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STRUCTURES OF A_1-BARRIGENOL AND R_1-BARRIGENOL

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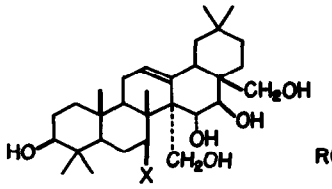
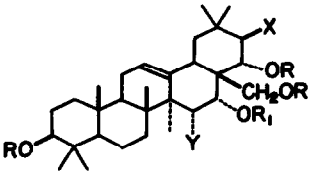
The pentahydroxy pentacyclic triterpene sapogenol, A_1-barrigenol, $C_{30}H_{50}O_5$, was first isolated by Nozoe from Barringtonia asiatica Kurz. (1), and Schima kankaoensis Hay. (2) and later by White and his coworkers from Pittosporum undulatum Vent. (3). The similar sapogenol, R_1-barrigenol, $C_{30}H_{50}O_6$, isolated by Nozoe (4) and Lin et al (5) from Barringtonia racemosa Blume, was also found by White and his coworkers in P. undulatum (3) and P. phillyraeoides DC (6,7). The Australian authors have correlated these two sapogenols and proposed the structures A and B for A_1- (3) and R_1-barrigenols (7), respectively. The NMR spectra of derivatives of these two sapogenols revealed features incompatible with the structures proposed (3,7), when measured in connection with our structural studies on the polyhydroxyoleanenes isolated from Camellia species (8,9), on samples prepared and kindly provided by Professor Nozoe. The present paper describes the result of our reinvestigation which correlates the former compound with camelliagenin A (8) and thus enable us to establish structures I and II for A_1- and R_1-barrigenols. These structures coincide with the ones recently deduced by Errington et al (10) on the basis of an NMR study.

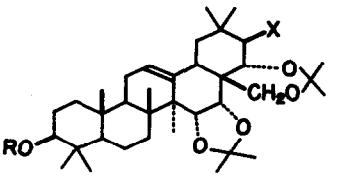
Structure of A_1-barrigenol (I). The NMR spectra (11) of all the A_1-barrigenol derivatives show signals corresponding to seven methyl groups attached to quaternary carbons (Table I). The singlet-nature of the methyl signals and the appearance of a vinyl hydrogen signal near 5.5 ppm (Table II) in the NMR spectra of all these derivatives reinforces the evidence provided by White et al (3) for his assumption that olean-12-ene is the carbon skeleton of this sapogenol. Furthermore, comparison of the methyl regions in the NMR spectra of A_1-barrigenol pentaacetate III (1) and camelliagenin A tetraacetate IV (8) revealed the structural similarity of these two compounds. While signals assignable to 23-, 24-, 25-, 29- and 30-methyl groups in III appear at exactly the same field, suggesting the presence



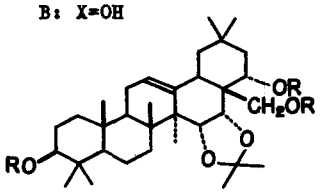
A: X=H
B: X=OH



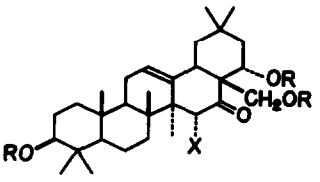
I R=R$_1$=X=H, Y=OH
II R=R$_1$=H, X=Y=OH
III R=R$_1$=Ac, X=H, Y=OAc
IV R=R$_1$=Ac, X=Y=H
VII R=Ac, R$_1$=X=H, Y=OAc
XIII R=R$_1$=X=Y=H
XIV R=R$_1$=Ac, X=Y=OAc
XV R=Ac, R$_1$=H, X=Y=OAc
XVIII R=R$_1$=H, X=OH, Y=H
XIX R=R$_1$=Ac, X=OAc, Y=H



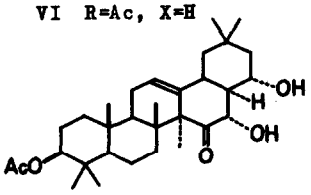
IX R=X=H
X R=Ac, X=H
XVI R=H, X=OH
XVII R=Ac, X=OAc



V R=X=H
VI R=Ac, X=H



VIII R=Ac, X=OAc
XII R=Ac, X=H



XI

of a 3β-acetoxyl group, those due to the 26- and 27-methyl groups in III appear at lower field than in IV, suggesting that the additional acetoxyl group in III is located close to these two methyl groups (12).

The NMR spectrum of III exhibits signals due to <u>six</u> carbinyl hydrogens (Table II) and five acetoxy methyl signals. Of the six hydrogens, two (H_a and $H_{a'}$) show as an AB type at the highest field, suggesting that they are the nonequivalent methylene hydrogens in a $-\dot{C}-CH_aH_{a'}-O-Ac$; two others (H_b and H_c) also appear as an AB type, indicating the presence of the grouping $-\dot{C}-CH_b(O-Ac)-CH_c(O-Ac)-\dot{C}-$; while the remaining two carbinyl hydrogens (H_d and H_e) both appear as doublets of doublets indicating that they are situated in either $-\dot{C}-C\underline{H}(OAc)-CH_2-$ and/or $-\dot{C}H-C\underline{H}(OAc)-\dot{C}H-$ groupings.

