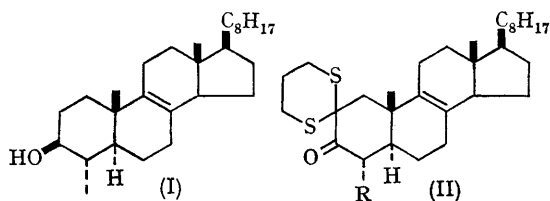


The Synthesis of 4 α -Methylcholest-8(9)-en-3 β -ol

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THE isolation from a transplantable, preputial tumour of a novel, steroidal metabolite which was characterised as 4 α -methylcholest-8(9)-en-3 β -ol (I) has been recorded,¹ together with evidence² that (I) is an intermediate in the biosynthesis of cholesterol from lanosterol. We now report the synthesis of this biologically significant steroid (I).



Thus, hydrogenation of 3 β -acetoxycholesta-8(9),14(15)-diene³ in alcohol with W-4 Raney nickel at atmospheric temperature and pressure during 90 min. gave 3 β -acetoxycholest-8(9)-ene in 45% yield (contrast Barton and Cox,⁴ and Gautschi and Bloch⁵). Oppenauer oxidation of the resultant cholest-8(9)-en-3 β -ol gave cholest-8(9)-en-3-one,⁶ which was converted by way of the 2-hydroxy-methylene derivative into the 2,2'-spiro-dithian (II; R = H), m.p. 160°. Methylation of (II;

R = H) with methyl iodide-potassium t-butoxide-benzene gave (II; R = Me), m.p. 141–143°, which was desulphurised with Raney nickel in ethanol to furnish a mixture of 4 α -methylcholest-8(9)-en-3 β -ol (I) and the corresponding 3 α -ol, m.p. 107–108°. Separation by chromatography gave 4 α -methylcholest-8(9)-en-3 β -ol (I) which was identical (m.p., mixed m.p., mass spectrum, and g.l.c.) with a specimen from the preputial tumour. The acetate of synthetic (I) was identical (m.p., mixed m.p., and mass spectrum) with the acetate of natural (I).

Oxidation of (I) and of its 3 α -epimer, by the Oppenauer procedure gave 4 α -methylcholest-8(9)-en-3-one (70% yield), m.p. 113°, [α] + 44° which was reduced by sodium borohydride-methanol-benzene to (I), unaccompanied by the 3 α -epimer.

Synthetic (I) exhibits an unusual degree of instability similar to that of the natural material.¹

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All new compounds had the requisite spectral and analytical properties.

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