A New Example of Backbone Rearrangement in Steroids

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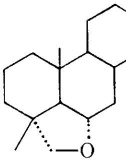
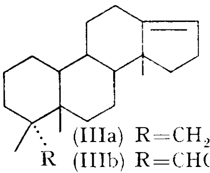
WHEN 4,4-dimethyl-5α-androstan-6α-ol (I) is treated with lead tetra-acetate and iodine in boiling cyclohexane, a new compound, $C_{21}H_{34}O$, (II), is isolated in 75% yield. Its structure is based upon the following evidence: (a) the i.r. spectrum shows a strong band at 990 cm.$^{-1}$, and no carbonyl nor hydroxyl bands; (b) there are only three tertiary methyl peaks in the n.m.r. spectrum, at 40·5, 50·5, and 65·5 c./sec., and a $\equiv C–CH_2–O$ system (quadruplet at 209 c./sec.)† Many related reactions are known in the steroid[1] or terpenoid[2] series. Compound (II), dissolved in a mixture of boron trichloride and methylene chloride[3] at – 70° gives two alcohols: (a) a saturated alcohol, $C_{21}H_{35}OCl$ (23%), m.p. 165—168°, $[\alpha]_D$ ($CHCl_3$) + 10°, whose structure has not been investigated and (b) an unsaturated primary alcohol, (IIIa), $C_{21}H_{34}O$ (45%), m.p. 118·5—121°, $[\alpha]_D$ ($CHCl_3$) + 4·5°.

The n.m.r. spectrum of (IIIa) indicates the presence of three tertiary methyl groups (singlets at 50·5 c./sec., 1 Me, and 55·5 c./sec., 2 Me) one olefinic proton (multiplet, 306 c./sec.) and of an AB system (222 c./sec., J = 10·7 c./sec.). The shift of the *C*-methyl signal from 40·5 in (II) to either 50·5 or 55·5 c./sec. in (IIIa) strongly suggests the proximity of a double bond. In fact, oxidation of (IIIa) to the aldehyde (IIIb) and the Wolff–Kishner reduction of the latter compound leads to a new hydrocarbon (IIIc), $C_{21}H_{34}$, m.p. 80—81·5°, $[\alpha]_D$ ($CHCl_3$) + 4°, which is different from 4,4-dimethylandrost-5-ene. Its n.m.r. spectrum indicates the presence of four tertiary methyl groups (47·5 and 52 c./sec., 1 Me, 55 c./sec., 2 Me) and one olefinic proton (multiplet 306 c./sec.). Hydroboration of (IIIc), followed by chromic acid oxidation affords a ketone, (IV), $C_{21}H_{34}O$, m.p. 155—156·5,° $[\alpha]_D$ ($CHCl_3$) + 120°, ν(C=O) 1750 cm.$^{-1}$ (CCl_4).

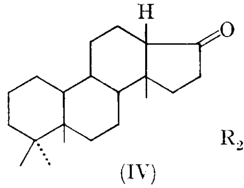
This ketone must have the partial structure $R–CO–CH_2–CH_2–R^1$, since the mass spectrum of its ethylene ketal shows virtually only one peak at *m/e* 99.[4] As it is a cyclopentanone, according to its i.r. spectrum it must be either a 17-keto- or a 15-keto-compound. These two features rule out any *abeo*-structure, *e.g.*, a C-nor-D-homo-androstane derivative.



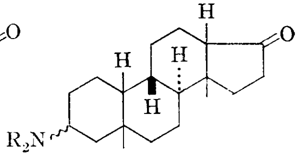
(II)



(IIIa) R=CH_2OH
(IIIb) R=CHO
(IIIc) R=Me



(IV)



(V) R=Me

The ketone (IV), which is stable under equilibration conditions, exhibits a large positive Cotton effect (Δε 295mμ + 3·42, Δε 305mμ + 3·58, dioxan) fitting with a 17-keto-structure and a stable *cis* C/D ring junction. A 15-keto-compound, with a *cis* C/D ring junction, would have a strong negative Cotton effect.[5] Moreover, the circular dichroism curve of (IV) is identical with that of the ketone (V), whose structure has recently been established.[6] The formation of (IV) can be rationalized if a backbone rearrangement of the steroid is postulated; various related examples of such rearrangements have recently been reported.[7]

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† N.m.r. spectra were recorded at 60 Mc/sec. on a Varian A 60, in $CDCl_3$, with tetramethylsilane as internal standard, at 25°.

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