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OLEAN-18-ENE DERIVATIVES WITH A 13αH-CONFIGURATION

Tadashi HONDA, Tatsushi MURAE, Takahiko TSUYUKI, and Takeyoshi TAKAHASHI
Department of Chemistry, Faculty of Science,
The University of Tokyo, Bunkyo-ku, Tokyo 113

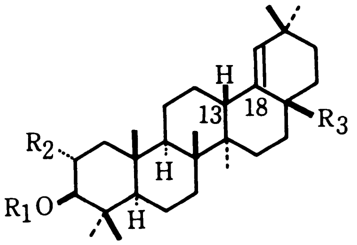
13αH-Olean-18-ene derivatives (4 and 5) were prepared from olean-12-en-19-one derivatives (6 and 24, respectively) by a forced Wolff-Kishner reduction and subsequent acetylation and methylation. Methyl 2,3-di-O-acetylarjunate (15) was transformed, *via* 16 and 17, into a 13βH-olean-18-ene derivative (21), which proved to be not identical with 4. A 13αH-configuration was therefore shown for 4. A signal due to a $C_{(19)}$-H of the 13αH-olefins (4 and 5) was observed at δ 5.30, while that of the 13βH-olefin (21) at δ 5.10.

Germanicol (1),[1] miliacin (2),[2] and morolic acid (3),[3,4] are triterpenes with a 13βH-olean-18-ene framework. However, no isolation nor synthesis of olean-18-ene derivative with a 13αH-configuration has yet been reported. The present paper deals with a preparation and a characterization of 13αH-olean-18-ene derivatives (4 and 5).

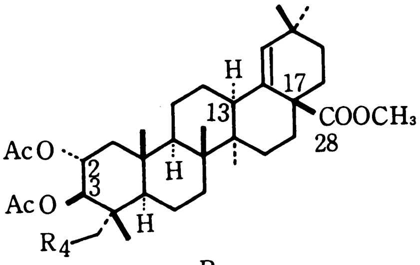
Methyl 2α,3β-diacetoxy-19-oxoolean-12-en-28-oate (6)[5] derived from arjunic acid (7)[5] was subjected to a forced Wolff-Kishner reduction (by Barton's procedures[6]) followed by acetylation (Ac_2O/Pyr., room temperature) and methylation (CH_2N_2) to give an olefin (4 ; yield: 46 %), mp 224-225 °C, $[\alpha]_D$ + 71° (EtOH); IR (KBr) 1740 and 1630 cm^{-1}; PMR ($CDCl_3$) δ 1.98 and δ 2.05 (each 3H, s; 2 X CH_3COO-), δ 3.64 (3H, s; -$COOCH_3$), and δ 5.30 (1H, sharp s; C=CH ; $C_{(19)}$-H); mass spectrum m/e 570.3830 (M^+; m/e 570.3917 calcd. for $C_{35}H_{54}O_6$), m/e 249,[7] m/e 248,[7] m/e 203, and m/e 189[7](base peak; characteristic for an olean-18-ene structure[7]), together with an α,β-unsaturated ketone (8; y: 20 %), mp 223-224 °C, $[\alpha]_D$ - 154° ($CHCl_3$); IR (KBr) 1730 and 1680 cm^{-1}; UV (EtOH) λ_{max} 253 nm (log ε 3.81); PMR ($CDCl_3$)[8] absence of olefinic proton; mass spectrum m/e 584.3682 (M^+; m/e 584.3709 calcd. for $C_{35}H_{52}O_7$) and m/e 188 (base peak). No formation of an expected deoxygenated product, methyl 2α,3β-diacetoxyolean-12-en-28-oate (9; methyl 2,3-di-O-acetylmasulinate[9]) was observed.

The olefin (4) was oxidized with selenium dioxide in acetic acid to yield a known 12,18-diene (10).[5,10] This evidence and the spectral data described above suggested an 18-ene structure (4) for this olefin; a 13αH-configuration of 4 was deduced as follows.

