Unexpected Inversion of Configuration at a Quaternary Centre during the Acetolysis of D-Homo-5α-androstan-17aβ-yl Tosylate

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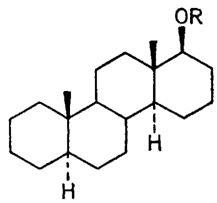
Summary Acetolysis of D-homo-5α-androstan-17aβ-yl tosylate (I) gave the 17aβ-yl acetate (II) accompanied by D-homo-5α,13α-androstan-17aα-yl acetate (III), resulting from inversion of configuration at the quaternary centre adjacent to the reaction site.

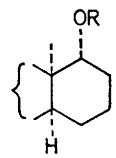
Acetolysis of D-homo-5α-androstan-17aβ-yl tosylate (I) in unbuffered acetic acid gave the 17aβ-yl acetate (II)[1] as the major product; Hirschmann[2] has recorded similar behaviour in a 17α-methyl substituted analogue. Minor products from (I) included a small olefinic fraction, the 17aα-acetoxy-derivative (trace, detected only by g.l.c.), and a new acetoxy-compound to which we assign structure (III), D-homo-5α,13α-androstan-17aα-yl acetate, m.p. 102—103°, needles from acetone; τ (CCl_4) 9·02 (18-Me), 9·26 (19-Me), 8·00 (Ac), and 4·74 ($W_{\frac{1}{2}}$ 10 Hz, C*H*OAc). The proportion of (III) depended upon the reaction temperature, being *ca.* 4% in acetic acid at reflux, and *ca.* 20% from a slow reaction (70 h) at 74° (g.l.c.).

The acetate (III), as well as the derived alcohol (IV) and ketone (V), m.p. 127—129°; ν_{max} 1710 cm^{-1}, differed from the corresponding 17a-, 17-, and 16-substituted D-homo-5α-androstanes.[1] The width of the signal due to the C(17a) proton in the n.m.r. spectrum of the acetate (III) showed the ester group to be equatorial.[3] Hydrolysis of the acetate (KOH–MeOH) was abnormally slow, and all compounds of the new series were less polar (t.l.c., g.l.c.) than the known isomers substituted in ring-D, implying a relatively hindered location for the functional group. The n.m.r. spectrum of the 13α,17a-ketone showed the 18-Me protons to be strongly deshielded (τ 8·81); the 19-Me protons (τ 9·29) however, were slightly *shielded* by ring-D with its magnetically anisotropic carbonyl group,[4] despite the spatial separation. The c.d. curve [$\Delta\epsilon$ +2·6 (297 nm), MeOH] showed the dominant effect of the α-axial C(18) methyl group, which is located in a positive octant.

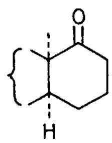
Molecular models of compounds (III)—(V) show that the 13α-formulation is consistent with all their observed properties. The 13α-configuration received further support when the ketone (V) was also obtained by photoisomerisation of D-homo-5α-androstan-17a-one (VI). Brief irradiation of the ketone (VI) in dioxan (Pyrex vessel) caused partial isomerisation at C(13) to give (V), separable by t.l.c.; prolonged irradiation caused further photochemical reactions



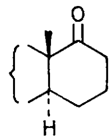
(I ; R = Ts)
(II; R = Ac)



(III; R = Ac)
(IV; R = H)



(V)



(VI)

leading to unidentified non-ketonic products. The photoisomerisation at C(13) is similar to that already known in androstan-17-ones, which occurs through rupture and regeneration of the C(13)–C(17) bond.[5]

The inversion of configuration at C(13) under ionizing conditions implies a mechanism of unusual complexity, which is under investigation.

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