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TRITERPENES FROM *MAYTENUS HORRIDA*

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Key Word Index—*Maytenus horrida*; Celastraceae; triterpenes; 1β, 3β, 11α-trihydroxyolean-12-ene.

Abstract—The new triterpene 1β,3β,11α-trihydroxyolean-12-ene and the already known compounds, lupeol, germanicol, 3β-hydroxy-glutin-5-ene, β-amyrin, 3β-hydroxyolean-9(11),12-diene, 3-oxo-olean-9(11),12-diene, 3β,11α-dihydroxyolean-18-ene,3β,11α-dihydroxyolean-12-ene, 3β,29-dihydroxy-glutin-5-ene and dulcitol, were isolated from the root bark of *Maytenus horrida*.

INTRODUCTION

As part of a study of the chemical components of the flora used in Latin American folk medicine, new metabolites were isolated from Peruvian [1] and Mexican [2–4] Celastraceae. *Maytenus horrida* Reiss [5], a rare species found among Cactaceae in clay soils in Bajo Chaco, Paraguay, is the subject of this paper. Elsewhere we have reported the structure of a new sesquiterpene alkaloid [6] and triterpenes and methylene quinone derivatives of the friedo-oleane series [7] from the same plant.

RESULTS AND DISCUSSION

Repeated chromatography on silica gel of extracts of the root bark of *M. horrida* yielded a new compound **1**, with a $[M]^+$ at m/z 458. This was assigned the structure 1β, 3β, 11α-trihydroxyolean-12-ene on the basis of the following considerations. The mass spectrum showed fragments at m/z 440, 422 and 404 indicating the loss of three water molecules. The ^{1}H NMR spectrum taken in pyridine-d_5 showed signals for eight methyls at δ0.92 (×2), 1.15, 1.16, 1.28, 1.31, 1.38 and 1.40, three protons geminal to secondary alcohol groups as multiplets at 3.68 and 4.20 and a vinylic proton as a doublet at 5.60. When **1** was treated with acetic anhydride in pyridine for 24 hrs at room temperature, the mono- and di-acetylated derivatives **2** and **3** were obtained while, if the reaction time was extended to six days, the triacetate **4** was also produced.

The monoacetate **2** had the molecular formula $C_{32}H_{54}O$. It showed bands for hydroxyl groups and an ester in the IR spectrum while in its ^{1}H NMR spectrum there was an acetate methyl signal at δ2.03 whth its geminal proton as a double doublet at 4.51 and 4.57 (J = 12, 5 Hz), the protons geminal to the other two hydroxyl groups as double doublets at 3.54 and 3.59 (J = 11, 5 Hz) and 4.29 and 4.33 (J = 8, 3.5 Hz), respectively, the last as part of an AMX system which was coupled with the vinyl proton which resonated as a doublet at 5.21 (J = 3.5 Hz). When a N.O.E. experiment was carried out to irradiate the doublet at δ3.54 and 3.59, a 10% increase in the intensity of the signals appearing at 4.51 and 4.57 as a double doublet was observed; both signals (3.54, 3.59 and 4.51, 4.57) collapsed in a double resonance experiment with irradiation at 1.85. Furthermore, when a solution of **1** in dry benzene was heated to 50° at 20 mm pressure and the benzene was distilled off, diol **5** was obtained with the vinyl protons at δ5.45 and 6.51 as doublets (J = 6.0 Hz), the shift to 6.51 being due to the effect of a neighbouring group as both 3β-hydroxyolean-9(11), 12-diene (**7**) and 3-oxo-olean-9(11), 12-diene (**8**) have the vinyl protons at 5.58 and 5.64 (J = 6.0 Hz).

These data, and the ^{1}H NMR spectra of **3** and **4**, as well as the mass spectral fragmentation pattern of **1** [8], all confirm the structure proposed. Nepetidin [9], 1β,3β,11α-trihydroxylup-20(29)-ene and 3β,11α-dihydroxy-lup-20(29)-ene [10] isolated from *Nepeta handistana*, are similar to our products **1** and **6** although the behaviour of nepetidin and **1** differs in that the former is not acetylated at C-11, nor can it be easily dehydrated and when this does occur, an ether bridge is formed between C-1 and C-11.

The difference in behaviour of the two compounds could be due to the fact that in the compound with the lupane skeleton, the 1β- and 11α-substituents are practically coplanar and slightly closer than they are in our product where an unsaturation prevents them from being coplanar and sets them slightly further apart, as can be seen from a study of the Dreiding models.

The triterpene dienes 3β-hydroxyolean-9(11),12-diene (**7**) and 3-oxo-olean-9(11),12-diene (**8**) [11], together with 3β,11α-dihydroxyolean-12-ene (**6**) [12], may be artefacts formed in the course of the extraction process or laboratory handling and tests are now being conducted to determine if this hypothesis is correct. Three more compounds isolated from *M. horrida* were identified as the oleane triterpenes β-amyrin, germanicol [13] and nivadiol [14] (3β,11α-dihydroxyolean-18-ene).

