Pergamon

Tetrahedron Vol. 50, No. 13, pp. 3869-3878, 1994

0040-4020/94 $6.00+0.00

0040-4020(94)E0126-E

Isolation and Relay Synthesis of 11α-Hydroperoxy Diacetyl Hederagenin, a Novel Triterpenoid Derivative from *Serjania triquetra* (Sapindaceae). Biogenetic Implications.[1]

María Isabel Chávez and Guillermo Delgado*

Instituto de Química de la Universidad Nacional Autónoma de México. Ciudad Universitaria, Circuito Exterior. Coyoacán 04510. México, D. F.

Key Words: *Serjania triquetra*, Sapindaceae, medicinal plant, sapogenins, 11α-hydroperoxy-diacetyl hederagenin, β-amyrin derivatives, biogenetic intermediate, chemical intermediate, pentacyclic triterpenes, biogenesis, relay synthesis.

Abstract: Stigmasterol, oleanolic acid, morolic acid, hederagenin, and 11α-hydroperoxy-hederagenin were isolated and characterized as the sapogenins present in the aerial parts of the medicinal plant *Serjania triquetra* (Sapindaceae). The structure of the novel triterpenoid derivative, 11α-hydroperoxy-diacetyl hederagenin, considered as a key biogenetic and chemical intermediate, was confirmed by relay synthesis from diacetyl hederagenin, *via* bromo-lactonization, dehydrobromination, and oxidation with H_2O_2. Biogenetic relationships are briefly described.

Various species of the Sapindaceae family are highly appreciated in traditional medicine in many parts of the world,[2] due to its remarkable array of biological activities. Saponins,[3-5] diterpenes,[6-8] flavonoids,[9] cyanogenic compounds,[10] and aminoacids,[11,12] among other constituents,[13-15] have been characterized from this group of plants.

The medicinal plant *Serjania triquetra* Radlk. belongs to this large family and is located in central and southern parts of Mexico, where the traditional medicine uses an infusion of leaves and stems as diuretic.[16] Continuing our program on the chemistry of organic constituents of Mexican plants,[17] this paper describes the isolation and structure determination of the sapogenins present in this plant. 11α-Hydroperoxy-hederagenin, considered as a key intermediate in the biosynthesis of several triterpenes, was a new sapogenin and the structure of its diacetyl derivative was confirmed by relay synthesis from diacetyl hederagenin.

The dried aerial parts of *S. triquetra* were defatted by extraction with *n*-hexane and then extracted with MeOH. The ethyl acetate insoluble portion of the methanol extract was hydrolyzed with HCl-MeOH-H_2O followed by acetylation with acetic anhydride-pyridine. Chromatography of the resulting mixture afforded stigmasteryl acetate, acetyl oleanolic acid (**1**),[18] acetyl morolic acid (**14**),[19] and diacetyl hederagenin (**2**),[20] whose structures were identified by spectroscopic methods (IR, ^1H and ^{13}C NMR, EIMS) and direct comparison with authentic samples.

The new triterpenoid **8**, also isolated from this mixture, displayed IR absorptions for hydroxyl (3522 cm^{-1}), carboxyl (3200-2500 cm^{-1}) and acetyl (1727 cm^{-1}) groups. Treatment of **8** with CH_2N_2 afforded the methyl ester **13**, which had the molecular formula $C_{35}H_{54}O_8$ (EIMS and elemental analysis), thus indicating nine degrees of unsaturation in the molecule. Since the ^{13}C NMR of **8** contained three carbonyls (δc 170.5, 171.0, 183.4; two acetyls, one carboxylic acid) and one double bond (δc 151.3 and 121.6), the molecule was judged to be a pentacyclic triterpene, similar to **1**, **2** and **14**.

The ^1H NMR spectrum of **8** showed signals for six methyl groups (δH 1.23, 1.07, 0.96, 0.94, 0.84, 0.79; assignments shown in Table 1 were made according previous reports[21]). A single proton doublet of doublet at δ H 2.92 (J=13,4 Hz) indicated an oleanane skeleton.[22] The doublets at δH 3.87 and δH 3.65 (J=11.5) established an acetoxy group at C-23,[23] and the one-proton doublet of doublet at δH 4.79 (J=10,7 Hz) indicated an acetoxy group at C-3β. These data were quite similar with those of diacetyl hederagenin (**2**). An additional one proton doublet of doublet at δH 4.48, which showed vicinal correlation with the vinylic proton H-12 (δH 5.53, d, J=4 Hz) and the angular H-9 (δH 1.88) in the 2D COSY experiment, indicated the presence of a hydroperoxide at C-11, in agreement with the molecular formula. The large pseudo-*trans*-diaxial coupling between H-9 and H-11 (J = 9.8 Hz) established the α-orientation of the hydroperoxide. Mass spectrum data of **13** (M^+ 602) showed direct lose of H_2O (*m/z* 584) and O_2 (*m/z* 570), confirming the presence of the hydroperoxide, and the key mass spectral peaks (see experimental) were those expected for the characteristic retro Diels-Alder fragmentation of Δ^{12}-pentacyclic triterpenes.[24] Thus, the structure of this substance was determined to be 11α-hydroperoxy diacetyl hederagenin (**8**).

