

Hydrogenolyses of 3-Hydroxycholest-4-enes by Mixed Hydrides

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Hydrogenolysis of 3 α -hydroxycholest-4-ene by aluminium chloride and lithium aluminium deuteride probably proceeds through the formation of an allyl carbonium ion. In the case of 3 β -hydroxycholest-4-ene, the results seem to indicate that the reaction does not proceed only through an S_N1 mechanism.

WE have previously reported¹ that the reduction of 6 β -methoxy-3 α ,5-cyclo-5 α -steroids by lithium aluminium hydride-aluminium chloride yields 3 α ,5-cyclo-5 α -steroids, and that the reaction occurs *via* an intermediate resonance-stabilised carbonium ion.

Allyl alcohols are reduced by mixed hydrides. A mechanism proposed by some authors² for this reaction involves the formation of an allyl carbonium ion. We have studied the reaction by use of lithium aluminium deuteride-aluminium chloride, and now report results for reduction of 3 α - and 3 β -hydroxycholest-4-ene. The mixture of 3-deuteriocholest-4-enes obtained by treatment with mixed deuteride was analysed in each case by

¹ A. Romeo and M. P. Paradisi, *J. Org. Chem.*, 1972, **37**, 46.

² J. Broome, B. R. Brown, A. Roberts, and A. M. S. White, *J. Chem. Soc.*, 1960, 1406; J. H. Brewster and H. O. Bayer, *J. Org. Chem.*, 1964, **29**, 116; E. L. Eliel, *Rec. Chem. Progr.*, 1961, **22** (3), 129.

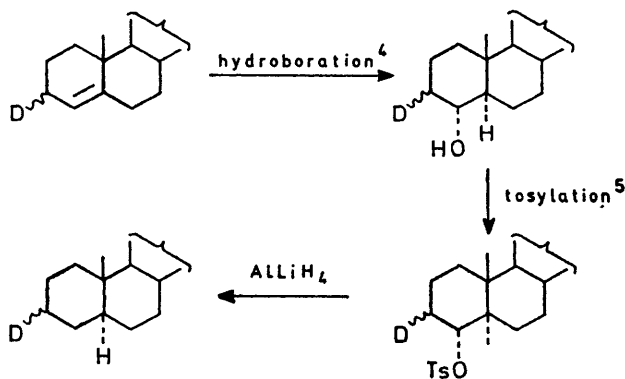
transformation (Scheme) into a mixture of 3-deuterio-5 α -cholestanes, the composition of which was determined by examining the relative intensity of the i.r. spectral peaks in the region 2190–2100 cm⁻¹.^{1,3}

Following reduction with a 1:1 ratio of lithium aluminium deuteride and aluminium chloride, 3 β -hydroxycholest-4-ene eventually gave a 65:35 mixture of 3 β - and 3 α -deuterio-5 α -cholestanes. After the same treatment, 3 α -hydroxycholestene gave a 15:85 mixture of the same products. The analyses were made by comparing i.r. spectra of the reaction mixtures with those of mixtures of known composition (see Figure).

These results indicate that the reduction by mixed deuteride cannot involve an S_N1 mechanism for both 3 α - and 3 β -hydroxycholest-4-ene. Both compounds

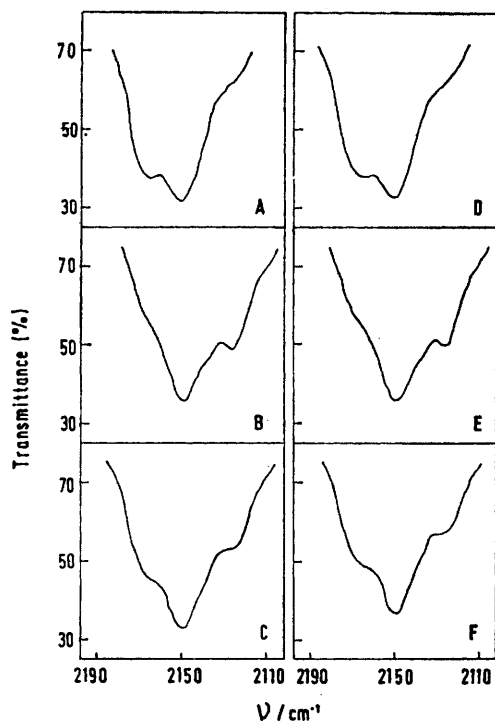
³ E. J. Corey, M. G. Howell, A. Boston, R. L. Young, and R. A. Sneen, *J. Amer. Chem. Soc.*, 1956, **78**, 5036.

would give the same carbonium ion and an identical product distribution would be expected.