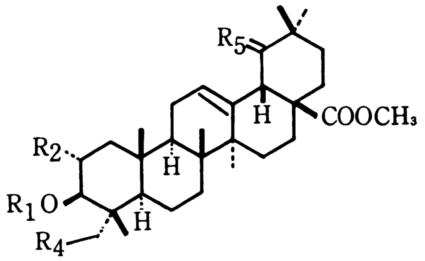
A conversion of methyl 3-O-acetylsiaresinolate (11) into methyl O-acetylmorolate (12), *via* a 12-keto-19α-ol (13) and a 19α-ol (14), has been reported by Barton et al.[3b] The same procedures were applied to methyl 2,3-di-O-acetyl-



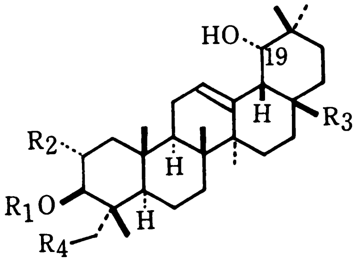
	R_1	R_2	R_3
1	H	H	CH_3
2	CH_3	H	CH_3
3	H	H	COOH
12	Ac	H	$COOCH_3$
21	Ac	OAc	$COOCH_3$



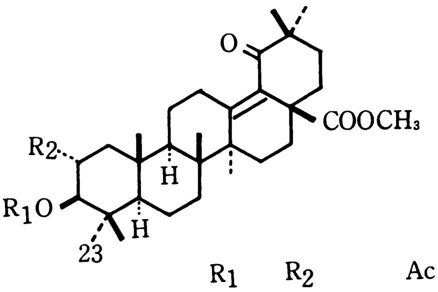
	R_4
4	H
5	OAc



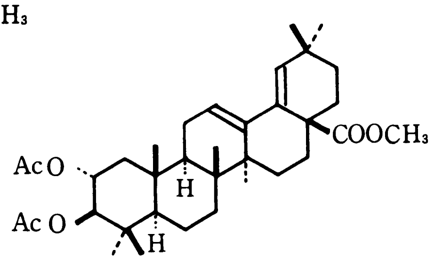
	R_1	R_2	R_4	R_5
6	Ac	OAc	H	O
9	Ac	OAc	H	H_2
24	Ac	OAc	OAc	O
26	H	OH	OH	H_2
27	Ac	OAc	OAc	H_2



	R_1	R_2	R_3	R_4
7	H	OH	COOH	H
11	Ac	H	$COOCH_3$	H
15	Ac	OAc	$COOCH_3$	H
25	H	OH	COOH	OH



	R_1	R_2
8	Ac	OAc
28	H	OH



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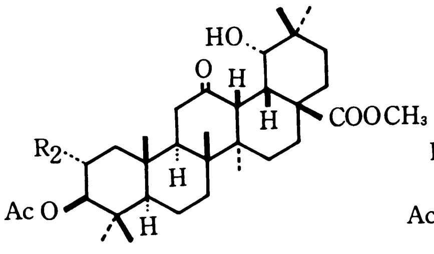
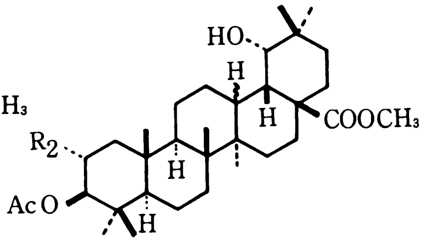
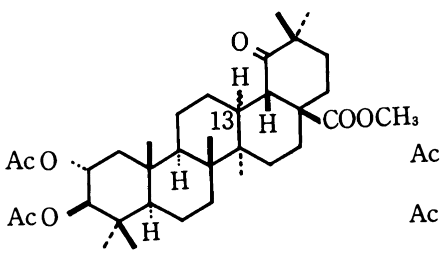