Several 11-hydroxylated amyrins have been recently characterized as natural products;[25-28] but to our knowledge, compound **8** represents the first natural oleanene bearing a hydroperoxide at C-11. The possible characterization of **8** as an artifact (eventually produced by oxidation of **2** during the isolation process) was ruled out, due to the well-known stability of Δ^{12}-amyrin derivatives toward standard isolation and hydrolysis conditions.

From the biogenetic point of view, 11-hydroperoxy-amyrins (**b**, Chart 1) (presumably formed from Δ^{12}-precursors (**a**)) may be proposed as key intermediates in the biosynthesis of different naturally occurring triterpenes; namely, the 11-hydroxy (**c**), 11,12-epoxy (**d**), and Δ^{11}-amyrin derivatives (**e**), *inter alia*, *via* a series of biogenetic transformations outlined in Chart 1 (oxidations, reductions, dehydrations). In particular, the biogenesis of eupteleogenine has been proposed *via* the 11α-hydroperoxy-derivative.[29] In addition, 11α-hydroperoxides have been also postulated as intermediates in some oxidative transformations of α- and β-amyrins, although they were not detected nor characterized.[30-32]

These observations, along with the chemical evaluation of the biogenetic relationships showed in Chart 1, as well as the confirmation of the structure of the new triterpene, made of interest to synthesize **8**.

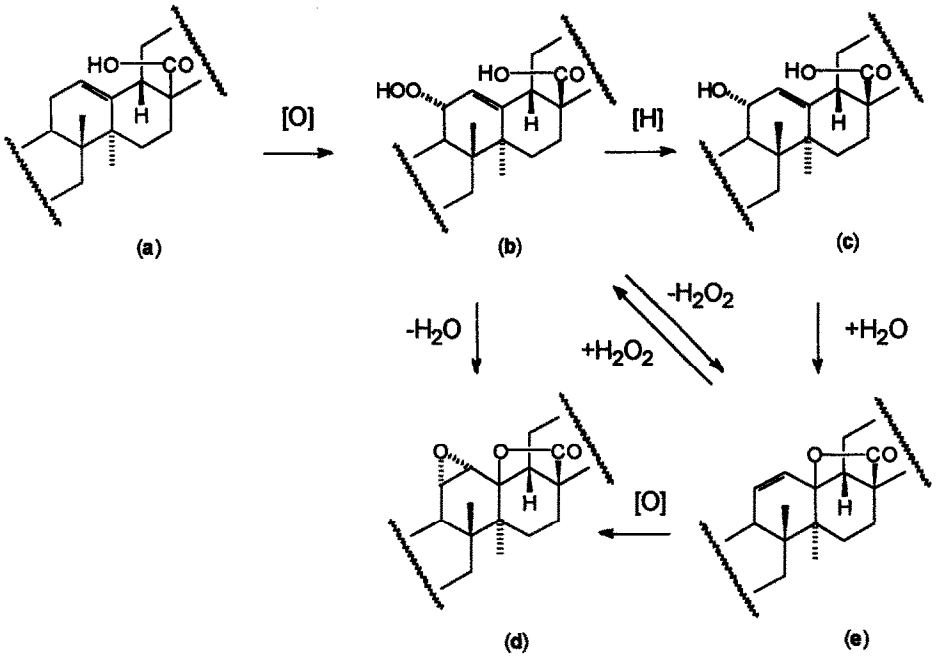
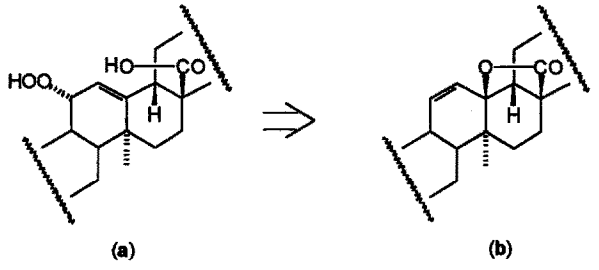


Chart 1. Biogenetic relationships of amyrin derivatives.

Based on mechanistic arguments, it was envisaged that the hydroperoxide group (**a**, Scheme 1) could be introduced directly to the Δ^{11}-derivative (**b**, Scheme 1) *via* a SN2' reaction, by means of the reaction of the olefin with H_2O_2. Although this reaction has been used to obtain the 11α,12α-epoxide, drastic conditions have been employed,[30,33] avoiding the isolation and characterization of the presumed hydroperoxy intermediate.



