Tetrahedron Letters No.26, pp. 2229-2232, 1965. Pergamon Press Ltd.
Printed in Great Britain.

THE STRUCTURE OF ISOAESCIGENIN

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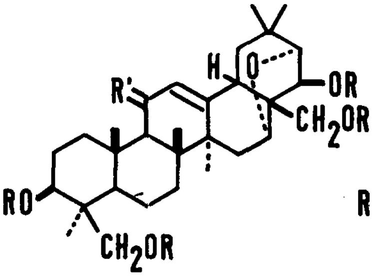
(Received 10 May 1965)

When the ether ring in aescigenin (I) (1) is opened, by means of a variety of reagents (2), the major product is isoaescigenin, $C_{30}H_{48}O_5$, or its penta-acetate. On the grounds that isoaescigenin penta-acetate epoxide, $C_{40}H_{58}O_{11}$, is saturated to tetranitromethane, isoaescigenin has been considered to be mono-unsaturated and hexacyclic (2). Isoaescigenin is now shown to be a di-unsaturated triterpene, olean-12,15-diene-3β,21α,22β,24,28-pentol (II).

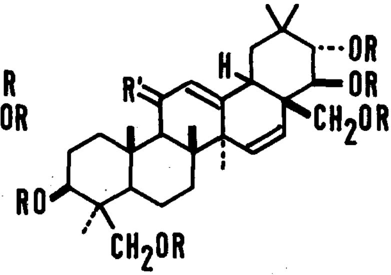
The NMR spectrum of isoaescigenin penta-acetate (III) shows an AB quartet (doublets centred at τ 4.68 and 5.05, J = 2.8 c.p.s.) indicative (3) of the presence of a 1,2-glycol system. The magnitude of the coupling constant does not enable a distinction to be made between 21α-H and 21β-H, but the high degree of steric hindrance (2) at the 15,16 double bond and the slow rate of reaction of isoaescigenin with $NaIO_4$ in aqueous EtOH (0.2 mole $NaIO_4$ consumed after 20 hrs. at room temp.) require a 21α-OAc in a *trans*-diaxial glycol system, i.e. isoaescigenin is a 21α,22β-diol. Isoaescigenin is smoothly cleaved (4) by HIO_4 in pyridine-MeOH (5).

The presence of a 12,13 double bond, deduced (2) from the identity of the ketone (now considered to be IV) prepared by oxidation of



(I, R = H, R' = H_2)

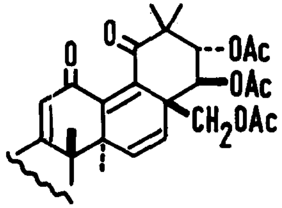
(V, R = Ac, R' = O)



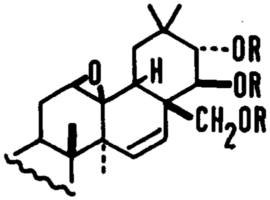
(II, R = H, R' = H_2)

(III, R = Ac, R' = H_2)

(IV, R = Ac, R' = O)



(VI)



(VII, R = Ac)

(VIII, R = H)

isoaescigenin penta-acetate with that obtained by scission of the ether ring in 11-ketoaescigenin tetra-acetate (V), was confirmed by the preparation of a dienedione (VI), m.p. 221-222° (vacuum sealed capillary), $[\alpha]_D$ +22° ($CHCl_3$), $\lambda_{max.}$ (EtOH) 271 mμ (ε 9700), τ 4.00 (11-H, singlet). The 12-H signal (multiplet centred at τ 4.6) in the NMR spectrum of the penta-acetate (III) shifts to τ 4.17 (singlet) for the ketone (IV), and to τ 7.01 (triplet, J = 2.5 c.p.s., $W^{\frac{1}{2}}$ = 5 c.p.s.) for isoaescigenin penta-acetate epoxide (VII) which must, therefore, be a 12,13-epoxide. The latter is assigned the 12β,13β structure as the 17β-CH_2OAc signal changes from a singlet (τ 6.18, $W^{\frac{1}{2}}$ = 3 c.p.s.) for the diene (III) to an AB quartet (doublets centred at τ 5.84 and 6.13, J = 12 c.p.s.) for the epoxide (VII). For all the acetates mentioned here, the 4β-CH_2OAc signal is an AB quartet in the τ 5.8 region (J ~ 12 c.p.s.) (6), and the 3α-H is a triplet (J ~ 8 c.p.s., $W^{\frac{1}{2}}$ = 17 c.p.s.) of multiplets at τ 5.4.

Also present in the spectra of these compounds is an AB quartet (doublets centred at τ 4.2 and 4.5, J ~ 11 c.p.s.). This signal, of particular significance in the spectrum of the "saturated" epoxide (VII), is indicative of the presence of a disubstituted double bond, the protons on which are magnetically isolated from others in the molecule. That (VII) is indeed a monoepoxide was confirmed by mass spectrometric determination (4) of the molecular weight of the corresponding alcohol (VIII), m.p. 328-330° (decomp., vacuum), $[\alpha]_D$ +11° (EtOH), $\lambda_{max.}$ (EtOH) 204 mμ (ε 2500).

The formation of the dienedione (VI), together with the presence of six tertiary-Me groups (NMR singlets) and two tertiary-CH_2OAc groups

(A_2 singlets and/or AB quartets) in all of the acetates, shows that no rearrangement has taken place on opening the ether ring in aescigenin (I). The only possible position, then, for the disubstituted double bond is 15,16 and isoaescigenin must be the diene (II).

The mass spectra of isoaescigenin, its penta-acetate, and the epoxide (VIII) are consistent with the proposed structures. Details of these and other experiments will be published elsewhere.

I am indebted to Prof. Dr. R. Kuhn and Dr. I. Low for permission to publish the results of experiments carried out by them in the Max Planck Institut für Medizinische Forschung (Institut für Chemie, Heidelberg), to Profs. O. Jeger (Zurich) and G. Ourisson (Strasbourg) for NMR spectra, and to Drs. Erskine and West (B.P., Sunbury-on-Thames) for a NMR spectrum and a mass spectrum.

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