many functional groups will tolerate exposure to this reagent under the recommended reaction conditions.[1] This makes possible the anti-Markovnikov reductive opening of aryl epoxides containing a large variety of substituents in the molecule.

The diborane–boron trifluoride anti-Markovnikov reductive cleavage of aryl substituted ethylene oxides appears to be quite general although it fails for epoxides which do not contain aryl groups on the epoxide structure. Fortunately, many of these aliphatic or alicyclic epoxides undergo anti-Markovnikov ring opening with diborane–borohydride.[3]

These results make it clear that the reductive possibilities with diborane can be greatly modified by using it in the presence of a nucleophilic component, such as lithium or sodium borohydride, or an electrophilic component, such as boron trifluoride.

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† It has been reported that the tetrahydrofuran solvent also participates in the uncatalyzed reaction of diborane with styrene oxide, and that (24%) 2-phenyl-2-butoxyethanol was also formed (D. J. Pasto, C. C. Cumbo, and J. Hickman, *J. Amer. Chem. Soc.*, 1966, **88**, 2201). However, it should be noted that both 2-phenylethanol and this butoxy-derivative require only 1 equivalent of "hydride" per mole of epoxide.

‡ Boron trifluoride does not, like other boron halides (*e.g.* boron trichloride), react with diborane in the presence of ether to form chloroborane etherates (H. C. Brown and P. A. Tierney, *J. Amer. Chem. Soc.*, 1958, **80**, 1552; *J. Inorg. Nuclear Chem.*, 1959, **9**, 51).

[1] H. C. Brown and B. C. Subba Rao, *J. Amer. Chem. Soc.*, 1960, **82**, 681; H. C. Brown and P. Heim, to be published.

[2] E. L. Eliel and D. W. Delmonte, *J. Amer. Chem. Soc.*, 1958, **80**, 1744; E. L. Eliel, *Rec. Chem. Progr.*, 1961, **22**, 129.

[3] H. C. Brown and N. M. Yoon, *J. Amer. Chem. Soc.*, 1968, **90**, 2686.