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THE STRUCTURES OF A_1-BARRIGENOL AND R_1-BARRIGENOL

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The triterpenoid sapogenin A_1-barrigenol was originally isolated from *Barringtonia asiatica* Kurz. (1) and *Schima kankaoensis* Hay (2). A_1-barrigenol was subsequently isolated from *Pittosporum undulatum* Vent. (3) where it occurs with a second sapogenin, later isolated from *B. racemosa* Blume (4) and termed R_1-barrigenol. The latter compound has also been isolated from *P. phillyraeoides* DC (5).

White and co-workers (3) proposed the structure I for A_1-barrigenol on the basis of degradative evidence. Knight and White (6) subsequently converted an R_1-barrigenol derivative to an A_1-barrigenol derivative, and proposed the structure II for R_1-barrigenol.

We now report the results of a n.m.r. study* of some A_1-barrigenol and R_1-barrigenol derivatives which shows that the structures previously proposed for the two sapogenins are incorrect, and leads to the structures III and IV for A_1-barrigenol and R_1-barrigenol respectively.

The n.m.r. spectra (Table 1) of A_1-barrigenyl pentacetate and R_1-barrigenyl hexacetate in deuterochloroform solution suggest that each compound contains seven quaternary methyl groups. This is confirmed by the spectra of A_1-barrigenol and R_1-barrigenol in pyridine, where the

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* The preparation and characterisation of the compounds used in this work have been reported previously (3,6).

N.m.r. spectra were recorded using Varian A60 and HR100 High Resolution N.M.R. spectrometers. Spectra were run in deuterochloroform as solvent except where otherwise noted.

Chemical shifts are recorded in p.p.m. from the internal standard tetramethylsilane.

seven methyl signals are clearly resolved. Comparison of the 60 Mc and 100 Mc spectra further confirms that all the methyl groups are quaternary: this is consistent with the olean-12-ene skeleton proposed (3,4) earlier on the basis of infrared evidence, but inconsistent with an urs-12-ene skeleton.

TABLE 1

Methyl Signals* in N.m.r. Spectra of

A_1-barrigenol and R_1-barrigenol and their Acetates

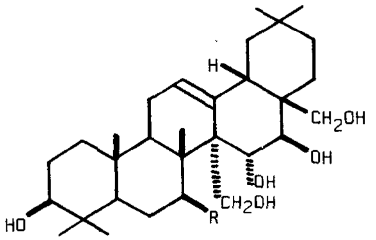
A_1-barrigenyl pentacetate†	A_1-barrigenol ‡	R_1-barrigenyl hexacetate†	R_1-barrigenol ‡
0.87 (6H)	0.98	0.87 (6H)	0.99
0.97 (6H)	1.03	0.92 (3H)	1.04
1.01 (6H)	1.05	0.98 (6H)	1.10
1.44 (3H)	1.09	1.03 (3H)	1.22
	1.13	1.43 (3H)	1.32
	1.21		1.34
	1.80		1.80

* P.p.m. from t.m.s. † $CDCl_3$ solution ‡ Pyridine solution

The n.m.r. spectra also show that each compound contains only one acetoxymethyl (with non-equivalent methylene protons, $|J| = 11.5$ c.p.s.). The chemical shifts are 3.78 and 4.11 p.p.m. in A_1-barrigenyl pentacetate and 3.78 and 4.02 p.p.m. in R_1-barrigenyl hexacetate.

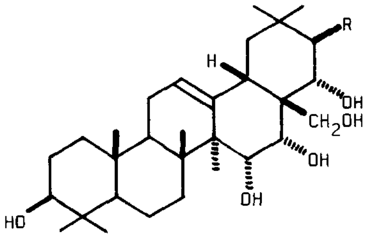
These results are clearly incompatible with the structures previously proposed for A_1-barrigenol and R_1-barrigenol, viz. I and II respectively. The n.m.r. results can, however, be reconciled with the earlier chemical evidence (3,6) if A_1-barrigenol has the structure III and R_1-barrigenol has the structure IV.

