

## Enol Acetate Hydroboration

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The mechanism of enol acetate hydroboration has been studied by examination of the hydroboration-protonolysis of cyclohex-1-enyl acetate. It has been shown that in this case the initial hydroboration proceeds not by exclusive  $\beta$ -addition of the boron to the enol acetate double bond but by both  $\alpha$ - and  $\beta$ -addition modes. The mechanism has been further investigated by using perdeuteriodiborane.

THE hydroboration of alkenes has proved a valuable method for accomplishing hydration, reduction, and related processes. The orientation of addition of the boron atom (either  $\alpha$  or  $\beta$  to a double bond substituent) is likely to be affected by both steric and electronic influences of the substituent.<sup>1</sup> Predominant addition

of the boron at the  $\beta$ -position is reported by Butler and Soloway<sup>2</sup> in the hydroboration of *N*-vinylurea and by Lewis and Pearce<sup>3</sup> when diborane in tetrahydrofuran is treated with *N*-cyclohex-1-enylpiperidine. Hydroboration of enol ethers also usually results in predominant

<sup>2</sup> D. N. Butler and A. H. Soloway, *J. Amer. Chem. Soc.*, 1966, **88**, 484.

<sup>3</sup> J. W. Lewis and A. A. Pearce, *Tetrahedron Letters*, 1964, 1029.

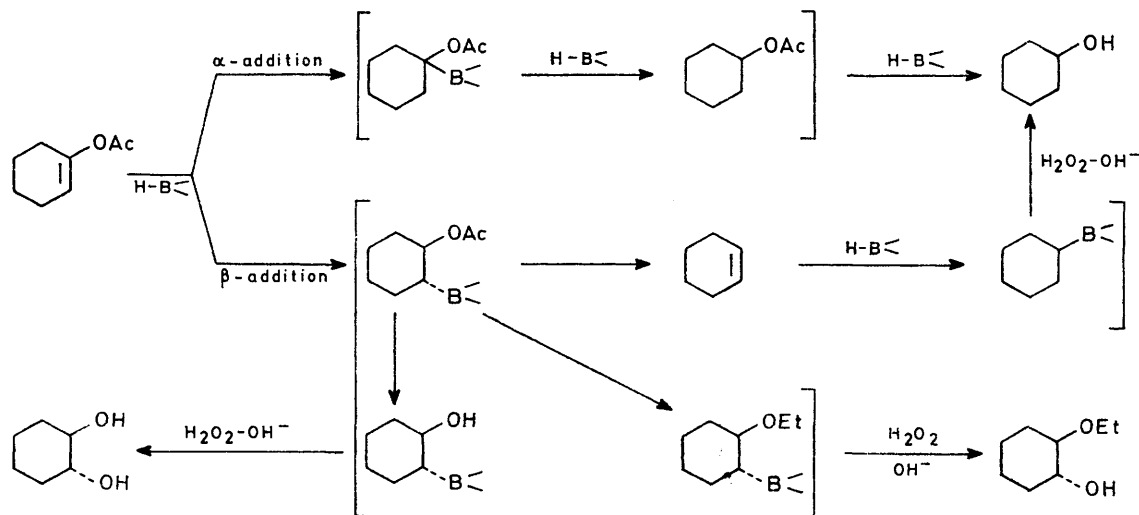
<sup>1</sup> H. C. Brown, 'Hydroboration,' Benjamin, New York, 1962, p. 121.

$\beta$ -addition,<sup>4,5</sup> 1-ethoxycyclohexene, for example, giving *trans*-2-ethoxycyclohexanol in 77% yield.<sup>4a</sup>

In the hydroboration of enol acetates the reaction is complicated by the tendency of the intermediate organoborane to undergo elimination. Brown and Heim<sup>6</sup> observed that hydroboration of isopropenyl acetate showed uptake of 4 equiv. of hydride per mol of compound. The products after oxidation were propan-1- and -2-ols in the ratio corresponding to the products of

cyclohexanol (38%) formed in the cyclohexenyl acetate reaction reflected the proportion of  $\alpha$ -addition but pointed out<sup>5</sup> that, as in analogous cases, it was not possible to distinguish unequivocally between the two possible mechanisms to account for the alcohol fraction.

