Communications TO THE EDITOR

A Convenient Modification of the Brown Hydration Reaction. Hydration of Unsaturated Steroids

Sir:

Recently H. C. Brown and co-workers have described an excellent method for the anti-Markownikoff hydration of double bonds, through conversion to the trialkylborane and subsequent oxidation. The method used for carrying out the hydroboration step involved passing diborane (generated from sodium borohydride and boron trifluoride etherate in diglyme) into a solution of the olefin in an ether[1] or alternatively allowing the olefin to react *in situ* with sodium borohydride and aluminum chloride[2] or boron trifluoride[3] in diglyme solution.

Diglyme (the dimethyl ether of diethylene glycol) not being available to us, we studied the *in situ* reaction of olefins with lithium aluminum hydride and boron trifluoride in ether solution, since the latter hydride (unlike sodium borohydride) is ether soluble and this combination is known also to generate diborane.[4] This modification when applied to simple olefins was found to give as excellent results as the original procedures. Thus 1-octene and cyclohexene by this method after oxidation with alkaline hydrogen peroxide furnished 1-octanol and cyclohexanol, respectively, in over 80% yield. In this way the necessity of generating diborane separately, or using the high boiling diglyme [b.p. 160–162° (740 mm.)] *in situ* is avoided.

We have successfully applied the Brown hydration method to steroids. By use of our modification, Δ^4-cholestene gave 60% of cholestan-4α-ol [m.p. 187–188°, $[\alpha]_D$ +3° (all rotations in chloroform)] and Δ^5-cholestene gave 75% of cholestan-6α-ol (m.p. 128–129°, $[\alpha]_D$ +35°). No isomeric alcohols were detected (the remainder was mainly unchanged starting material in each case) and these results confirm the conclusion that the hydration proceeds by *cis* addition from the less hindered side of the double bond.[1b] The yields of the cholestanols were 30% and 40%, respectively, when the hydroboration was carried out by passing diborane into the sterols dissolved in ether.[5]

Cholesterol by either method after acetylation furnished 70% of cholestane-3β,6α-diol diacetate (m.p. 104–105°, $[\alpha]_D$ +41°) and 15–20% of coprostane-3β,6β-diol diacetate (m.p. 136–138°, $[\alpha]_D$ +16°).[6] Cholesterol 2-(2′-tetrahydropyranyl) ether by our modification after acid treatment and acetylation gave these diacetates in 45% and 35% yield, respectively. It is of interest to note that the direction of attack of the Δ^5-double bond appears to depend on the bulk of the substituent at C-3.

Other unsaturated steroids have also been hydrated by the lithium aluminum hydride–boron trifluoride method, as will be reported in the full paper. In addition, the method has been found to proceed well and stereospecifically in the decalin series, *e.g.* 7,7,10-trimethyl-$\Delta^{1(9)}$-octalin gave 7,7,10-trimethyl-*cis*-decal-1β-ol (m.p. 82–83°) in 80% yield.

The following hydration of cholesterol is typical. A solution of 0.6 g. of lithium aluminum hydride in 30 cc. of dry ether was added dropwise to a solution containing 2 g. of cholesterol and 3.0 g. of boron trifluoride etherate in 75 cc. of ether under nitrogen. After 1 hr. at room temperature, the mixture was treated with a saturated sodium sulfate solution and solid sodium sulfate, and was filtered and evaporated. The residue in tetra hydrofuran was then oxidized with 30% aqueous hydrogen peroxide and alcoholic sodium hydroxide,[1,2] and the product was isolated with ether, acetylated and chromatographed on alumina.

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(1) H. C. Brown and B. C. Subba Rao, *J. Org. Chem.*, **22**, 1136, 1137 (1957); (b) H. C. Brown and G. Zweifel, *J. Am Chem. Soc.*, **81**, 247 (1959); (c) R. Dulou and Y. Chrétien-Bessière, *Compt. rend.*, **248**, 416 (1959)

(2) H. C. Brown and B. C. Subba Rao, *J. Am. Chem. Soc.*, **78**, 5694 (1956); R. Pappo, *J. Am. Chem. Soc.*, **81**, 1010 (1959).

(3) H. C. Brown and G. Zweifel, abstracts of papers, 135th Meeting of the American Chemical Society, Boston, Mass., April 1959, p. 39-O.

(4) I. Shapiro, H. G. Weiss, M. Schmich, S. Skolnik, and G. B. L. Smith, *J. Am. Chem. Soc.*, **74**, 901 (1952).

(5) The rest of the material was again unchanged starting material in each case despite a large excess of diborane being used. The yield could therefore probably be improved by use of an even larger excess.

(6) These results are in accord with those reported independently by W. J. Wechter [*Chem. & Ind.* (*London*), 294 (1959)].

(7) N. R. C. Postdoctoral Overseas Fellow, 1957–58.