The NMR spectra of A_1-barrigenol monoacetonide V (1) and its triacetate VI (1) indicate that the 1,2-glycol grouping in I is converted into an acetonide in V (Table II). The ease of formation of V and the coupling constant (4 cps) between H_b and H_c in III establish a <u>cis</u>-orientation for the glycol. Formation of the tetraacetate VII on acetylation of I in pyridine (1) suggests the axial nature of the remaining hydroxyl group.

TABLE I. Methyl Signals of A_1- and R_1-Barrigenol Derivatives (11)†

	†CH_3						$-O\diagdown\diagup^{CH_3}_{CH_3}$	$-OCOCH_3$
	23	24	25	26	27	29,30		
III	0.85	0.85	0.96	1.00	1.44	0.96, 1.00	—	1.92, 1.96, 2.02, 2.06, 2.09
IV	0.86	0.86	0.96	0.92	1.30	0.96, 1.03		1.97, 2.02(2), 2.07
V	0.98	0.79	0.92	0.92	1.54	0.89, 0.92	1.22, 1.35	—
VI	0.85	0.85	0.94	0.92	1.56	0.93, 1.02	1.23, 1.35	2.00, 2.02, 2.04
VII	0.85*	0.87*	0.96	1.00	1.53	0.96, 1.00	—	2.03(3), 2.08
VIII	0.88	0.88	0.98	1.15	1.25	0.93, 0.98	—	2.00, 2.03, 2.05, 2.12
IX	0.97	0.78	0.93	0.91	1.53	0.88, 1.02	1.22, 1.40, 1.43, 1.44	—
X	0.86	0.86	0.94	0.94	1.54	0.88, 1.03	1.23, 1.40, 1.43, 1.45	2.03
XI	0.86*	0.88*	0.96		0.78,0.93,1.03,1.27		—	2.02
XII	0.87	0.87	0.98	1.05	1.25	0.93, 0.98		2.00, 2.04(2)
XIV	0.85	0.85	0.95	0.97	1.42	0.91, 1.02		1.92(2), 1.97, 2.02, 2.07, 2.24
XV	0.86*	0.88*	0.97	0.99	1.53	0.89, 1.05		2.00(2), 2.04, 2.06, 2.08
XVI	0.98	0.78	0.91	0.88	1.53	0.98, 1.01	1.21, 1.33, 1.38, 1.41	
XVII	0.86	0.86	0.93	0.89	1.58	0.86, 1.01	1.22, 1.40(3)	2.02(2)
XIX	0.87	0.87	0.96	0.91	1.30	0.91, 1.05		1.93, 1.98, 2.03(2) 2.23

† Numbers in parentheses denote the number of methyl groups overlapped.
* Assignment is tentative.

Comparison of the NMR spectra of III and VII clearly revealed that the unacetylated hydroxyl group is a part of the 1,2-glycol (Table II) and is in a 1,3-diaxial relationship with the 27-methyl group (Table I). The latter relationship was also demonstrated by a comparison of the NMR spectra of the hydroxy-acetate VII and the ketone VIII, m.p. 201-202° (15), obtained by the CrO_3 oxidation of VII. Thus this 1,2-glycol is located at the 15α(eq), 16α(ax)-position in the olean-12-ene skeleton.

The presence of a 3β-hydroxyl group and the absence of any other oxygen function in the A and B rings of I, implied by the chemical shift of the methyl signals (vide supra), was further ascertained by the appearance of H_d in all derivatives in exactly the same position as in other 3β-hydroxyolean-12-ene derivatives (8).

The 1,3-disposition of the primary hydroxyl and the remaining secondary hydroxyl was clearly indicated by the formation of the diacetonide IX from I (3). A comparison of the