Scheme 1. Retrosynthetic analysis for the introduction of the hydroperoxy residue.

It was decided to attempt first this transformation with Δ^{11}-acetyl oleanolic lactone (**5**), because the availability of acetyl oleanolic acid (**1**) from this and earlier work.[18,34] Δ^{11}-Acetyl oleanolic lactone (**5**) was obtained as previously described *via* bromination of **1** to afford **3**,[35] followed by dehydrobromination to give

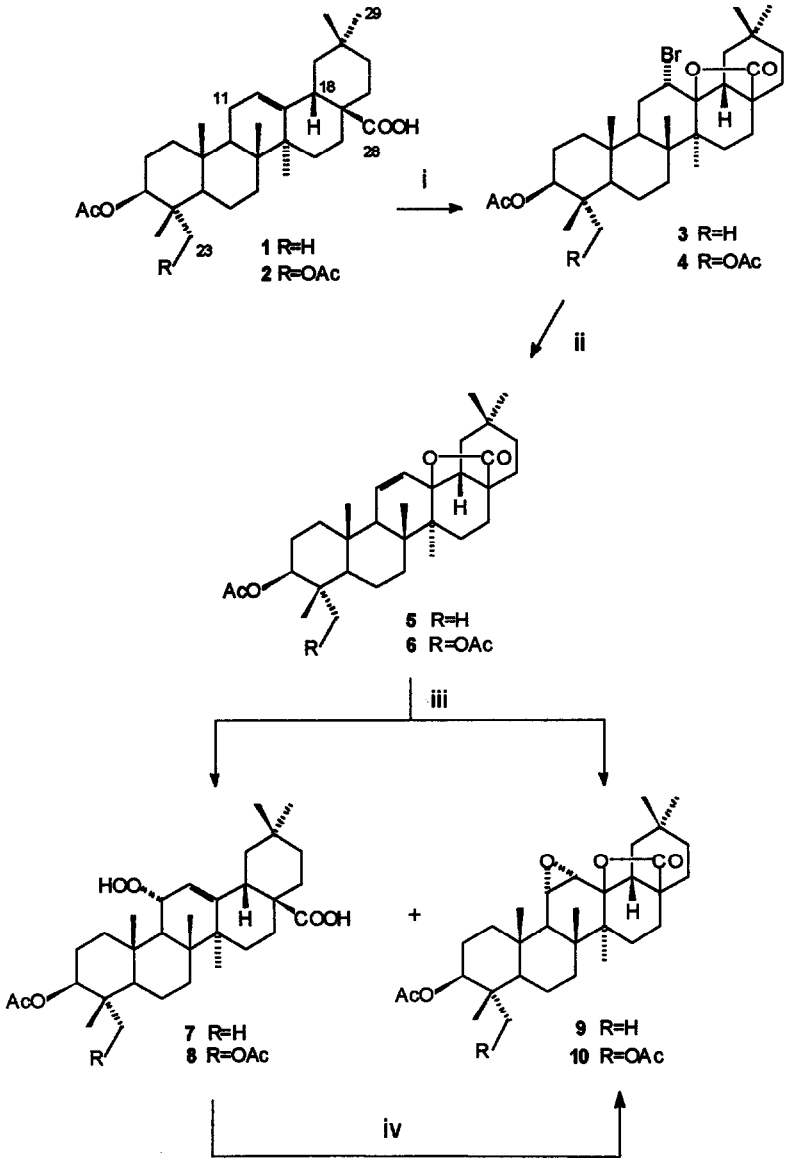
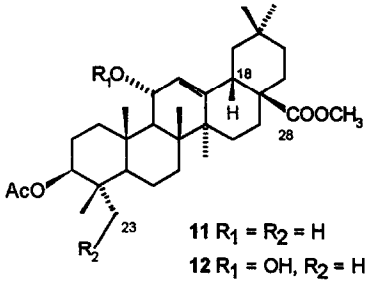


Chart 2. i: Br_2/MeOH; ii: DBU/*o*-xylene; iii: H_2O_2/CH_3COOH; iv: glacial CH_3COOH

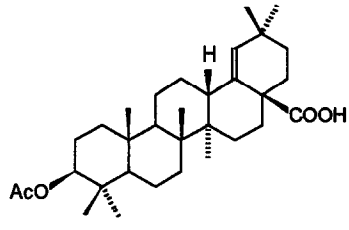
5[36] (see Chart 2). Physical and spectroscopic properties of **3** and **5** were quite similar with those previously obtained for the deacetyl analogs.[33,37] Exposure of **5** to H_2O_2-glacial acetic acid (CH_2Cl_2, room temperature, 22 h) gave two products. The main and less polar compound was acetyl-11α,12α-epoxyolean-28,13β-olide **9**, according to its mass, ^1H and ^{13}C spectral data (see experimental). The more polar compound (7) was methylated and characterized as methyl 11α-hydroperoxy-oleanolate **12** (see Table 1). Control of the reaction (tlc and ^1H NMR) at different periods (3, 6, 12, 18 h) indicated that tne epoxide **9** was formed from the hydroperoxide 7, although some starting material (**5**) was still present. After 48 hrs of reaction, all the starting material (**5**) disappeared and the 11α,12α-epoxide (**9**) was the only product in the reaction mixture. When the 11α-hydroperoxy derivative 7 was allowed to stand with glacial acetic acid for 24 h at room temperature, it was transformed to **9** (see Chart 2).

