Tetrahedron Letters No.43, pp. 5235-5237, 1966. Pergamon Press Ltd.
Printed in Great Britain.

THE SYNTHESIS OF 3β-HYDROXY-4,4-DIMETHYL-5α-CHOLEST-8-EN-11-ONE FROM LANOSTEROL

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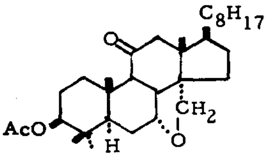
(Received 18 July 1966)

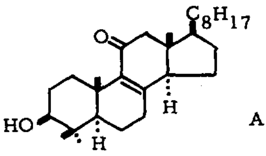
Recent publications have described the functionalization of the 14α-methyl group in derivatives of 5α-lanostane[1,2] and 5α-lanostan-11-one[3,4,5]. We found[5] that cleavage of the ether (I) with pyridinium hydrochloride in acetic anhydride[2,6] for 24 hr. at 140° gave 3β-hydroxy-4,4-dimethyl-5α-cholest-8-en-11-one (II) - together with an almost equal amount of the diacetate (III), which failed to rearrange to the 8-ene-11-ketone (IV) on acidic or basic hydrolysis. We now report a rapid and almost quantitative conversion of the ether (I) to 3β-hydroxy-4,4-dimethyl-5α-cholest-8-en-11-one (II) by cleavage with boron trifluoride.

The ether (I) was treated with boron trifluoride etherate in acetic anhydride[7] for 10 min. at 20° to give as the sole product the enol acetate (V); this by brief alkaline hydrolysis gave the 8-ene-11-ketone (II), probably by conversion of the enol (VI) to the 8-en-11-one (IV), followed by a retroaldol reaction to give formaldehyde and 3β-hydroxy-4,4-dimethyl-5α-cholest-8-en-11-one (II).

The enol acetate (V) possessed $\nu_{\text{max.}}^{CCl_4}$ 1735 ($CO.CH_3$) 1598 ($C = C$), 1220 and 1248 cm.$^{-1}$ (–OAc), $\lambda_{\text{max.}}$ 243 mμ (log ε 4.14) with shoulders at 236 and 251 mμ. The n.m.r. spectrum revealed signals at τ 8,04 (14α-CH_2OAc), τ 7.97 (3β-OAc), τ 7.89 (11-OAc), an AB quartet τ 6.02, 5.74 [J 11 c/s.] (14α–CH_2–), τ 5.46 (3α-H), and τ 4.34 (7-H). 3β-Hydroxy-4,4-dimethyl-5α-cholest-8-en-11-one (II) was identical with the sample previously prepared^5, m.p. 119 - 122° from ether, $\nu_{\text{max.}}^{CCl_4}$ 3620 (OH), 1665 cm.$^{-1}$ (C=O), $\lambda_{\text{max.}}$ 250 mμ (log ε 3.84), n.m.r. spectrum: τ 6.72 (3α-H) and no other low field proton [Found: C, 81.0; H, 11.0; calc. for $C_{29}H_{48}O_2$ C, 81.3; H, 11.3%; M(mass spectrum), 428].



(I)



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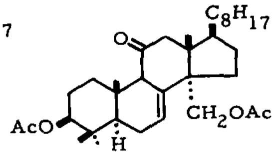

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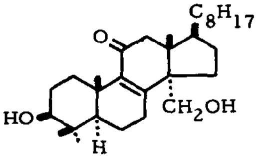

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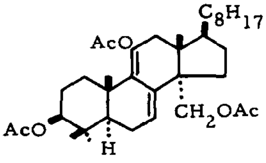

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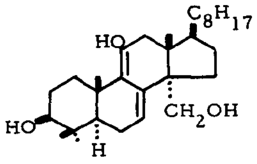

(VI)

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