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THE CONFIGURATION AT C-21 AND C-22 IN BARRINGTOGENOL C (AESCINIDIN), BARRINGTOGENOL D, PROTOAESCIGENIN, AESCIGENIN, AND ISOAESCIGENIN (1)

T. Nakano and M. Hasegawa

Department of Chemistry, Instituto Venezolano de Investigaciones Cientificas (I.V.I.C.), Apartado 1827, Caracas, Venezuela

J. B. Thomson

Department of Chemistry, University College, Dublin, Ireland

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In a recent communication (2), two of us (T. N. and M. H.) proposed structure Ia for jegosapogenol, a triterpene from Styrax japonica Sieb. et Zucc. The diequatorial (21β,22α) configuration for the α-glycol system was assigned on the basis of the NMR spectra of the tri- (Ib) and tetra- (Ic) acetates, in both of which a large, diaxial coupling constant (J = 10 cps) between H-21 and H-22 was observed (see Table). Furthermore, $J_{H-21,H-22}$ for the 16α,21α-epoxy derivatives (IIb, IIc, and IId) of jegosapogenol is near zero, i.e. the dihedral angle is near 90° (3). Since H-21 is necessarily β-equatorial in II, H-22 must be β-axial.

During this work, a striking similarity was noted between jegosapogenol and barringtogenol C (4). The only difference between the proposed constitutions of these compounds lies in the configuration of the α-glycol system in ring E. The trans-diaxial (21α,22β) assignment for barringtogenol C was based (4) mainly on the slow rate of reaction of this compound with lead tetra-acetate. However, it has been reported (5) that the NMR spectrum of barringtogenol D (the 16α,21α-epoxy derivative of barringtogenol C) triacetate shows a singlet at τ 6,35 for the proton at C-21. If the acetoxyl group at C-22 were β-axial some degree of coupling between H-21 and H-22 should be

observed (3) since the dihedral angle approximates 45° (Dreiding models). Consequently, the C-22 hydroxyl group of the barringtogenols should be α-equatorial and barringtogenol C should be jegosapogenol. Through the courtesy of Prof. Tschesche, barringtogenols C and D, and barringtogenol D triacetate, have been obtained and have been found to be identical with the corresponding derivatives of jegosapogenol. Thus, the structures of barringtogenol C (aescinidin) and barringtogenol D should be revised to Ia and IIa,respectively.

The same line of reasoning recently led (6) to the establishment of the identity of barringtogenol C and theasapogenol B. These workers also suggested (7), but did not demonstrate, that the structures of protoaescigenin (8), aescigenin (9), and isoaescigenin (10) should be revised to Id, IIe, and III, respectively. This suggestion has now been shown to be correct.

The NMR spectrum of aescigenin tetra-acetate shows (5) a singlet at τ6.35 for the C-21 proton; H-22 must, therefore, be β-axial (see discussion above). Furthermore, the epoxy alcohol (IV), derived from barringtogenol D (IIa), has been shown (4) to be identical with the corresponding derivative from proto-aescigenin or aescigenin.* Aescigenin is, therefore, correctly represented by IIe and the 22-hydroxyl group in protoaescigenin, and hence in isoaescigenin, is α-equatorial.

While the NMR spectra of protoaescigenin penta- (Ie) and hexa- (If) acetates show multiplets at τ 5.3 from which coupling constants are not readily extracted, the spectra of the acetonides (V and VI) derived (11) from proto-aescigenin exhibit AB quartets (Table) with J = 9 and 11 cps, respectively. Thus, H-21 and H-22 are <u>trans</u>-diaxial and protoaescigenin is correctly represented by Id.

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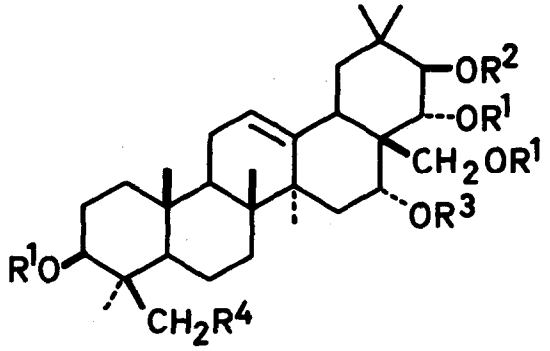
* It should be noted that the original assignment of the β-configuration to the 22-hydroxyl group was based solely on molecular rotation data (9).



