Photolysis of the Nitrite Esters of 4,4-Dimethyl-6β-hydroxy-steroids

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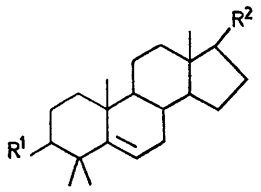
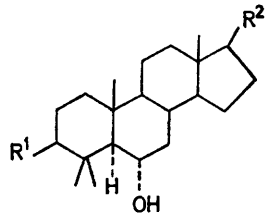
Summary Photolysis of the nitrite esters of three 4,4-dimethyl-6β-hydroxy-steroids leads to exclusive functionalization at C-19; the stereochemical implications are discussed.

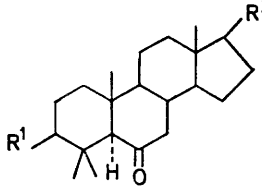
ALTHOUGH considerable work has been carried out on the effects of triaxial interactions in the steroid A-ring[1] almost no study has been devoted to the situation involving one of the groups in the B-ring.† We have investigated the abstraction by 6β-alkoxy radicals of hydrogen atoms from the 4β (31) and 10β (19) methyl groups of 4,4-dimethyl steroids.[2,3]



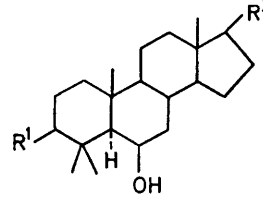
(Ia; R^1 = H, R^2 = C_8H_{17})
(Ib; R^1 = R^2 = H)



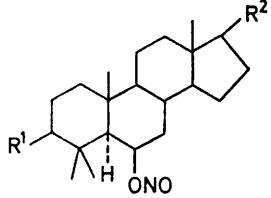
(IIIa; R^1 = H, R^2 = C_8H_{17})



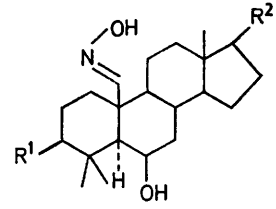
(IIIa; R^1 = H, R^2 = C_8H_{17})
(IIIb; R^1 = R^2 = H)
(IIIc; R^1 = OAc, R^2 = H)



(IVa; R^1 = H, R^2 = C_8H_{17})
(IVb; R^1 = R^2 = H)
(IVc; R^1 = OH, R^2 = H)
(IVd; R^1 = OAc, R^2 = H)



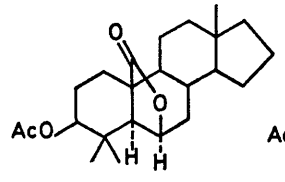
(Va; R^1 = H, R^2 = C_8H_{17})
(Vb; R^1 = R^2 = H)
(Vc; R^1 = OAc, R^2 = H)



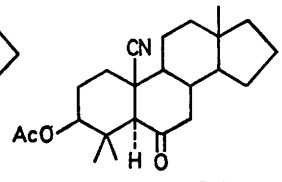
(VIa; R^1 = H, R^2 = C_8H_{17}
(VIb; R^1 = R^2 = H)
(VIc; R^1 = OAc, R^2 = H)

Prolonged hydroboration of (Ia), followed by Jones oxidation of the resulting 5α-H,6α-ol (IIa) gave (IIIa), m.p. 108—109°, ν_{max} 1710 cm^{-1}. Reduction with ($LiAlH_4$; 24 h; 35°) gave in high yield (IVa), m.p. 106—107°; δ 4·30 p.p.m. (6α-H, $W_{\frac{1}{2}}$ 6 Hz). Analogously (Ib) was converted into (IVb), m.p. 125—126°, δ 4·40 p.p.m. (6α-H, $W_{\frac{1}{2}}$ 7 Hz). (IVd), m.p. 134—135°, ν_{max} 3600 and 1740 cm^{-1}, δ 4·40 p.p.m. (3α-H, 6α-H) was obtained by selective acetylation of the 3β,6β-diol (IVc), m.p. 157—159°, prepared by prolonged reduction ($LiAlH_4$) of (IIIc).[4] Alternatively (IVd) was prepared directly from 4,4-dimethyl-androst-5-en-3-one.[4]

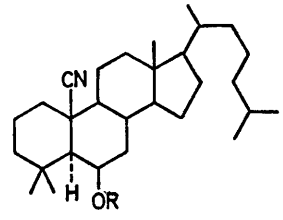
Photolyses of the nitrite esters (Va and b) from alcohols (IVa and b), proceeded similarly to furnish the 19-oximes (VIa and b), m.p. 211—212 and 209—210°, in yields of 44 and 42% respectively, together with small amounts of the 6β-alcohols (IVa and b), and the 6-ketones (IIIa and b). No trace of the 31-oximes could be found.



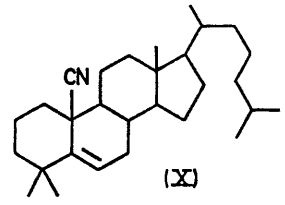
(VII)



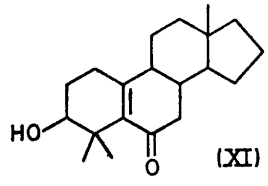
(VIII)



(IXa; R = Ac)
(IXb; R = SO_2Me)



(X)



(XI)

Photolysis of the nitrite ester (Vc) gave a more complex mixture, from which the 6β-alcohol (IVd) and 6-ketone (IIIc) were separated in small amount from the 19-oxime (VIc) (42%), m.p. 207—209°. The most polar chromatography fraction consisted of a mixture of 19-oxime (VIc) and the 6β,19-lactone (VII), m.p. 232—234°, whose identity was confirmed by its preparation from oxime (VIc) by chromic oxide–acetone oxidation.[5] Repeated photolyses revealed no trace of the 31-oxime.

Further transformations were carried out to confirm the 19- as opposed to 31-functionalisation. (VIc) was oxidized (CrO_3–pyridine) to (VIII), m.p. 250—251°. In refluxing dilute methanolic KOH (VIII) was converted into the

† Whalley and his co-workers are engaged in similar complementary studies.

αβ-unsaturated ketone (XI). (VIa) was converted by sodium acetate in refluxing acetic anhydride into (IXa), m.p. 137—138°. Finally, (VIa) was converted *via* the cyano-mesylate (IXb) into (X), m.p. 88—90°.

By analysis of the chemical shift values of the 18- and 31-methyl groups in the cyano-compounds [(VIII): δ 0·82 (Me-18), 1·50 (Me-31); (IXa): 0·79 (Me-18), 1·19 (Me-31); (X) 0·78 (Me-18), 1·32 (Me-31) p.p.m.] and consideration of the spatial shielding characteristics of the CN group,[6,7] the 10β-location of the CN group has been proved conclusively.

The abstraction by a 6β-alkoxy-radical of a hydrogen atom exclusively from the 19-methyl group in compounds (IVa, b, and d) indicates, as in Whalley's studies, that A-ring conformations other than ideal chairs are involved. In the case of the 3β-acetoxy steroid (IVd) a flattened chair is indicated, since a boat or twist conformation would be ruled out by 3β-acetoxy–19-methyl interaction. In the 3-deoxy series either a flattened chair or twist conformation is consistent with the results.

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[2] D. H. R. Barton, J. M. Beaton, L. E. Geller, and M. M. Pechet, *J. Amer. Chem. Soc.*, 1960, **82**, 2640; D. H. R. Barton and J. M. Beaton, *ibid.*, 1960, **82**, 2641.
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