Neighbouring Group Participation in 17-Hydroxy-16-hydroxymethyl-steroids

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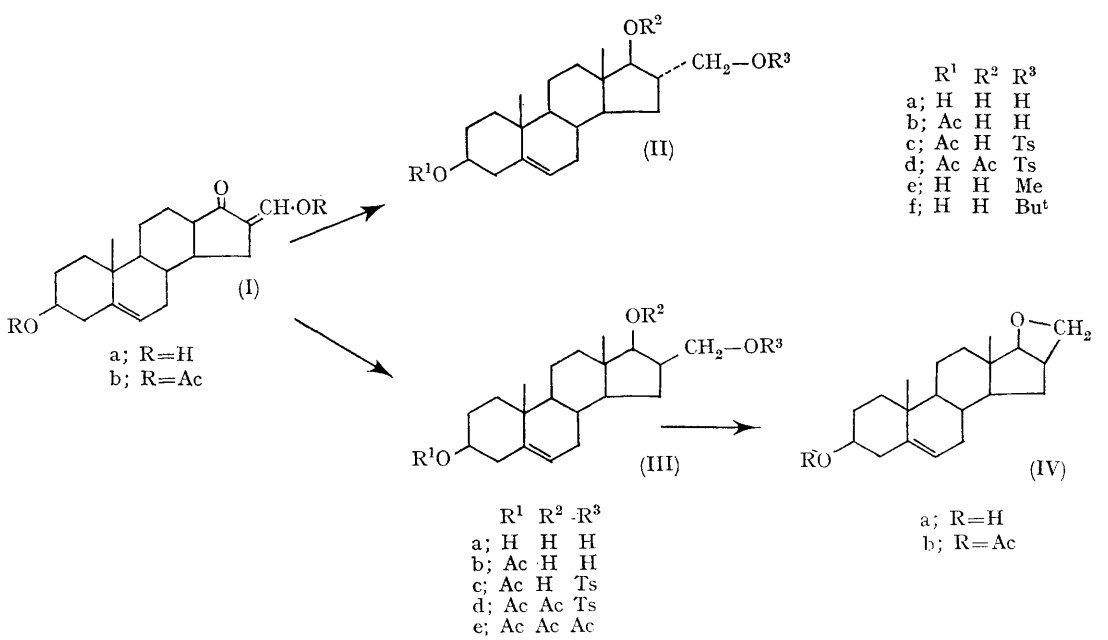
REDUCTION with sodium borohydride of 3β-hydroxy-16-hydroxymethyleneandrost-5-en-17-one (Ia)[1] led to the formation of a mixture of C-16 epimeric 16-hydroxymethylandrost-5-ene-3β,17β-diols (IIa and IIIa).[2] On the basis of the o.r.d. of the products,[3] the 16β-configuration was assigned



to the compound of higher melting point. Under the same conditions 3β,16-diacetoxymethylene-androst-5-en-17-one (Ib) afforded 3β-acetoxy-16α- and 3β-acetoxy-16β-hydroxymethyl-17β-ols (IIb and IIIb).

3β-Acetoxy-16β-*p*-tolyl sulphonyloxymethyl-androst-5-en-17β-ol (IIIc) and the corresponding 3,17-diacetate (IIId) reacted in methanol with sodium borohydride to give an apolar substance (IVa) as the only product. According to i.r. spectral evidence (IVa) was a cyclic oxetan derivative; ν_{max} (KBr) 3600—3300, 1450, and 950 cm.$^{-1}$, $[\alpha]_D$ — 62 ± 2° (*c* 0·5, dioxan), m.p. 185—187°. Compound (IVa) was also obtained as the main product, when (IIIc) or (IIId) was treated with potassium t-butoxide in t-butyl alcohol at room temperature, according to Henbest's method.[4] Acetylation with acetic anhydride in pyridine at room temperature gave the corresponding 3-acetate (IVb), m.p. 119—121°; $[\alpha]_D$ — 72 ± 2° (*c* 0·5, dioxan).

Under similar conditions, 3β-acetoxy-16α-*p*-tolylsulphonyloxymethylandrost-5-en-17β-ol (IIc) and the corresponding 3,17-diacetate (IId) gave 16α-methoxymethylandrost-5-ene-3β,17β-diol (IIe) and the 16α-t-butoxymethyl derivative (IIf).

The 16β,17β-epoxymethylene androst-5-en-3β-ol (Va) can be opened in two ways. In the presence of toluene-*p*-sulphonic acid in ethereal solution it transforms into the triol (IIIc), but proton catalysis in acetic anhydride gives the triacetate (IIIe); in both cases the configuration is retained.

The formation of the four-membered cyclic ether (IVa) from the toluene-*p*-sulphonyl acetate (IIIc and IIId) is the result of O$^-$–4 neighbouring group participation which, in general, can be induced in case of favoured steric orientation of the substituents only.[5] This is the case here with 16β-substituted-17β-hydroxy-derivatives (IIIc and IIId) but no such participation can be found in the 16α-substituted-17β-hydroxy-compounds (IIc and IId).

Among pregnane derivatives the formation of a similar oxetan ring, fused in α-position to ring D, was observed with 16α-chloromethyl-17α-hydroxy-[6] and 16α-*p*-tolylsulphonyloxymethyl-17α-hydroxy-derivatives.[7]

The occurrence and failure, respectively, of the stereospecific ring-closure reaction afford chemical evidence for the steric orientation of the C-16 substituent.

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