Chemical evidence of the presence of the hydroperoxy group in **12** was further achieved by its reduction with PPh_3 to afford the 11α-hydroxy derivative (**11**), whose structure was determined by spectroscopic analysis. Particularly noteworthy were the chemical shifts for H-11, H-12 and H-18 of **11** (δH 4.19, 5.35, 2.87, respectively), which shifted upfield compared to those of the hydroperoxy compound **12** (δH 4.46, 5.55 and 2.90), confirming the functional group transformation (see Table 1).

Due to these good results attained in the introduction of the hydroperoxy at C-11 by the SN2' reaction, the same transformations were applied to diacetyl hederagenin (**2**). Bromination of **2** gave **4**, which on dehydrobromination yielded the Δ^{11}-olefin **6**. Reaction of **6** with H_2O_2-acetic acid yielded 11α,12α-epoxy-diacetyl derivative **10** and 11α-hydroperoxy-diacetyl hederagenin **8**. This last compound was identical by direct comparison with that isolated from the acetylated mixture of the natural sapogenins of *Serjania triquetra*, confirming the structure of the new triterpene.



11 $R_1 = R_2 = H$
12 $R_1 = OH$, $R_2 = H$
13 $R_1 = OH$, $R_2 = OAc$



14

These results and the characterization of **8** as a natural derivative confirm, on chemical grounds, previous proposals which postulate 11α-hydroperoxy amyrin derivatives as biogenetic and chemical intermediates.

Table 1. ^{1}H NMR Data ($CDCl_3$, 80 MHz) of β-Amyrin Derivatives.[a,b]

	2	3	4	5	6	8[c]	9	10	11	12[c]	13[c]
H-3	4.75 dd	4.53 dd	4.75 dd	4.49 dd	4.76 dd	4.79 dd	4.50 dd	4.78 dd	4.52 dd	4.51 dd	4.81 dd
	(9,7)	(12,6)	(10,8)	(9.5,7)	(10,6)	(10,7)	(9.5,7)	(10,6)	(12,3)	(9.5,7)	(10,7)
H-9						1.88 d					1.88 d
						(9.8)					(9.8)
H-11				5.42 dd	5.38 dd	4.48 dd	3.02brs	3.01 brs	4.19 dd	4.46 dd	4.50 dd
				(10,3)	(10,3)	(9.8,4)	(w/2=3)	(w/2=3)	(9,4.5)	(10,6)	(9.8,4)
H-12	5.26 m	4.29 brs	4.25 dd	6.03 dd	6.00 dd	5.53 d	3.02 brs	3.01 brs	5.35 d	5.55 d	5.55 d
	(w/2=7)	(w/2=9)	(5,3)	(10,1.5)	(10,1.5)	(4)	(w/2=3)	(w/2=3)	(4)	(4)	(4)
H-23a	3.89 d		3.86 d		3.87 d	3.87 d		3.85d			3.86 d
	(11.5)		(12)		(11.5)	(11.5)		(11.5)			(11.5)
H-23b	3.65 d		3.62 d		3.67 d	3.67 d		3.65 d			3.70 d
	(11.5)		(12)		(11.5)	(11.5)		(11.5)			(11.5)
H-18	2.78 dd					2.92 dd			2.87 dd	2.90 dd	2.95 dd
	(13,5)					(13,4)			(13,5)	(12,5)	(13,4)
H-23		0.87		0.86			0.86		0.86	0.90	
H-24	0.84	0.84	0.83	0.86	0.90	0.84	0.86	0.84	0.86	0.90	0.84
H-25	0.99	0.91	1.00	0.97	1.00	1.07	1.04	1.09	1.04	1.07	1.06
H-26	0.77	1.22	1.21	1.05	1.08	0.79	1.06	1.09	0.74	0.78	0.76
H-27	1.10	1.43	1.43	1.05	1.08	1.23	1.10	1.16	1.22	1.27	1.22
H-29	0.92	0.91	0.91	0.88	0.90	0.94	0.92	0.99	0.94	0.95	0.92
H-30	0.94	1.00	0.95	0.93	0.95	0.96	1.00	0.99	0.95	0.97	0.94

[a] Assignments for the methyl groups were made according to data reported in the literature.[21]

[b] Coupling constants (Hz) in parentheses.