The two mechanisms differ in that the alcohol can be formed *via* the  $\alpha$ -adduct without involving the alkaline peroxide reagent. We have therefore sought to distinguish between the mechanisms by concluding the



SCHEME 1

hydroboration of propene. This suggested that the reaction involved hydroboration at the terminal  $\beta$ -position ( $1H^-$ ), elimination of the acetoxyboron system, rehydroboration of the propene ( $1H^-$ ), and reduction of the acetoxyboron system to the alcohol stage ( $2H^-$ ). Bigley and Payling<sup>7</sup> showed that enol acetates also react with bis-(1,2-dimethylpropyl)borane by boron addition  $\beta$  to the acetoxy-group, followed by elimination and rehydroboration.

Brown and Sharp<sup>5</sup> reported that in the hydroboration of enol acetates the directive influence of the acetoxy-group appeared to be small. Whereas isobutenyl acetate gave 100%  $\alpha$ -addition,  $\geq 30\%$   $\alpha$ -addition was suggested for 1-acetoxybutene. Hydroboration was usually effected at 0 °C over 30–60 min. In the hydroboration of cyclohex-1-enyl acetate,<sup>5</sup> the production of *trans*-cyclohexane-1,2-diol (57%) and *trans*-2-ethoxycyclohexanol (3%) indicated that at least 60%  $\beta$ -addition occurred (Scheme 1). Hassner and Braun<sup>8</sup> had earlier obtained comparable results using either diborane or bis-(1,2-dimethylpropyl)borane. *trans*-Diols have also been obtained by the hydroboration-oxidation of steroidal enol acetates.<sup>9</sup>

Brown and Sharp<sup>5</sup> suggested, however, that the

<sup>4</sup> (a) D. J. Pasto and C. C. Cumbo, *J. Amer. Chem. Soc.*, 1964, **86**, 4343; (b) H. C. Brown and R. M. Gallivan, *ibid.*, 1968, **90**, 2906.

<sup>5</sup> H. C. Brown and R. L. Sharp, *J. Amer. Chem. Soc.*, 1968, **90**, 2915.

<sup>6</sup> Results cited in ref. 5.

<sup>7</sup> D. B. Bigley and D. W. Payling, *J. Chem. Soc.*, 1965, 3974.

hydroboration with a protonolysis step using propionic acid, in place of the oxidative procedure. Under these conditions the  $\beta$ -addition mechanism would give cyclohexene instead of cyclohexanol, whereas the latter would be the product only of the  $\alpha$ -addition route. The *trans*-cyclohexane-1,2-diol and *trans*-2-ethoxycyclohexanol formed in the oxidative procedure would correspond to cyclohexene formed in the protonolysis.

Hydroboration of cyclohexenyl acetate was carried out at 7 °C in tetrahydrofuran and the mixture was then maintained at room temperature for 48 h. After treatment with boiling propionic acid and work-up, g.l.c. of the product mixture revealed the presence of cyclohexanol (67%) and cyclohexene (33%). This therefore substantiates the proposal of Brown and Sharp<sup>5</sup> that hydroboration by  $\alpha$ -addition accounts for the cyclohexanol formed. The higher percentage found by us may be compared with the findings of Hassner *et al.*,<sup>10</sup> who observed that in the hydroboration-oxidation process the proportion of cyclohexanol was raised with increasing temperature and increasing amount of diborane. The failure of the cyclohexene to undergo rehydroboration, as indicated by the absence of cyclohexane, may be due to a temperature effect. Alternative

