Reactions of 5α-Hydroxy-steroids: the Mechanism of Backbone Rearrangement in Sulphuric Acid–Acetic Acid–Acetic Anhydride

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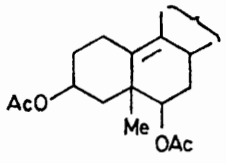
Summary Reaction of 4β-acetoxy-5α-hydroxycholestane (**4**) with D_2SO_4–DOAc–Ac_2O gives the acetoxy-olefins (**5**)—(**7**) with no incorporation of deuterium; these observations exclude the intermediacy of olefin and cyclopropane intermediates in the backbone or partial backbone rearrangement.

THE backbone rearrangement of steroids and triterpenoids with a range of deuteriated acids has generally led to incorporation of deuterium and hence has suggested olefin or cyclopropane intermediates.[1] However, rearrangement of compound (**2**) with DF, followed by treatment with MeOH–KOH has been shown[2] to give compound (**3**) with deuterium incorporation exclusively at C(11). This contrasts with other backbone rearrangements induced by DF and D_2SO_4, in proceeding entirely by a non-stop mechanism, but the influence of the hydroxy-substituent on the five-membered ring is unknown.



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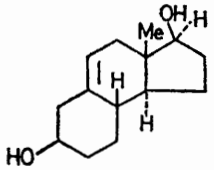

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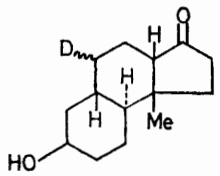

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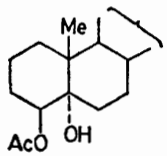

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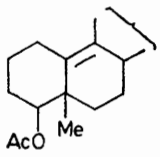

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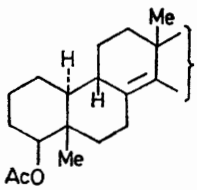

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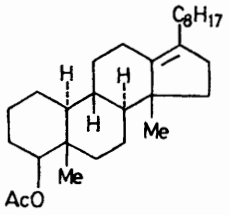

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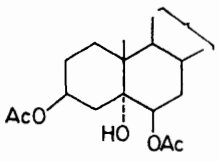

(8)

We now report the study of a steroid system where olefin products of both partial and complete backbone rearrangement can be isolated. Reaction of 4β-acetoxy-5α-hydroxycholestane (**4**) (500 mg) in DOAc–Ac_2O–D_2SO_4 (66 ml; 50 : 16 : 0·005) gives the olefins (**5**)—(**7**), which were isolated by preparative t.l.c. and their identity established by comparison with authentic samples.[3] The deuterium enrichments of the product olefins were determined mass spectrometrically. Within the limits of experimental accuracy (±5%) no deuterium incorporation could be detected in any of the products. Similarly, reaction of 3β,6β-diacetoxy-5α-hydroxycholestane (**8**) with CD_3CO_2D–Ac_2O–D_2SO_4 gives the olefin (**1**) without incorporation of deuterium. These observations contrast with other studies[1] and exclude olefin or cyclopropane intermediates in the backbone and partial backbone

rearrangement of compounds (**4**) and (**8**). Methyl migration, involving either edge- or corner-protonated cyclopropane intermediates and hydride shifts in the systems examined are therefore more rapid than proton loss to cyclopropane or olefin intermediates.

The authors acknowledge grants from the Research Committee of the New Zealand University Grants Committee.

(*Received*, 12*th November*, 1973; *Com.* 1558.)

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[2] J. P. Berthelot and J. Levisalles, *Chem. Comm.*, 1970, 1162.
[3] J. M. Coxon and M. P. Hartshorn, *Tetrahedron Letters*, 1969, 105.