The n.m.r. spectrum of A_1-barrigenyl pentacetate contains an AB doublet pair (δ 5.22 and 5.65 p.p.m., $|J| = 3.9$ c.p.s.) attributed to the ring protons adjacent to a vicinal diacetate system. The doublets could be reduced in turn to sharp singlets by spin-decoupling. The magnitude of the coupling constant requires the acetoxy groups to be cis-oriented in agreement with



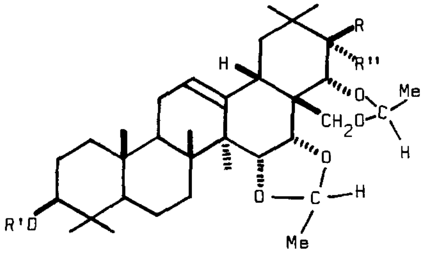
I R = H

II R = OH



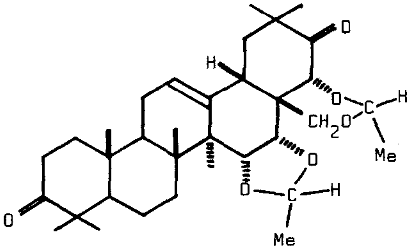
III R = H

IV R = OH

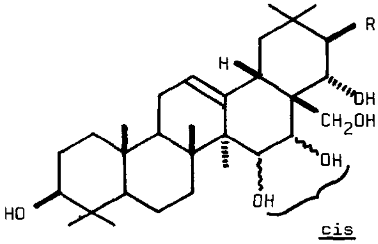


V R = β-OH, R' = H, R'' = H

XI R'' = α-OH, R' = Ac, R = H

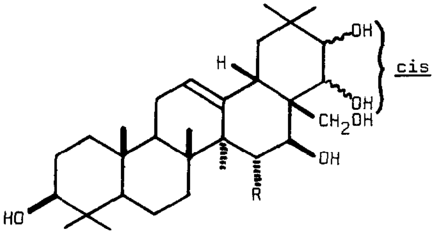


VI



VII R = H

VIII R = OH



IX R = H

X R = OH

the ease of formation of cyclic acetals and ketals by the vicinal glycol system in A_1-barrigenol. The corresponding protons in R_1-barrigenyl hexacetate give rise to an AB quartet, δ 5.18 and 5.53 p.p.m., $|J| = 4.0$ c.p.s.

Both A_1-barrigenyl pentacetate and R_1-barrigenyl hexacetate give rise to a broad multiplet at δ 4.51 attributed to the 3α-proton; the shape and position of this multiplet is common to all olean-12-ene compounds containing only a 3β-acetoxy substituent in ring A.

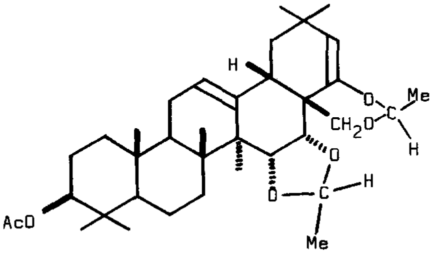
The proton adjacent to the remaining acetoxy group of A_1-barrigenyl pentacetate gives rise to a multiplet at 5.21 p.p.m. which is clearly the X part of an ABX system. The line spacing within the multiplet gives $|J_{AX} + J_{BX}| = 18.0$ c.p.s., requiring the acetoxy group to be equatorial. This multiplet is replaced in the spectrum of R_1-barrigenyl hexacetate by a sharp singlet at 5.24 p.p.m., suggesting that the protons adjacent to two of the acetoxy groups are accidentally equivalent. The relationship between the two protons is apparent from the spectrum of bisethylidene-R_1-barrigenol (V). This contains three pairs of AB doublets: at 3.21 and 3.69 p.p.m. ($|J| = 11.5$ c.p.s.) arising from the C-28 methylene protons, at 4.33 and 4.56 p.p.m. ($|J| = 7.0$ c.p.s.) due to the protons adjacent to what was originally the cis-glycol, and at 3.43 and 4.14 p.p.m. ($|J| = 10.5$ c.p.s.) due to a pair of trans-diaxial protons one of which is attached to a carbon atom involved in the six-membered cyclic acetal. The last pair of doublets is replaced by a sharp singlet in the spectrum of the bisethylidene diketone (VI).

The results above imply that A_1-barrigenol has the structure VII or IX and R_1-barrigenol has the structure VIII or X. The trans-diequatorial arrangement of the second vicinal glycol system of R_1-barrigenol is consistent with the previously reported (6) ready dehydration by phosphorus oxychloride of "y-epi-bisethylidene-R_1-barrigenyl 3β-acetate" (XI). The n.m.r. spectrum of the product (XII) contains a sharp singlet at 5.22 p.p.m. showing that the new double bond is trisubstituted rather than disubstituted as previously thought.

