

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

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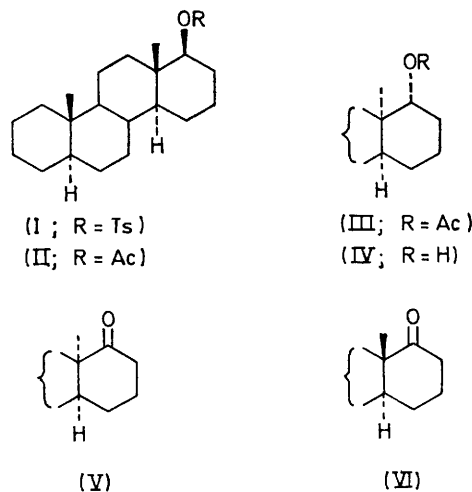
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Summary Acetolysis of D-homo-5 α -androstan-17 $\alpha\beta$ -yl tosylate (I) gave the 17 $\alpha\beta$ -yl acetate (II) accompanied by D-homo-5 α ,13 α -androstan-17 $\alpha\alpha$ -yl acetate (III), resulting from inversion of configuration at the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

ACETOLYSIS of D-homo-5 α -androstan-17 $\alpha\beta$ -yl tosylate (I) in unbuffered acetic acid gave the 17 $\alpha\beta$ -yl acetate (II)¹ as the major product; Hirschmann² has recorded similar behaviour in a 17 α -methyl substituted analogue. Minor products from (I) included a small olefinic fraction, the 17 $\alpha\alpha$ -acetoxy-derivative (trace, detected only by g.l.c.), and a new acetoxy-compound to which we assign structure (III), D-homo-5 α ,13 α -androstan-17 $\alpha\alpha$ -yl acetate, m.p. 102–103°, needles from acetone; τ (CCl₄) 9.02 (18-Me), 9.26 (19-Me), 8.00 (Ac), and 4.74 ($W_{\frac{1}{2}}$ 10 Hz, CHOAc). 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 17 α -, 17-, and 16-substituted D-homo-5 α -androstanes.¹ The width of the signal due to the C(17 α) 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 13 α ,17 α -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 13 α -formulation is consistent with all their observed properties. The 13 α -configuration received further support when the ketone (V) was also obtained by photoisomerisation of D-homo-5 α -androstan-17 α -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



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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³ N. S. Bhacca and D. H. Williams, 'Applications of NMR Spectroscopy in Organic Chemistry,' Holden-Day, San Francisco, 1964, pp. 79–83.

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