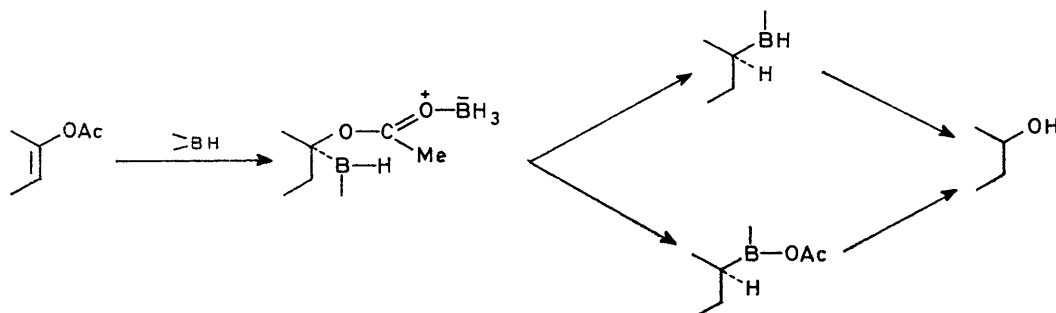
<sup>8</sup> A. Hassner and B. H. Braun, *Univ. Colorado Studies, Ser. Chem. Pharm.*, 1962, **4**, 48.

<sup>9</sup> F. S. Alvarez and M. Arreguin, *Chem. and Ind.*, 1960, 720; L. Caglioti, G. Cainelli, G. Maina, and A. Selva, *Gazzetta*, 1962, **92**, 309.

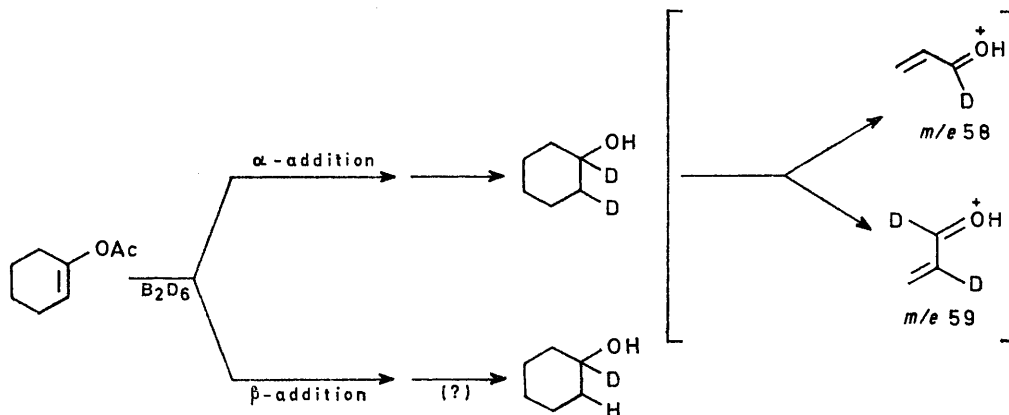
<sup>10</sup> A. Hassner, R. E. Barnett, P. Catsoulacos, and S. H. Wilen, *J. Amer. Chem. Soc.*, 1969, **91**, 2632.

routes to monoalcohols which involve nucleophilic displacement of the acetate group (Scheme 2)<sup>10,11</sup> in the hydroboration-oxidation process would not apply in our case with the protonolysis work-up. The likelihood of obtaining cyclohexanol as a result of reductive removal of boron from the  $\beta$ -adduct was thought unlikely in view of the absence of cyclohexyl ethyl ether in Brown's work.<sup>5</sup>

There is a possibility that if the elimination step in the  $\beta$ -addition sequence (Scheme 2) is not rapid, this could permit an alternative route to cyclohexanol involving direct protonolysis of the organoboron intermediate in



SCHEME 2



SCHEME 3

the acid treatment step. We repeated the hydroboration-protonolysis of cyclohexenyl acetate but with perdeuteriodiborane. Cyclohexanol formed by the alternative process would contain only one C-D bond, whereas the  $\alpha$ -addition route would provide cyclohexanol containing two C-D bonds (at C-1 and C-2; Scheme 3). The cyclohexanol isolated showed a parent ion at  $m/e$  102, a base peak at  $m/e$  59, and a strong peak at  $m/e$  58, consistent with the presence of 1,2-dideuterio-cyclohexanol, the latter two ions arising from the two possible  $\alpha$ -cleavages (*i.e.* of the 1,2- or the 1,6-bond) in the unsymmetrically substituted ring.<sup>12</sup> Thus the  $\alpha$ -addition mechanism is further supported.