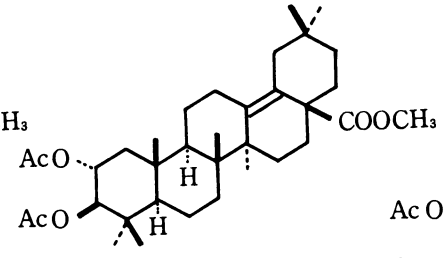
	R_2
13	H
16	OAc



	R_2	13H
14	H	β
17	OAc	β
18	OAc	α



19	13βH
20	13αH



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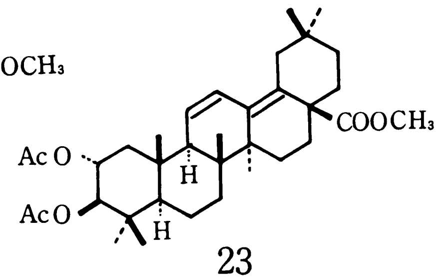

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arjunate (15).$^{5)}$ Treatment of 15 with hydrogen peroxide in acetic acid at 75 °C gave a ketone (16),$^{11)}$ mp 272-273 °C, $[\alpha]_D$ - 25° ($CHCl_3$), IR (Nujol) 3500, 1750, 1730, 1720, and 1690 cm^{-1}; PMR ($CDCl_3$)$^{8)}$ δ 4.55 [1H, t-like; $C_{(19\beta)}$-H; changed into a doublet (J = 3.5 Hz) on addition of D_2O], δ 3.10 (1H, d, J = 7 Hz; $C_{(13\beta)}$-H), and δ 2.90 (1H, dd, J = 7 and J = 3.5 Hz; $C_{(18\beta)}$-H); mass spectrum m/e 602 (M^+; $C_{35}H_{54}O_8$$^{12)}$). The Huang-Minlon reduction of 16, followed by methylation and acetylation yielded a mixture (1.4:1.0) of deoxygenated products (17 and 18), which was separated by silica gel column chromatography to give an alcohol (17), amorphous solid, IR (Nujol) 3530 and 1740 cm^{-1}; PMR ($CDCl_3$)$^{8)}$ δ 3.37 (1H, d, J = 2 Hz; $C_{(19\beta)}$-H); mass spectrum m/e 570 [$(M - H_2O)^+$] and m/e 528 [$(M - AcOH)^+$], and a diastereomeric alcohol (18), amorphous solid, IR (Nujol) 3530 and 1740 cm^{-1}; PMR ($CDCl_3$)$^{8)}$ δ 3.40 (1H, d, J = 5 Hz; $C_{(19\beta)}$-H); mass spectrum m/e 570 [$(M - H_2O)^+$] and m/e 528 [$(M - AcOH)^+$]. The alcohol (17) was then oxidized with the Jones' reagent to yield a ketone (19), amorphous solid, IR (KBr) 1730 and 1710 (sh) cm^{-1}; PMR ($CDCl_3$)$^{8)}$ δ 3.15 (1H, d, $J_{13\beta,18\beta}$ = 4 Hz; $C_{(18\beta)}$-H); CD (EtOH) $\Delta\varepsilon_{302}$ = + 1.60; mass spectrum m/e 586.3899 (M^+; m/e 586.3867 calcd. for $C_{35}H_{54}O_7$). The Jones' oxidation of 18 gave a diastereomeric ketone (20), mp 204-209 °C, IR (KBr) 1730 cm^{-1}; PMR ($CDCl_3$)$^{8)}$ δ 3.28 (1H, d, $J_{13\alpha,18\beta}$ = 12 Hz; $C_{(18\beta)}$-H); CD (EtOH) $\Delta\varepsilon_{302}$ = - 0.11; mass spectrum m/e 586.3879 (M^+; m/e 586.3867 calcd. for $C_{35}H_{54}O_7$). The $J_{13,18}$ values described above led to a 13βH- and a 13αH-configuration for 19 and 20, respectively.$^{13)}$ A configuration at $C_{(13)}$ of the alcohol (17) was therefore infered to be 13βH (with an axial 19α-OH), and that of 18 13αH (with an equatorial 19α-OH). Treatment of 17 with phosphoryl chloride in pyridine afforded an 18-ene (21) whose configuration at $C_{(13)}$ must be βH, mp 232-233 °C, $[\alpha]_{450}$ - 38° (EtOH), IR (KBr) 1740 and 1630 cm^{-1}; PMR ($CDCl_3$)$^{8)}$ δ 5.10 (1H, s; $C_{(19)}$-H); mass spectrum m/e 570.3912 (M^+; m/e 570.3917 calcd. for $C_{35}H_{54}O_6$), m/e 249,$^{7)}$ m/e 203, and m/e 189$^{7)}$(base peak), while a dehydration ($POCl_3$/Pyr.) of 18 gave a 13(18)-ene (22), mp 205.5-206.5 °C, IR (KBr) 1720 cm^{-1}, PMR ($CDCl_3$)$^{8)}$ absence of olefinic proton; mass spectrum m/e 570.3916 (M^+; m/e 570.3917 calcd. for $C_{35}H_{54}O_6$), m/e 249, m/e 203, and m/e 189 (base peak). The latter olefin (22) was obtained by hydrogenation (Pt, AcOH, at room temperature) of the known 11,13(18)-diene (23).$^{5)}$