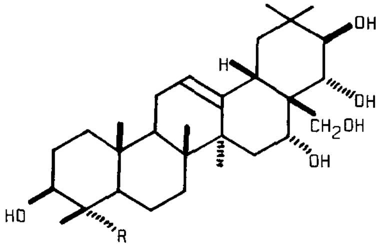
A choice between structures VIII and X for R_1-barrigenol can be made on the basis of infrared evidence. The spectrum of XI has been reported (6) to reveal the presence of a very strongly hydrogen-bonded hydroxyl group. Such a strong hydrogen bond could be formed between a 21α-hydroxy group and an oxygen atom attached axially to C-16. On the other hand, if the "extra" hydroxyl were at C-15 no such bonding could take place either before or after epimerisation.

It follows that R_1-barrigenol must be represented by IV and hence A_1-barrigenol by III.

Our confidence in these structures is confirmed by the recent elucidation (7) of the structures of theasapogenol A (XIII) and barringtogenol C (theasapogenol B) (XIV), which are

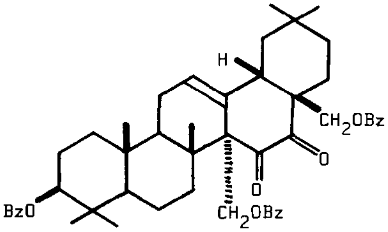


XII

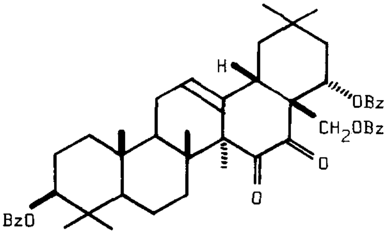


XIII R = CH_2OH

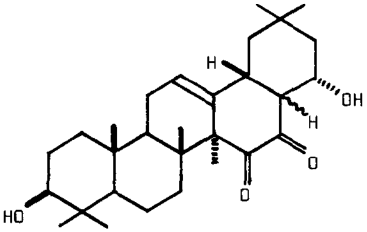
XIV R = Me



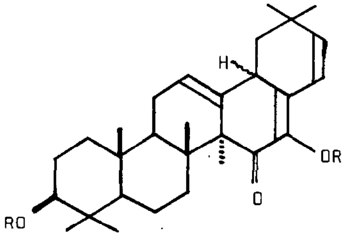
XV



XVI



XVII



XVIII R = H

XIX R = Ac

clearly related biosynthetically to A_1-barrigenol and R_1-barrigenol. Barringtogenol C is, like A_1-barrigenol, a deoxy-R_1-barrigenol and differs only in lacking the C-15 rather than the C-21 hydroxy group.

Our revised structures can be reconciled with the key piece of chemical evidence which lead to the incorrect structures previously reported (3,6), viz. the alleged elimination of two moles of formaldehyde on hydrolysis of the A_1-barrigenyl tribenzoate diketone of supposed structure XV. We believe that the correct structure of the diketone is XVI, and that on hydrolysis one mole of formaldehyde is lost by a retro-aldol reaction to give XVII. Subsequent elimination of water from the β-hydroxyketone (XVII) would give rise to XVIII.

The n.m.r. spectrum of the corresponding diacetate (XIX) shows signals at 0.88 (6H), 0.98 (6H), 1.08 (3H), 1.17 (3H), and 1.33 p.p.m. (3H), corresponding to seven methyl groups, at 2.03 (3β-acetoxy) and 2.23 p.p.m. (enol acetate), broad multiplets at about 5.68 p.p.m. (one vinyl proton) and 4.50 p.p.m. (3α-proton), and a pair of doublets ($|J|$ = 10 c.p.s.) at 5.85 and 6.27 p.p.m. (protons on cis-disubstituted double bond). This is completely consistent with the structure XIX.*

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* The reported (3) analysis of the compound (Found: C, 75.4; H, 8.8; $COCH_3$, 13.6%) is not inconsistent with structure XIX ($C_{33}H_{46}O_5$ requires C, 75.8; H, 8.9; 2 x $COCH_3$, 16.5%).