[c] Data taken at 300 MHz

EXPERIMENTAL

General. Melting points were obtained on a Fisher-Johns apparatus and are uncorrected. ^{1}H and ^{13}C NMR spectra were recorded on Varian FT 80 and Varian VXR 300 instruments. IR spectra were taken on a Nicolet 5 SX FTIR spectrophotometer. EIMS were obtained on a Hewlett-Packard 5985-b at 70 eV. Preparative separations were carried out on silica gel (230-400 mesh, Merck) and tlc on Alugram Sil g/UV254 plates.

Plant Material and Isolation of Products. The plant material (*S. triquetra)* used for the preparations in folk medicine, was collected and identified by Drs. Robert Bye and Edelmira Linares (Botanical Garden, Instituto de Biología de la Universidad Nacional Autónoma de México). Reference specimenes are deposited in the National Herbarium, Instituto de Biología, UNAM.

Dried and finely powdered aerial parts of the plant (3 Kg) were extracted with *n*-hexane followed by exhaustive extraction with MeOH. After filtration, the extract was evaporated to dryness to give a gummy material (326 g). This residue was extracted with EtOAc and the insolubles were filtrated to give a brown solid (145 g). Part of this solid (30 g) was hydrolyzed (30 ml HCl 8% and 300 ml of H_2O-MeOH (1:1) at room temperature for 24 h). After usual work up, the obtained residue was acetylated (25 ml Ac_2O, 25 ml anh. Py, room temperature, 8 h) to afford the mixture (14 g) of acetylated sapogenins. This mixture was carefully chromatographed *via* VCC[38] on silica gel, eluting with *n*-hexane and mixtures of *n*-hexane-EtOAc. The low polarity fractions afforded stigmasteryl acetate (220 mg, mp: 143-144 °C). Fractions eluted with *n*-hexane-EtOAc (98:2) yielded acetyl oleanolic acid (**1**, 2100 mg, mp: 266-268 °C). Subsequent fractions eluted with the same polarity (*n*-hexane-EtOAc; 98:2) left a residue (170 mg) which was further purified by prep. tlc developed with *n*-hexane-EtOAc, 95:5) to give acetyl morolic acid[19] (**14**, 18 mg, mp: 248-250 °C; lit:[19] 256 °C); IR ν_{max} cm^{-1} ($CHCl_3$): 1721, 1693, 1602, 1452, 1373, 1255, 1125, 1110, 1027, 980, 903, 862, 814.

Fractions eluted with *n*-hexane-EtOAc (95:5) afforded diacetyl hederagenin (**2**, 650 mg), isolated as a powder. (Mp: 160-162 °C; lit:[20] 168 °C), IR ν_{max} cm^{-1} ($CHCl_3$): 3300-2500, 1727, 1695, 1455, 1420, 1380, 1370, 1255, 1190, 1105, 1028, 1010; ^1H NMR (80 MHz, $CDCl_3$): see Table 1.

Elution of the column chromatography with *n*-hexane EtOAc (9:1) yielded a residue (140 mg) which was further purified by prep. tlc (eluting with $CHCl_3$-acetone, 20:1, two developments) to give 11α-hydroperoxy-diacetyl hederagenin (**8**, 68 mg) as a colourless powder. Mp 122-123 °C; IR ν_{max} cm^{-1} ($CHCl_3$): 3522, 3300-2500, 1727, 1466, 1522, 1370, 1144, 1039, 974, 940; ^1H NMR (300 MHz, $CDCl_3$): see Table 1 (assignments made by 2D COSY experiments); ^{13}C NMR (75 MHz, $CDCl_3$, APT and DEPT experiments): 37.5 (C-1), 22.7 (C-2), 74.0 (C-3), 40.6 (C-4), 47.7 (C-5), 17.8 (C-6), 32.1 (C-7), 42.8 (C-8), 50.0 (C-9), 41.6 (C-10), 81.0 (C-11), 121.6 (C-12), 151.3 (C-13), 42.8 (C-14), 27.7 (C-15), 22.9 (C-16), 46.0 (C-17), 40.5 (C-18), 45.6 (C-19), 30.6 (C-20), 33.6 (C-21), 32.5 (C-22), 65.2 (C-23), 13.0 (C-24), 17.2 (C-25), 18.7 (C-26), 24.6 (C-27), 183.4 (C-28), 32.9 (C-29), 23.5 (C-30), 21.2 ($CO\mathit{CH_3}$), 20.9 ($CO\mathit{CH_3}$), 171.0 ($\mathit{CO}CH_3$), 170.5 ($\mathit{C}OCH_3$).