Ia $R^1 = R^2 = R^3 = R^4 = H$

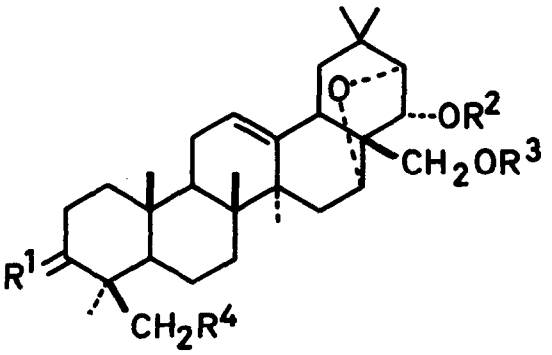
Ib $R^1 = Ac$, $R^2 = R^3 = R^4 = H$

Ic $R^1 = R^2 = Ac$, $R^3 = R^4 = H$

Id $R^1 = R^2 = R^3 = H$, $R^4 = OH$

Ie $R^1 = R^2 = Ac$, $R^3 = H$, $R^4 = OAc$

If $R^1 = R^2 = R^3 = Ac$, $R^4 = OAc$



IIa $R^1 = H, \beta\text{-}OH$, $R^2 = R^3 = R^4 = H$

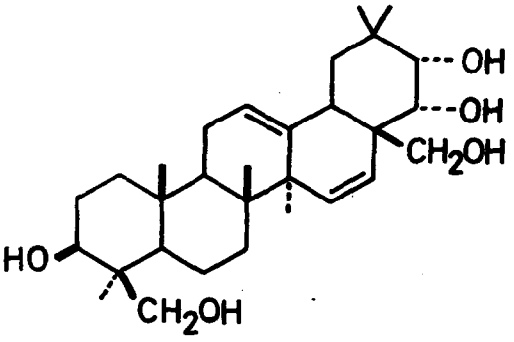
IIb $R^1 = H, \beta\text{-}OAc$, $R^2 = R^3 = Ac$, $R^4 = H$

IIc $R^1 = O$, $R^2 = R^3 = Ac$, $R^4 = H$

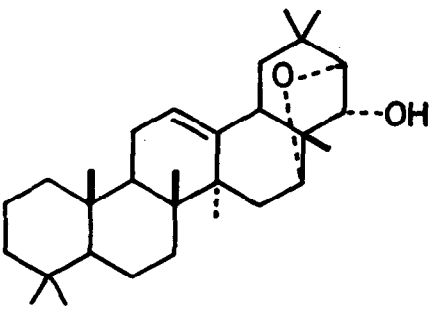
IId $R^1 = O$, $R^2 = R^4 = H$, $R^3 = Ac$

IIe $R^1 = H, \beta\text{-}OH$, $R^2 = R^3 = H$, $R^4 = OH$

IIf $R^1 = H, \beta\text{-}OAc$, $R^2 = R^3 = Ac$, $R^4 = OAc$



III



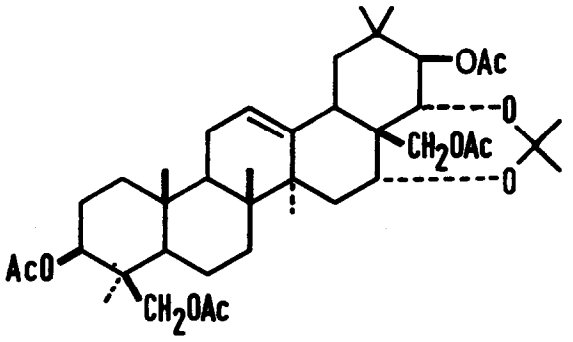
IV

TABLE. NMR data* for H-21 and H-22

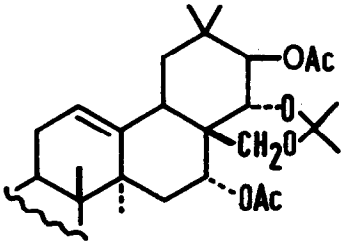
Compound	τ ($CDCl_3$)	J(cps)	Ref.
Ib	5.97(d), 4.72(d)**	10	2
Ic	4.39(d), 4.60(d)	10	2
IIb	6.40(s), 4.70(s)**	0	2
IIc	6.42(s), 4.72(s)**	0	2
IId	6.44(s), 6.04(s)**	0	2
Ie	5.3(3H, mult.)	-	11
If	5.3(4H, mult.)	-	11
IIf	6.35(s) 5.40(s)	0	5, 11
V	4.05(d), 5.22(d)	9	11
VI	3.82(d), 5.36(d)	11	11

* Unless otherwise indicated, the spectra were determined with a Varian HR-100 spectrometer using tetramethylsilane as internal standard.

** Obtained with a Varian A-60 instrument.



V



VI

The trans-diaxial, 21α-OH,22β-OH, assignment for isoaescigenin was based on the slow rate of its reaction with sodium metaperiodate. The small (~ 3 cps) value of $J_{H-21,H-22}$ for isoaescigenin derivatives is consistent with the revised structure (III) since the relevant dihedral angles are approximately equal (Dreiding models).

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