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THE BAEYER-VILLIGER OXIDATION OF Δ^4-3-KETOSTEROIDS: A ROUTE TO SOME NOVEL A-NORSTEROIDS

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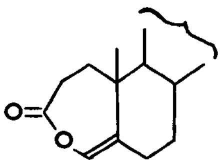
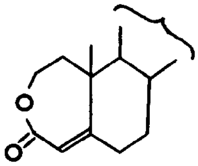
The products obtained from the peracid oxidation of Δ^4-3-ketosteroids have been shown[1,2,3] to vary greatly depending on the reagent used. However, for the systems studied the product of initial oxygen insertion is the enol lactone (I) rather than the αβ-unsaturated lactone (II)



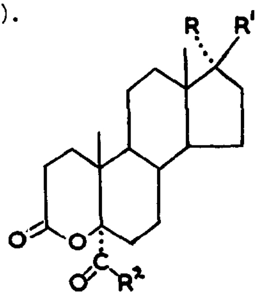
I



II

We have found it necessary to reinvestigate the Baeyer-Villiger oxidation of some Δ^4-3-ketosteroids. Using trifluoroperoxyacetic acid we obtained rather different results from those of Caspi, Chang and Dorfman[3] who investigated the reaction of perbenzoic acid with some of these compounds and Salamon[1] and Pettit and Kasturi[2] who used persulphuric acid in their study of the reaction.

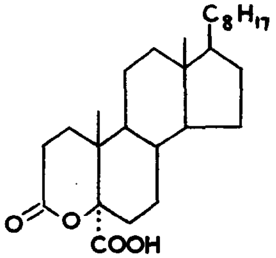
Treatment of cholest-4-ene-3-one with trifluoroperoxyacetic acid gave in good yield a lactone aldehyde* (m.p. 131°, $[\alpha]_D^{21}$ + 11.2) to which we assign structure (IIIa) since it can be oxidised to the known[4] lactone carboxylic acid (IV).



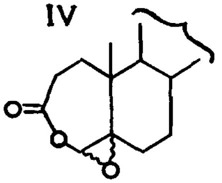
IIIa R = H, R' = C_8H_{17}, R^2 = H

b R = CH_3, R' = OH, R^2 = H

c R = H, R' = C_8H_{17}, R^2 = CH_3



IV



V

We suggest that the aldehyde is formed by an acid-catalysed rearrangement of an epoxide of the enol lactone (V). We were unable to isolate such an intermediate, however Caspi _et al_[2] obtained a compound from the perbenzoic acid oxidation of 11β-hydroxyandrost-4-ene-3,17-dione to which they

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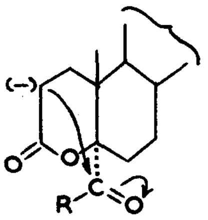
* All new compounds gave satisfactory analyses and had I.R. and P.M.R. spectra consistent with the assigned structures. Rotations are for approximately 1% chloroform solutions.

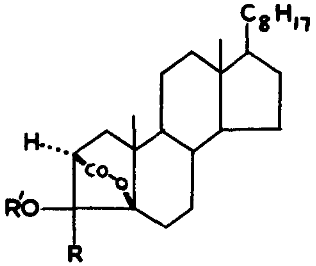
assigned a structure of this type.

This reaction of Δ^4-3-ketosteroids with trifluoroperoxyacetic acid would appear to be a general one since 17β-hydroxy-17α-methylandrost-4-ene-3-one gave an analogous lactone aldehyde* (IIIb; m.p. 150°, $[\alpha]_D^{20}$ - 10.5°) under the same conditions. Also, in a similar manner 4-methylcholest-4-ene-3-one gave the keto-lactone* (IIIc; m.p. 185°, $[\alpha]_D^{24}$ + 84.5°).

The three δ-lactones (IIIa), (IIIb) and (IIIc) undergo extraordinarily facile internal Claisen-type condensations (see VI) when treated with base to give A-norsteroids with a 3,5-lactone bridge. For example, in the presence of alkali, compound (IIIc) gave the lactone (VIIa; m.p. 224°, $[\alpha]_D^{17}$ + 63°), while acetic anhydride containing potassium acetate converted (IIIc) in good yield to (VIIb; m.p. 132°, $[\alpha]_D^{19}$ + 23°), which was identical with the product of acetylation of (VIIa)



VI



VII a R = CH_3, R' = H

b R = CH_3, R' = Ac

c R = βH, R' = Ac

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* The 5α-configuration is assigned by analogy. In addition, the reaction of these compounds in base would suggest they all have the same configuration at C-5.

The lactone aldehyde (IIIa) could be converted with acetic anhydride and potassium acetate to the A-norsteroid (VIIc; m.p. 117°, $[\alpha]_D^{17}$ + 31.5°) to which we tentatively assign the βH configuration at C-3 for the following reason. The spin-spin coupling constant[5] of the proton on C-3 (δ 5.0 ppm., $J_{2,3}$ = 0.9 c/s) indicates that the dihedral angle between the protons on C-2 and C-3 should be close to 90°. Therefore, since the formation of (VIIc) from (IIIa) requires the αH configuration at C-2, the configuration at C-3 should be βH.

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5. The p.m.r. spectrum was recorded for a deuteriochloroform solution on a Varian A60 spectrometer operating at 60 Mc/S.