8 (30 mg) was methylated (CH_2N_2/Et_2O) to give **13** (95% yield) as a white powder: mp 119-120 °C; $[\alpha]_D^{25}$ 45° (*c* 0.01, $CHCl_3$); IR ν_{max} cm^{-1} ($CHCl_3$): 3690, 1723, 1602, 1463, 1368, 1254, 1166, 1124, 1039, 930; ^1H NMR (300 MHz, $CDCl_3$): see Table 1; EIMS *m/z* (rel. int): M^+ 602 (1), 584 (10), 570 (79), 262 (10), 249 (14), 247 (12), 203 (55), 189 (100), 133 (95). Anal. Calcd. for $C_{35}H_{54}O_8$: C, 69.74; H, 9.04. Found: C, 69.90; H, 9.18.

12α-Bromo-acetyl-oleanolide 3. **1** (996 mg, 2 mmol) in MeOH (50 ml) was treated with a solution of bromine (1.25 g, 7.7 mmol) in MeOH (50 ml). After 30 min the reaction mixture was cooled (ice bath) and the formed solid (**3**, 700 mg, 63% yield) was filtered. Mp 193-195 °C; IR ν_{max} cm^{-1} ($CHCl_3$): 1763, 1720, 1463, 1390, 1360, 1301, 1256, 1160, 1135, 1106, 1077, 1059, 1026, 985; ^1H NMR (80 MHz, $CDCl_3$): see Table 1; ^{13}C NMR data previously reported.[39]

Δ^{11}-Acetyl-oleanolide 5. **3** (250 mg, 0.43 mmol) was refluxed with DBU (1.9 ml, 0.0125 mmol) and *o*-xylene (4 ml) for 16 hr.[36] The reaction mixture was partitioned in Et_2O and H_2O, and the ethereal layer was washed with HCl (5%), $NaHCO_3$ and brine. Elimination of the solvent under reduced pressure yielded **5** (160 mg, 72% yield) as colourless powder. Mp 233-235 °C; IR ν_{max} cm^{-1} ($CHCl_3$): 1754, 1720, 1497, 1390, 1366, 1320, 1301, 1257, 1138, 1083, 1027, 987; ^1H NMR (80 MHz, $CDCl_3$): see Table 1; ^{13}C NMR data previously reported.[39]

Oxidation of 5. 11α,12α-Epoxy-acetyl-oleanolide (9) and Methyl-11α-hydroperoxy-acetyl-oleanolate (12). **5** (56 mg, 0.122 mmol) was dissolved in CH_2Cl_2 (12 ml) and a mixture of 30% H_2O_2 (3 ml, 0.088 mmol) and glacial acetic acid (3 ml) was added dropwise during 20 min with stirring, while the mixture was cooled intermittently, after which time the solution was kept at room temperature. Tlc and ^1H NMR analysis of the reaction (after 3, 6, 12 and 18 h) indicated the presence of two products, in addition to the starting material, and that the less polar product, **9**, was formed from the more polar **7**. After 22 h of reaction, the starting material almost disappeared and the mixture was extracted with CH_2Cl_2. The organic residue was washed ($NaHCO_3$, brine) and dried (Na_2SO_4). Elimination of the solvent under reduced pressure and crystallization with CH_2Cl_2-acetone yielded 11α,12α-epoxy-acetyl-oleanolic lactone **9** (35 mg, 61% yield). Mp: 327-329 °C; IR ν_{max} cm^{-1} ($CHCl_3$): 1765, 1721, 1470, 1392, 1367, 1251, 1044, 1028, 970, 929; ^1H NMR (80 MHz, $CDCl_3$): see Table 1; ^{13}C NMR (75 MHz, $CDCl_3$) data previously reported.[39]

The mother liquors were concentrated and then treated with CH_2N_2/Et_2O. Elimination of the solvent yielded methyl-11α-hydroperoxy-acetyl-oleanolate **12** (12 mg, 20% yield) as a colourless solid. Mp 188-190 °C; IR ν_{max} cm^{-1} ($CHCl_3$): 3685, 3540, 1721, 1463, 1368, 1320, 1259, 1174, 1126, 1027, 984, 938; ^1H NMR (80 MHz, $CDCl_3$): see Table 1, EIMS *m/z* (rel. int.): M^+ 544, 526 (5), 511 (11), 262 (4), 249 (12), 203 (50), 189 (65), 175 (63), 121 (55), 119 (100). When the reaction mixture was allowed to react for 48 h, **9** (*ca.* 75%) was the only product. Treatment of **7** with glacial acetic acid (24 h, room temperature) afforded **9** (80%).