TABLE II. Lower Field Signals of A_1- and R_1-Barrigenol Derivatives (11)*

	3α-H	15β-H	16β-H	21α-H	22β-H	28-H_2	12-H
III	4.48 (br.t, 7.5)	5.18† (d,4)	5.62 (d,4)		5.18† (q, 6,11)	4.07(d,12) 3.75(d,12)	5.48(m)
IV	4.47 (q,6.5,8.5)		5.1-5.5†		5.1-5.5†	3.73(d,11.5) 3.83(d,11.5)	5.1-5.5†
V	?	4.35§ (d,8)	4.58§ (d,8)		?	3.44(d,12) 3.13(d,12)	5.28(m)
VI	4.47 (br.t,7.5)	4.14§ (d,7)	4.23§ (d,7)		5.22 (q,6,12)	3.78(d,11.5) 3.67(d,11.5)	5.32(m)
VII	4.48 (br.t,7.5)	5.11 (d,4)	4.22 (d,4)		5.33† (q,6.5,11.5)	3.99(d,11.5) 3.70(d,11.5)	5.43(m)
VIII	4.48 (br.t,8)	5.48(s)	—		5.06 (q,5,12)	4.71(d,12) 4.12(d,12)	5.55(m)
IX	3.19 (br.t,7.5)	4.36 (d,7)	4.98 (d,7)		3.92 (q,5,12.5)	3.49(d,12) 3.37(d,12)	5.28(m)
X	4.48 (br.t,8)	4.37 (d,7)	4.98 (d,7)		3.92 (q,5,12.5)	3.47(d,12) 3.37(d,12)	5.28(m)
XI	4.48 (br.t,8)		4.10 (d,12.7)		3.92 (o,10.5,9,4.5)		5.61(m)
XII	4.47† (br.t,8)				5.01 (q,5,12)	4.42(d,11.5) 4.20(d,11.5)	5.44(m)
XIV	4.48 (br.t,7.5)	5.15 (d,4)	5.50† (d,4)	5.21(s)	5.21(s)	4.01(d,12) 3.76(d,12)	5.50(m)†
XV	4.48 (br.t,7.5)	5.08 (d,4)	4.16 (d,4)	5.64 (d,10)	5.33 (d,10)	3.92(d,12) 3.70(d,12)	5.46(m)
XVI	~3.20†	4.35 (d,7)	4.85 (d,7)	3.40§ (d,10.5)	4.17§ (d,10.5)	3.68(d,11.5) 3.19(d,11.5)	5.28(m)
XVII	4.47† (br.t,7.5)	4.34 (d,7)	4.91 (d,7)	5.58 (d,11)	3.80 (d,11)	3.43(br.s)	5.29(m)
XIX	4.49 (br.t,8)		5.22(m)†	5.30(s)	5.31(s)§	3.74(br.s)	5.39(m)†

* Coupling constants are listed in parentheses together with signal multiplicities which are abbreviated as s (singlet), br.s (broad singlet), d (doublet), t (triplet), br. t (broad triplet), q (qualtet), o (octet) and m (multiplet). †Overlaps with the other signals. §Assignment is tentative. ? Unobservable because of limited solubility.

NMR spectra of IX and its acetate X (3) shows that only the signal (H_d) assignable to the 3α-hydrogen exhibits an acetylation shift. Location of the 1,3-glycol function at 22- and 28-position was established by treatment of VIII with alcoholic alkali which afforded the norketone XI, m.p. 271-275° (decomp.) (16). The similarity in the multiplicity of the 22-hydrogen in the corresponding derivatives of A_1-barrigenol and of camelliagenin A (8) suggests an α(eq)-configuration for this secondary hydroxyl group.

All of these observations suggest that I is 15α-hydroxycamelliagenin A. This assumption was established by the reduction of VIII with zinc in acetic acid to give the

15-deacetoxyketo-triacetate XII, m.p. 206-207°, which is identical in every respect with the 16-keto-triacetate derived from camelliagenin A, XIII (8).

Structure of R_1-barrigenol. Since White et al (7) have clearly shown R_1-barrigenol II to be a hydroxy-A_1-barrigenol, only the position and configuration of the additional hydroxyl group remains to be determined. The NMR spectrum of R_1-barrigenol hexaacetate XIV exhibits signals due to seven tertiary C-methyls, six acetoxy methyls, and seven carbinyl hydrogens. The chemical shifts of the C-methyl signals, when compared with those of III, suggest that the additional hydroxyl group is not attached to the A or B ring (Table I). Furthermore, in the lower-field region of the NMR spectrum, the signal due to the 3α-hydrogen is clearly visible but the quartet due to 22β-hydrogen in III is absent and, instead, a sharp 2H-singlet appears at 5.21 ppm. This singlet becomes an AB type in the NMR spectra of R_1-barrigenol pentaacetate XV, m.p. 246-250°, the diacetonide XVI (7), and the diacetonide diacetate XVII, m.p. 275-276° (decomp.) (Table II), from which it can be concluded that the additional hydroxyl group is at C-21. The coupling constant (J= 10-11 cps) of the AB signals indicates an antiparallel disposition for these carbinyl hydrogens, hence trans-diequatorial hydroxyls at C-21 and C-22. A very similar substitution pattern is found in barringtogenol C, XVIII (9, 17) as can be seen from a comparison of the NMR spectrum of its pentaacetate XIX with that of XIV (Tables I, II).

A_2-Barrigenol, $C_{30}H_{50}O_4$, isolated from B. asiatica (1), and R_2-barrigenol, $C_{30}H_{50}O_5$, from B. racemosa (4), were found to be identical with camelliagenin A (8) and barringtogenol C (9,17), respectively, by comparisons of the corresponding derivatives.

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