SCHEME

It is known⁶ that use of the mixed reagent of structure AlHCl_2 is more liable to produce carbonium ions than a direct reduction. It is also known⁷ that species



C-D Stretching bands of $[3\text{-}^2\text{H}_1]$ cholestanes for 10% CCl_4 solutions at 25° : A, 35% $[3\alpha\text{-}^2\text{H}_1]$ cholestane, 65% $[3\beta\text{-}^2\text{H}_1]$ cholestane; B, 85% 3α , 15% 3β ; C, 65% 3α , 35% 3β ; D, E, F, $[3\text{-}^2\text{H}_1]$ cholestanes obtained (following the Scheme) from $[3\text{-}^2\text{H}_1]$ cholest-4-enes by reaction of: D, 3β -hydroxycholest-4-ene with $\text{LiAlD}_4\text{-AlCl}_3$ (1 : 1); E, 3α -hydroxycholest-4-ene with $\text{LiAlD}_4\text{-AlCl}_3$; F, 3β -hydroxycholest-4-ene with $\text{LiAlD}_4\text{-AlCl}_3$ (1 : 4)

of the structure AlHCl_2 are formed when the $\text{LiAlH}_4\text{-AlCl}_3$ ratio is not more than 1 : 3. To obtain further

⁴ M. Nussim, Y. Mazur, and F. Sondheimer, *J. Org. Chem.*, 1964, **29**, 1120.

⁵ C. W. Shoppee, M. I. Akhtar, and R. E. Lack, *J. Chem. Soc.*, 1964, 877.

information about the mechanism, reductions of the 3-hydroxycholestenes were carried out with an $\text{LiAlD}_4\text{-AlCl}_3$ ratio of 1 : 4. The 3β -hydroxy-compound eventually yielded a 35 : 65 mixture of 3β - and 3α -deuteriocholestanes, whereas the ratio of products from the 3α -hydroxy-compound was the same as produced by the 1 : 1 reagent (15 : 85) (see Figure).

These results seem to indicate that with the 3α -hydroxy-compound (axial OH) the reaction occurs through an $\text{S}_{\text{N}}1$ mechanism, whereas with the 3β -hydroxy-compound it proceeds only partially through a carbonium ion. Thus the reduction of allyl alcohols by aluminium chloride does not always take place through a carbonium ion. Moreover, it appears that aluminium chloride may interact with functional groups usually not reduced by lithium aluminium hydride, by a mechanism other than $\text{S}_{\text{N}}1$.

EXPERIMENTAL

M.p.s were taken with a Culatti capillary apparatus. I.r. spectra were recorded with a Perkin-Elmer 521 spectrophotometer for solutions in carbon tetrachloride. Optical rotations were measured with a Schmidt Haensch polarimeter for 1% solutions in a 1 dm cell. Woelm alumina was used for column chromatography. M.p.s and optical rotations of products agreed with literature data for the non-deuterated compounds.

Mixed Hydride Reductions of 3-Hydroxycholest-4-enes.—The mixed hydride reagents were prepared by slowly adding measured amounts of an ethereal solution of aluminium chloride to stirred solutions of known amounts of lithium aluminium deuteride in dry diethyl ether. The steroid in diethyl ether was then added dropwise to the reagent. After the reaction the mixture was carefully hydrolysed with a small amount of water. The ethereal solution was separated by filtration and the solid residue was washed with ether. The combined ethereal solution was washed with 2N-sulphuric acid and water, dried, and evaporated. The residue was chromatographed on a column of basic alumina (Brockmann I) with light petroleum (b.p. $30\text{--}35^\circ$) as eluant, to yield the 3-deuteriocholest-4-enes after crystallisation from acetone.

Hydroboration and oxidation of the cholestenes⁴ and tosylation of the resulting 4α -hydroxycholestanes⁵ were carried out as described in the literature.

Reduction of 4α -Tosyloxy-5 α -cholestanes.—A solution of the tosylate and lithium aluminium hydride in diethyl ether was refluxed for 24 h. The excess of lithium aluminium hydride was decomposed with water and the ethereal solution was filtered, washed with 2N-sulphuric acid, 2N-sodium hydroxide, and water, dried (Na_2SO_4), and evaporated under vacuum. The residue was chromatographed on basic alumina (Brockmann I) with light petroleum as eluant; crystallisation of the product from aqueous ethanol yielded the 3-deuteriocholestanes.

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⁶ E. C. Ashby and B. Cooke, *J. Amer. Chem. Soc.*, 1968, **90**, 1625.

⁷ E. C. Ashby and J. Prather, *J. Amer. Chem. Soc.*, 1966, **88**, 729.