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PYROLYSIS OF STEROID 9,11-EPOXY-5,7-DIENE MALEIC ANHYDRIDE ADDUCTS. PREPARATION OF 11-KETONEOERGOSTEROL (1)

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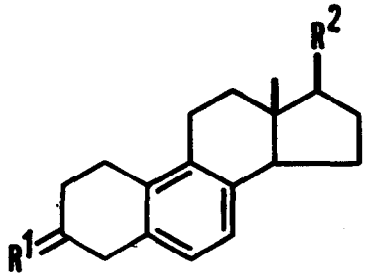
Neoergosterol (I) and its derivatives are very sensitive to oxidising agents and selective oxidation is difficult. Thus, even under carefully controlled conditions, with exclusion of oxygen during the reaction and subsequent isolation of the products, dihydroneoergosterol (II) gives only 41% yield of the corresponding ketone (IV) (2). Oxidation of dihydroneoergosteryl acetate (III) with Jones reagent (3), in an inert atmosphere, gives the 11-ketone (V) in only 15% yield (2) (*ca.* 4% overall yield from ergosterol). We wish to report that 11-ketoneoergosteryl acetate (VI) may be obtained in *ca.* 15% overall yield from ergosterol by introduction of the 11-oxygen atom before aromatisation of ring B.

An obviously useful intermediate would be 9,11-epoxyergosteryl acetate (VIII), a compound which is readily prepared in the form of its maleic anhydride adduct (*ca.* 30% overall yield from ergosterol), but all attempts to liberate the free epoxide have been unsuccessful (4). Bergmann and Stevens (4) reported that pyrolysis of the maleic anhydride adduct yields 15-30% of an aromatic compound, without loss of carbon, which they considered to be 11-keto-x-methyl-neoergosteryl acetate, m.p. 137-139°, $\lambda_{max.}$ 257 and 305 mμ (log ε 3.96 and 3.37, respectively). Later, in a U.S. Patent (5), it was reported, without comment, that pyrolysis of the maleic anhydride adduct of 3β-acetoxy-9,11-epoxy-20-ketopregna-5,7-diene (IX) affords the 1-methyl compound (X). However, it seemed to us that decomposition of the adducts would involve elimination of the angular methyl group and that Bergmann's compound would be the desired 11-ketoneoergosteryl acetate (VI). This has proved to be the case.

When the maleic anhydride adduct of the epoxide (VIII) is heated above its melting point under reduced pressure a vigorous evolution of maleic anhydride and methane takes place. Chromatography of the residue on alumina yields 50% 11-ketoneoergosteryl acetate (VI), m.p. 145-147° (corrected), $[\alpha]_D$ -33° ($CHCl_3$), $\lambda_{max.}$ (iso-octane) 211, 255, and 305 mμ (log ε 4.6, 4.2,

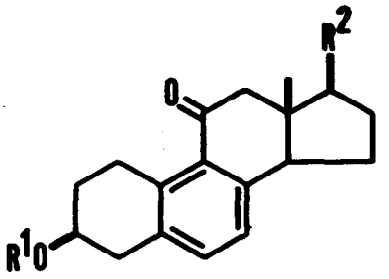


I R^1 = H, β-OH, R^2 = C_9H_{17}

II R^1 = H, β-OH, R^2 = C_9H_{19}

III R^1 = H, β-OAc, R^2 = C_9H_{19}

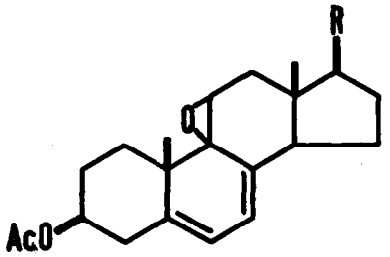
IV R^1 = O, R^2 = C_9H_{19}



V R^1 = Ac, R^2 = C_9H_{19}

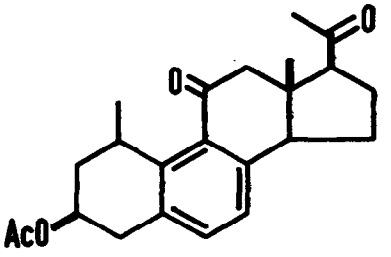
VI R^1 = Ac, R^2 = C_9H_{17}

VII R^1 = H, R^2 = C_9H_{17}

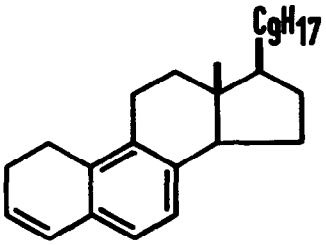


VIII R = C_9H_{17}

IX R = Ac



X



XI

and 3.5, respectively), $\nu_{max.}$ (KBr) 1733 and 1667 cm.$^{-1}$, together with a number of other compounds which will be discussed elsewhere. The N.M.R. spectrum of the 11-ketone (VI) shows the aromatic protons as an AB quartet with doublets centred at τ 2.85 and 3.11 (J = 8 cps), H-3 as a broad multiplet at τ 4.95, the olefinic protons of the side chain as a multiplet at τ 4.78, and the 12-methylene group as an AB quartet with doublets centred at τ 7.38 and 7.66 (J = -11 cps). The acetate and 13β-methyl groups resonate at τ 8.00 and 9.38, respectively.

Confirmation of the structure of the keto-acetate (VI) was obtained by Huang-Minlon reduction of the corresponding alcohol (VII), m.p. 148-149° (corrected), $\nu_{max.}$ (KBr) 1667 cm.$^{-1}$, to give 19-norergosta-3,5,7,9,22-pentaene (XI), m.p. 83-84°, $[\alpha]_D$ + 55° ($CHCl_3$), identical (IR and N.M.R. spectra) with an authentic sample (6).

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