16-Hydroxylation of Steroids with the Fungus *Rhizopus nigricans*

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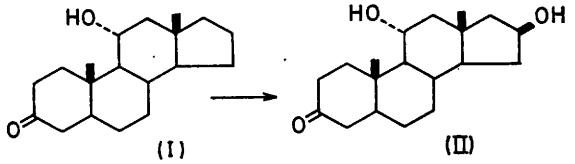
Summary 3-Oxosteroids lacking a 17-substituent are hydroxylated in the 16-position by *Rhizopus nigricans*.

THE FUNGUS *Rhizopus nigricans* is one of the original and best known 11α-hydroxylators of steroids, effective with a whole range of substrates.[1] A few instances of 7β-hydroxylation (in 12% yield or less) are recorded and 6β-hydroxylation often accompanies 11α-substitution. In further studies[2] of the influence of structural factors on the course of steroid microbiological hydroxylation we have observed (see Table) that with this fungus hydroxylation occurs in the 16-position with 5α-androstan-3-one and some of its 11-oxygenated derivatives as substrates. Thus, with 11α-hydroxy-5α-androstan-3-one (I), practically 80% of the products (II + its 3β-ol) result from the hitherto infrequently encountered 16β-hydroxylation. The switch to



(I) (II)

the more common 16α-substitution when the 11β-isomer of (I) is the substrate is quite dramatic.

Inhibition of microbiological hydroxylation by neighbouring groups is already known[3] and it is clear that the presence of the ubiquitous 17β-oxygenated side-chain in the previously studied substrates for *R. nigricans* has most effectively protected the 16-methylene group from attack. The efficiency with which 16β-hydroxy-5α-androstan-3-one is 11α-hydroxylated (85% yield) may well be of significance in connection with the geometry of the hydroxylation process.

TABLE

Substrate	Product(s)
5α-Androstan-3-one	11α,16β-$(OH)_2$-3-one (18) + s.m. (46)
5α-Androstane-3,11-dione	16β(OH)-3,11-dione (20) + s.m. (19)
11α-Hydroxy-5α-androstan-3-one (I)	11α,16β-$(OH)_2$-3-one (II) (30) + 3β,11α,16β-$(OH)_3$ (50)
11β-Hydroxy-5α-androstan-3-one	11β,16α-$(OH)_2$-3-one (56)
16β-Hydroxy-5α-androstan-3-one	11α,16β-$(OH)_2$-3-one (61) + 3β,11α,16β-$(OH)_3$ (23)

The incubation conditions were similar to those already described.[2] Most of the products are new compounds; their structures were established by chemical conversions and spectrometric methods.[4] The figures in brackets are percentages of the products or starting material (s.m.) isolated.

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