MICROBIOLOGICAL OXIDATION OF 16-DEHYDROPREGNENOLONE

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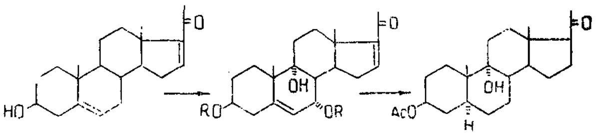
Continuing a study of the oxidizing capacity of the fungus Circinella muscae [1], we have fermented 3β-hydroxypregna-5,16-dien-20-one (16-dehydropregnenolone) (I) with this strain. 2.0 g of 16-dehydropregnenolone was added to a grown culture. After incubation, 1.25 g of a substance was obtained with the formula $C_{21}H_{30}O_4$ (II), mp 238–243° C, $[\alpha]_D^{18} - 98.0°$ (c 1.00 , UV spectrum: $\lambda_{max}^{C_2H_5OH}$ 241 mμ (log ε 4.04). The IR spectrum of compound II has absorption bands at 3250–3400 cm^{-1} (hydroxyl groups) and at 1660 and 1590 cm^{-1} (α,β-unsaturated keto grouping). Calculation of the protons in the NMR spectrum of II carried out before and after the displacement of the protons of the OH groups with trifluoroacetic acid showed the presence in the substance of two secondary and one tertiary hydroxyl groups. Product II is not oxidized by $NaIO_4$. The acetylation of II (acetic anhydride–pyridine, 36° C, 72 hr) gave a diacetate $C_{25}H_{34}O_6$ (III) with mp 165–167° C, $[\alpha]_D^{18} - 192.3°$ (c 1.05 ; chloroform).

Catalytic hydrogenation over platinum of the diacetate III, which was accompanied by hydrogenolysis of one of the acetate groups, and the subsequent oxidation of the reduced product with chromic anhydride led to 3β, 9α-dihydroxy-5α-pregnan-20-one 3-acetate (IV) [2], with mp 185–188° C, $[\alpha]_D^{25} + 64.9°$ (c 1.54; chloroform). Consequently, in compound II the tertiary hydroxyl group is located at $C_{(9)}$.



II R = H

III R = Ac

IV

The signal of the proton at $C_{(16)}$ in the NMR spectrum of the acetate of 16-dehydropregnenolone is found at 6.63 ppm (δ scale) and the proton at $C_{(6)}$ in the 5.30 ppm region. In compound III the form and position of the signal of the $C_{(16)}$ proton have not changed (6.62 ppm), while the signal of the $C_{(6)}$ proton has moved in the weak-field direction (5.52 ppm). This permits the assumption [3] that the allyl hydroxyl group formed in substance II is present at $C_{(7)}$.

The increment in the molecular rotation between II and 3β, 9α-dihydroxy-pregna-5, 16-dien-20-one [2] ($\Delta[M]_D$ −106.5°), and also between their acetates ($\Delta[M]_D$ −565.9°), shows the α-configuration of the hydroxyl at $C_{(7)}$ [4]. Thus, compound II is 3β, 7α, 9α-trihydroxypregna-5, 16-dien-20-one, and has been found among the products of the microbiological transformation of steroids for the first time, so far as we are aware.

REFERENCES

1. M. B. Gorovits, A. D Koveshnikov, and N. K. Abubakirov, KhPS [Chemistry of Natural Compounds], 5, 125, 1969.
2. G. Sato and S. Hagakawa, J. Org. Chem., 28, 2739, 1963.
3. N. Bhacca and D. Williams, Applications of NMR Spectroscopy in Organic Chemistry [Russian translation], Moscow, 1966.
4. U. Schwarz, J. Martinkova, J. Protiva, and K. Syhora, Coll., 31, 4703, 1966.

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