The 13βH-18-ene (21) thus prepared was found to be not identical with the 18-ene (4). The olefin (4) should therefore be represented by a 13αH-structure, methyl 2α,3β-diacetoxy-13αH-olean-18-en-28-oate (4).

The forced Wolff-Kishner reduction and successive acetylation and methylation of methyl 2α,3β,23-triacetoxy-19-oxoolean-12-en-28-oate (24)$^{14,15)}$ derived from arjungenin (25)$^{14)}$ gave also an 18-ene derivative, methyl 2α,3β,23-triacetoxy-13αH-olean-18-en-28-oate (5; y: 32 %), amorphous solid, $[\alpha]_D$ + 70° (EtOH), IR (Nujol) 1740 cm^{-1}; mass spectrum m/e 628 (M^+), m/e 249,$^{7)}$ m/e 248,$^{7)}$ m/e 203, and m/e 189$^{7)}$(base peak). It was shown that a proton on $C_{(19)}$ of the 13αH-18-ene (4) resonated at δ 5.30, while that of 13βH-18-ene (21) at δ 5.10.$^{16)}$ In the PMR spectrum ($CDCl_3$)$^{8)}$ of 5, a sharp singlet due to an olefinic proton at $C_{(19)}$ appeared at δ 5.30; this suggested a 13αH-configuration for 5.

It has been reported that the double bond of olean-12-en-19-one derivatives isomerizes in the presence of alkali (or under the conditions of Wolff-Kishner reduction) to give the corresponding olean-13(18)-en-19-one derivatives.$^{5,15,17)}$

A forced Wolff-Kishner reduction of the α,β-unsaturated ketone (8)[18] gave 4 (y: 19 %) after acetylation and methylation of the product. An intermediacy of 8 in the reaction of 6 giving rise to 4 was thus suggested.

The Wolff-Kishner reduction of α,β-unsaturated ketones is well documented.[19] The formation of 13αH-olean-18-ene derivatives (4 and 5)(and no formation of their 13βH-diastereomers) is considered to be stereospecific and may be due to a structure feature around the C/D/E rings of olean-13(18)-en-19-one derivatives (and of their nitrogen-containing intermediates).

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11) The ketone (16) was treated successively with KOH/EtOH (heated under reflux, 2 h) and with Ac$_2$O/Pyr. to recover the starting material (16; y: 50 %); this suggested a 13βH-configuration for 16.
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