12α-Bromo-3-acetyl-23-acetoxy-oleanolide (4). Diacetyl hederagenin (**2**, 100 mg, 0.179 mmol) was dissolved in MeOH (16 ml), and a solution of bromine (50 mg, 0.313 mmol) in MeOH (6 ml), was added with stirring. After 30 min the reaction mixture was cooled and the precipitated solid was filtrated, to give 83.3 mg (74% yield) of **4**. Mp 230-232 °C; IR ν_{max} cm^{-1} ($CHCl_3$): 1763, 1726, 1470, 1389, 1370, 1254, 1160, 1134, 1106,1078, 1040, 991, 925, 905; ^1H NMR (80 MHz, $CDCl_3$): see Table 1; ^{13}C NMR data previously reported.[39]

Δ^{11}-Acetyl-23-acetoxy-oleanolide (6). A mixture of **4** (150 mg, 0.236 mmol), DBU (1 ml, 0.007 mmol) and *o*-xylene (1.5 ml) was refluxed for 10 h. Following the same procedure to that described for the dehydrobromination of **3**, **6** (97 mg, 74%) was obtained. Mp 223-225 °C; IR ν_{max} cm^{-1} ($CHCl_3$): 1752, 1727, 1385, 1368, 1252, 1138, 1041, 922, 898, 868; ^1H NMR (80 MHz, $CDCl_3$): see Table 1; ^{13}C NMR data previously reported.[39]

Hydrogen Peroxide Oxidation of 6. To a solution of **6** (98 mg, 0.176 mmol) in CH_2Cl_2 (18 ml) was added a solution of H_2O_2 (30%, 4.6 ml, 0.135 mmol) and glacial acetic acid (4.6 ml), following the same procedure to that described for the oxidation of **5**. The mixture of products (95 mg obtained after 22 h of reaction) was separated *via* prep. tlc, using *n*-hexane-EtOH as eluting system (one development). **10** (65 mg, 66% yield) was obtained as a white solid. Mp 168-170 °C; IR ν_{max} cm^{-1} ($CHCl_3$): 1766, 1728, 1470, 1369, 1250, 1143, 1106, 1038, 930; ^1H NMR (80 MHz, $CDCl_3$): see Table 1; ^{13}C NMR data previously reported.[39] The more polar product **8** (28 mg, 27% yield) was identical by direct comparison with the acetylated derivative of the natural sapogenins of *S. triquetra.* After 48 h of reaction, **8** was the only product.

Preparation of 11. **12** (16.5 mg, 0.303 mmol) was added to a solution of PPh_3 (4.5 mg, 0.017 mmol) in CCl_4 (16 ml) with stirring at room temperature. After 5 min, the solvent was eliminated by reduced pressure and the residue was purified by prep. tlc (eluted with *n*-hexane-EtOAc, 9:1). 13 mg of **11** (72%) were obtained as a white solid. Mp 202-204 °C; $[\alpha]^{25}_D$ + 153 (*c* 0.05, $CHCl_3$); IR ν_{max} cm^{-1} ($CHCl_3$): 3650, 1718, 1464, 1370, 1257, 1199, 1165, 1125, 1029, 977; ^1H NMR (300 MHz, $CDCl_3$): see Table 1.

ACKNOWLEDGEMENTS

The authors thank Messrs R. Villena, M. Torres, L. Velasco, F. del Río, J. Espiñeira, R. Gaviño and R. Patiño (Instituto de Química de la UNAM) for technical assistance, and Drs. R. Bye and E. Linares (Botanical Garden, Instituto de Biología de la UNAM) for the supply and identification of the plant material. Financial support by Consejo Nacional de Ciencia y Tecnología, México, through a fellowship awarded to M. I. Chávez, is gratefully acknowledged.

REFERENCES

1. This paper (contribution 1193 from the Instituto de Química de la UNAM) is dedicated *in memoriam* to Prof. Humberto Flores Beltrán del Río (1923-1993). Taken in part from the M. Sc. thesis submitted by M. I. Chávez to the División de Estudios Superiores de la Facultad de Ciencias Químicas e Industriales. Universidad Autónoma del Estado de Morelos. Cuernavaca, Morelos, México.
2. Hegnauer, W. *Chemotaxonomie der Pflanzen.* Sapindaceae. Springer Verlag. **1970,** *6*, 271-287.
3. Encarnacion, R.; Kenne, L.; Samuelsson, G.; Sandberg, F. *Phytochemistry* **1981,** *20*, 1939-1942.
4. Kimata, H.; Nakashima, J.; Kokubun, S.; Nakayama, K.; Mitoma, Y.; Kitahara, J.; Yata, N.; Tanaka, O. *Chem. Pharm. Bull.* **1983,** *31*, 1998-2005.
5. Kasai, R.; Fukino, H.; Kasuki, T.; Wong, W.; Goto, Ch.; Yata, N.; Janaka, O.; Yasuhara, F.; Yamaguchi, Sh. *Phytochemistry* **1986,** *25*, 871-876.
6. Hsu, H-Y.; Chen, Y. P.; Kakisawa, H. *Phytochemistry* **1971**, *10*, 2813-2814.
7. Dawson, R. M.; Jarvis, M. W.; Jefferies, P. R.; Payne, T. G.; Rosich, R. S. *Aust. J. Chem.* **1966**, *19*, 2133-2142.

