Microbiological 18-Hydroxylation of Steroids

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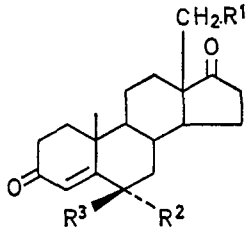
Summary Incubation of androst-4-ene-3,17-dione with *Aspergillus niger*, ATCC 9142, gives 18-hydroxyandrost-4-ene-3,17-dione.

MICROBIOLOGICAL 18-hydroxylation is unusual; it occurs in the case of certain steroids using *Cercospora melonis*[1] and *Corynespora cassiicola*.[2] 18-Hydroxylation has not previously been observed with *Aspergillus niger*, although *A. niger*, ATCC 9142, has been reported[3] to effect hydroxylation of the 21-methyl group of progesterone and derivatives, and 17- and 21-hydroxylation of progesterone have been observed[4] with *A. niger*, S. 100.

We now report that incubation of androst-4-ene-3,17-dione (I), (1 g) with a 2-day growth of *A. niger*, ATCC 9142, in Czapek Dox medium for 4 days gives 18-hydroxyandrost-4-ene-3,17-dione (II), (0·487 g), m.p. 168—170° (from EtOAc–hexane), $[\alpha]_D^{20}$ + 94° (*c* = 0·8 chloroform), and 6β-hydroxyandrost-4-ene-3,17-dione (III), (0·016 g). The known compound (III) was identified by m.p., rotation, and t.l.c. comparison with an authentic sample. Compound (II) has been reported[5] as a product of a chemical transformation and has been characterised as the acetate (IV).



(I) $R^1=R^2=R^3=H$
(II) $R^1=OH$; $R^2=R^3=H$
(III) $R^1=R^2=H$; $R^3=OH$
(IV) $R^1=OAc$; $R^2=R^3=H$

The structure of (II), resulting from the microbiological reaction, was confirmed by conversion into the known acetate (IV), m.p. 127—129°, and by the following spectral data: mass spectrum, *m/e* (%), 302 (100), 287 (9) (*M*—Me), 284 (10) (*M*—H_2O), and 271 (5) (*M*—CH_2OH), M^+ 302·1887; i.r. spectrum included bands at 3400, 1745, 1675, 1620, 1050, and 870 cm^{-1}; n.m.r. (100 MHz) absorptions included τ 4·24 (1H, s, 4-H), 8·77 (s, 19-Me), and 5·99 and 6·14 (AB, 2 non-equivalent 18-CH_2 protons, *J* 9 Hz).

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