The Backbone Rearrangement of Androst-5-ene-3β,17β-diol: a Chemical Proof

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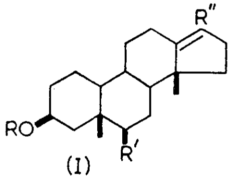
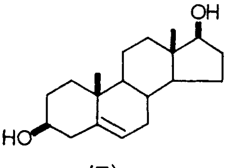
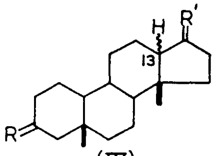
THERE have recently been several reports[1-3] on "backbone" rearrangements of steroidal 5,6α-epoxides and 5α,6β-diacetates, affording for instance (Ia).[3] In the course of a study on the reaction of anhydrous HF with cholesterol,[4,5] we obtained compounds which we believe to be also formed through a similar backbone rearrangement.



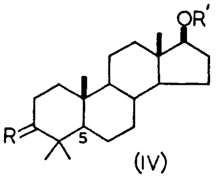
(I)
a: R=Ac; R'=OAc; R''= C_8H_{17}
b: R=H; R'=H; R''=OH



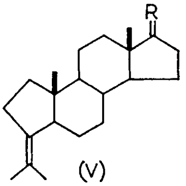
(II)



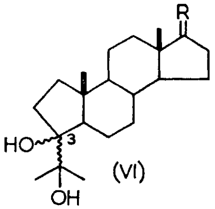
(III)
a: R=β-OH,H; R'=O; 13α-H
b: R=β-OH,H; R'=O; 13β-H
c: R=R'=O: 13β-H



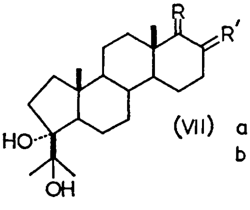
(IV)
a: R=O; R'=H; Δ^5
b: R=O; R'=Bz; Δ^5
c: R=β-OH,H; R'=Bz Δ^5
d: R=β-OH,H; R'= CO·C_6H_{11}; 5α-H



(V)
a: R=β-O·CO·C_6H_{11},H
b: R=β-OH,H
c: R=O



(VI)
a: R=O; 3β-OH
b: R=O; 3α-OH
c: R=CN,OH; 3α-OH
d: R=CH_2·NH_2,OH; 3α-OH



(VII) a: R=O; R'=H,H
b: R=H,H; R'=O

In order to arrive simply at a chemical proof, we turned to androst-5-ene-3β,17β-diol (II).[6] When treated at −60° with anhydrous HF in methylene chloride, (II) affords yields of *ca.* 50% of each of a polar fraction and of a less polar fraction. The less polar fraction, shows on thin-layer chromatography two spots, one of which disappears after the material has been treated with acid or crystallised from acetone. The permanent spot corresponds to a crystalline compound (m.p. 170—172·5°; ν_{CO} = 1735 cm.$^{-1}$). We assign structure (IIIb) to this compound, and (IIIa) to its labile isomer, on the basis of the following evidence: (IIIb) can be oxidised to a diketone (IIIc) (m.p. 144—146°; ν_{CO} 1710 and 1735 cm.$^{-1}$) which we have synthesised from the known compound (IVa).[7]

The sequence (IVa → IVb → IVc → IVd) is straightforward. Ring contraction of (IVd) to (Va) was achieved by using PCl_5 in benzene–toluene.[8] The sequence (Va → Vb → Vc) is again straightforward. Osmium tetroxide hydroxylation of (Vc) afforded two diols (VIa) and (VIb), the more abundant of which (VIb) was used for the sequence (VIb → VIc → VId → VIIa + VIIb) which is well known.[9] The minor D-homo-ketone (VIIb), after cleavage with periodic acid and treatment with trichloroacetic acid, gave a compound (m.p. 142·5—145°, mixed m.p. 141—145°; ν_{CO} 1710 and 1735 cm.$^{-1}$) indistinguishable from (IIIc).

This synthesis provides a chemical proof of the "backbone" rearrangement of (II) to (IIIb). It is hoped that the direct synthesis of (IIIa) will prove feasible. If (IIIa) is actually formed and isolated (otherwise than as a spot on thin-layer chromatography), it must mean that the rarrangement is wholly concerted, and that the enol (Ib) is *not* an intermediate, since it is well known[9,10] that *cis*-fused hydrindanones are more stable than *trans*-fused ones.

Those products which are new compounds have analytical figures and spectrosopic properties in agreement with the postulated structures.

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