8. Mata, R.; Contreras, J. L.; Crisanto, D.; Pereda-Miranda, R.; Castañeda, P.; del Río, F. *J. Nat. Prod.* **1991**, *54*, 913-917.
9. Venkateswara, R. K. *J. Indian Chem. Soc.* **1962**, *39*, 561.
10. Siegler, D.; Seaman, F.; Mabry, T. J. *Phytochemistry* **1971**, *10*, 485-487.
11. Fowden, L.; Anderson, J. W.; Smith, A. *Phytochemistry* **1970**, 9, 2349.
12. Fowden, L.; Smith, A. *Phytochemistry* **1969**, *8*, 437-443.
13. Plouvier, V. *Compt. Rend.* **1968**, *267 D*, 1883.
14. Fowden, L.; Mac Gibbon, C. M.; Mellon, F. A.; Sheppard, R. C. *Phytochemistry* **1972**, *11*, 1105-1110.
15. Johns, S. R.; Lamberton, J. A. *Aust. J. Chem.* **1969**, *22*, 1315-1316.
16. Martínez, M. *Las Plantas Medicinales de México*. 4th. ed., Editorial Botas, **1959**, 472. México, D. F.
17. Delgado, G., *Trends in Organic Chemistry* **1992**, *3*, 129-140.
18. Pereda-Miranda, R.; Gascón-Figueroa, M. *J. Nat. Prod.* **1988**, *51*, 996-998.
19. Majumder, P. L.; Maiti, R. N.; Panda, K. S.; Mal, D.; Raju, M. S.; Wenkert, E. *J. Org. Chem.* **1979**, *44*, 2811-2812.
20. Haynes, L. L.; Plimmer, J. R.; Sue-Ho, W. M. *J. Chem. Soc.* **1963**, 744-745.
21. Cheung, H. T.; Williamson, D. G. *Tetrahedron* **1969**, *25*, 119-128.
22. Cheung, H. T.; Yan, T. C. *Aust. J. Chem.* **1972**, *25*, 2003-2012.
23. Gaudemer, A.; Polonsky, J.; Wenkert, E. *Bull. Soc. Chim.* Fr. **1964**, 407-411.
24. Budzikiewiecz, H.; Wilson, J. M.; Djerassi, C. *J. Am. Chem. Soc.* **1963**, *85*, 3688-3699.
25. Ikuta, A.; Morikawa, A. *J. Nat. Prod.* **1992**, *55*, 1230-1233.
26. Hota, R. K.; Bapuji, M. *Phytochemistry* **1993**, *32*, 466-468.
27. Pistelli, L.; Bilia, A. R.; Marsili, A.; de Tommasi, N.; Manunta, A. *J. Nat. Prod.* **1993**, *56*, 240-244.
28. Mahato, S. B.; Nandy, A. K.; Roy, G. *Phytochemistry* **1992**, *31*, 2199-2249.
29. Kitagawa, I.; Kitazawa, K.; Yosioka, I. *Tetrahedron* **1972**, *28*, 907-921.
30. Majumder, P. L.; Bagchi, A. *Tetrahedron* **1983**, *39*, 649-655.
31. Yoshikawa, M.; Wang, H. K.; Tosirisuk, V.; Kitagawa, I. *Chem. Pharm. Bull.* **1982**, *30*, 3057-3060
32. Siddiqui, S.; Siddiqui, B. S.; Adil, Q.; Begum, S. *Tetrahedron* **1990**, *46*, 3569-3580.
33. Pereda-Miranda, R.; Delgado, G. *J. Nat. Prod.* **1990**, *53*, 182-185.
34. Delgado, G.; Hernández, J.; Pereda-Miranda, R. *Phytochemistry* **1989**, *28*, 1483-1485.
35. Razdan, T. K.; Kachroo, V.; Harkar, S.; Koul, G. L.; Dhar, K. L. *Phytochemistry* **1982**, *21*, 409-412
36. Parish, E. J.; Miles, D. H. *J. Org. Chem.* **1973**, *38*, 1223 1225.
37. Lewis, K. G.; Tucker, D. *J. Aust. J. Chem.* **1983**, *36*, 2297-2305.
38. Coll, C.; Bowden, E. *J. Nat. Prod.* **1986**, *49*, 934-936.
39. Chávez, M. I.; Delgado, G.; González-Chimeo, E.; Pereda-Miranda, R. *An. Esc. Nac. Cienc. Biol.* **1994** (In the press).

(*Received in USA* 18 *November* 1993; *accepted* 31 *January* 1994)