<sup>11</sup> A. Suzuki, K. Ohmori, H. Takenada, and M. Itoh, *Tetrahedron Letters*, 1968, 4937; A. Suzuki, K. Ohmori, and M. Itoh, *Tetrahedron*, 1969, **25**, 3707; D. J. Pasto, J. Hickman, and T. C. Cheng, *J. Amer. Chem. Soc.*, 1968, **90**, 6259.

## EXPERIMENTAL

Mass spectra were recorded on an A.E.I. MS12 instrument. Cyclohex-1-enyl acetate, b.p.  $90^\circ$  at 20 mmHg, was prepared according to the method of Leonard and Owens.<sup>13</sup>

*Purification of Solvents and Preparation of Diborane.*—Bis-(2-methoxyethyl) ether was kept over sodium wire overnight, then decanted and distilled from lithium aluminium hydride, and stored over molecular sieves (type 4A). Tetrahydrofuran was treated similarly. Boron trifluoride-diethyl ether complex was distilled from calcium hydride under dry nitrogen and stored over 4A molecular sieves. All apparatus was cleaned and oven-dried before use.

Boron trifluoride-diethyl ether complex (52.0 g, 0.28 mol) was slowly added to bis-(2-methoxyethyl) ether (100 ml). The diethyl ether was removed under reduced pressure at room temperature to give boron trifluoride-bis-(2-methoxyethyl) ether complex, which was used immediately. *m*-Sodium borohydride in bis-(2-methoxyethyl) ether (250 ml, 0.25 mol) was slowly added while the mixture was vigorously stirred at room temperature, and the diborane formed was swept over into tetrahydrofuran (350 ml), cooled to  $0^\circ\text{C}$ , by a slow stream of nitrogen. When all the sodium borohydride had been added the temperature of the mixture was raised to  $80^\circ\text{C}$  to complete the reaction. The exit from the flask containing the tetrahydrofuran was connected through

<sup>12</sup> H. Budzikiewicz, C. Djerassi, and D. H. Williams, 'Mass Spectrometry of Organic Compounds,' Holden-Day, San Francisco, 1967, p. 107.

<sup>13</sup> N. J. Leonard and F. H. Owens, *J. Amer. Chem. Soc.*, 1958, **80**, 6039.

a mercury safety valve to a wash-bottle containing acetone. The molarity of the tetrahydrofuran solution of diborane was determined by measuring the volume of hydrogen evolved on reaction of a sample with dilute hydrochloric acid.

*Hydroboration-Protonolysis of Cyclohex-1-enyl Acetate.*—To cyclohex-1-enyl acetate (3.0 g), cooled to 7 °C, was slowly added a standardised solution of diborane in tetrahydrofuran (0.656M; 100 ml). The mixture was allowed slowly to attain room temperature and left, securely stoppered, for 48 h. Most of the tetrahydrofuran was removed by use of a fractionating column and the remaining liquid was heated under reflux with propionic acid (7.4 g) for 4 h. Water (100 ml) was then added, the cooled mixture was extracted with ether (5 × 30 ml), and the combined extracts were washed with saturated aqueous sodium hydrogen carbonate and water and dried (K<sub>2</sub>CO<sub>3</sub>). Removal of ether (fractionating column) left the mixture of products. G.l.c. on a Pye 104 instrument incorporating a

Honeywell integrator (Carbowax column) revealed the presence of cyclohexanol (67%) and cyclohexene (33%) (relative yields). These were the only products observed other than a small amount (<10%) of unresolved material, b.p. >200°. Less than 10% of cyclohexenyl acetate was left unchanged. The cyclohexanol (b.p. 163—165°) was separated from the product mixture by fractional distillation (*m/e* 100 and 57).

*Deuterioboration-Protonolysis of Cyclohex-1-enyl Acetate.*—Perdeuteriodiborane in tetrahydrofuran was prepared and standardised as described for diborane, but with sodium borodeuteride in place of sodium borohydride. The deuterioboration-protonolysis was effected as before; g.l.c. of the product mixture showed the presence of cyclohexanol (68%) and cyclohexene (32%). The mixture was fractionally distilled; the mass spectrum of the cyclohexanol fraction (b.p. 161—164°) showed *m/e* 102, 59, and 58.

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