Product **9** had the molecular formula $C_{30}H_{50}O_2$ and the ^{1}H NMR spectrum revealed the presence of a vinyl proton at δ5.66, two protons of the hydroxymethylene

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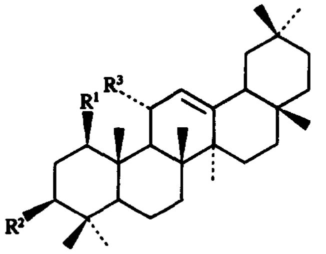
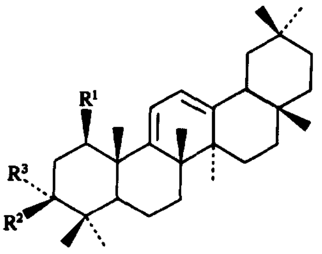
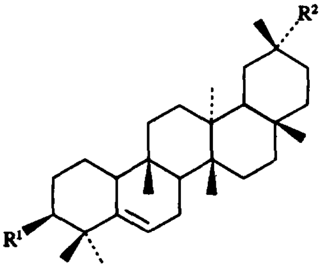


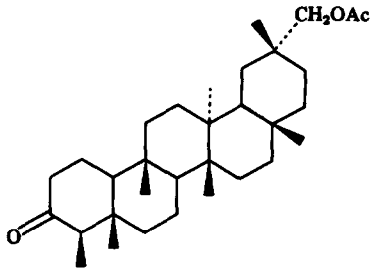
	R1	R2	R3
1	OH	OH	OH
2	OH	OAc	OH
3	OH	OAc	OAc
4	OAc	OAc	OAc
6	H	OH	OH



	R1	R2	R3
5	OH	OH	H
7	H	OH	H
8	H	=O	=O



	R1	R2
9	OH	CH_2OH
10	OH	Me
11	OAc	CH_2OAc
12	OAc	Me



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grouping as an AB system at 3.27 (J = 3.8 Hz), a geminal proton of a secondary alcohol group at 3.47 and signals for eight methyls. The spectral data of compound **10** showed it to be related. The ^{13}C NMR spectral data (Table 1), DEPT experiments [15] and correlation with the ^{13}C NMR spectrum of 3-oxo-29-acetoxyfriedo-oleane (**13**) [16] and data reported by other authors [17, 18], established the position of the carbons. Study of the mass spectral fragmentation showed retro-Diels–Alder type fragments plus those due to the breaking of rings C and D; the same behaviour has been observed in friedo-oleane triterpenes [19]. From the above data, compound **9** was identified as 3β,29-dihydroxyglutin-5-ene and **10** as 3β-hydroxyglutin-5-ene.

EXPERIMENTAL

M. uncorr. ^{1}H NMR and ^{13}C NMR spectra were obtained using $CDCl_3$ as solvent, unless otherwise stated. IR spectra were taken in $CHCl_3$. Dry CC was carried out on silica gel 0.05–0.2 mm. Voucher specimen No. 1232 has been lodged with the Herbarium of the Botany Department, Faculty of Chemical Sciences, Universidad National de Asuncion, Paraguay.

The finely-cut root bark of *Maytenus horrida* (2 kg) was extracted with hot EtOH, yielding a ppt. (44.9 g) soluble in $CHCl_3$. Repeated CC of the extract with petrol–EtOAc mixtures as eluent afforded, in order of separation: 3β,29-dihydroxyglutin-5-ene (**9**) (21 mg), 3β,11α-dihydroxyolean-18-ene (16 mg) and dulcitol (900 mg). When the ground root bark of *Maytenus horrida* (2 kg) was extracted with $CHCl_3$ at room temp. 75 g of extract was

Table 1. ^{13}C NMR Chemical shifts for compounds 9–13

Carbon	9	10	11	12	13
1	18.41	18.30	19.09	19.03	22.43
2	28.01	27.93	25.66	25.61	41.67
3	76.51	76.44	78.75	78.68	not recorded
4	41.01	40.90	39.31	39.24	58.38
5	141.83	141.76	142.17	142.07	42.02
6	122.14	122.10	120.12	120.14	41.43
7	23.78	23.74	23.66	23.64	18.40
8	48.09^a	47.55^a	47.90^a	47.51^a	53.48
9	35.05	34.94	35.02	34.95	37.59
10	49.90^a	49.83^a	50.03^a	49.98^a	59.62
11	32.79	33.24	32.55	33.27	35.78
12	30.68	30.45	30.71	30.55	30.73
13	37.91^b	37.95^b	38.00^b	38.03^b	38.41
14	38.79^b	39.40^b	39.70^b	39.43^b	40.04
15	34.83	34.72	34.80	34.75	32.77
16	36.00	35.19	35.98	36.17	35.97
17	30.78	30.18	30.65	30.24	30.63
18	42.20	43.21	42.32	43.27	42.30
19	29.74	35.19	30.04	35.23	30.19
20	31.35	28.32	31.91	28.37	31.84
21	28.12	32.20	28.50	32.18	28.21
22	39.54	39.05	39.15	39.10	39.21
23	29.13	29.04	29.28	29.25	6.98
24	25.61	25.51	25.20	25.16	14.82
25	16.23	16.26	16.09	16.15	18.04
26	18.21	18.47	18.17	18.53	18.55
27	20.56	19.69	20.20	19.67	20.77
28	32.19	32.46	32.17	32.53	32.23
29	74.64	32.12	75.01	32.18	75.31
30	26.24	34.60	26.79	34.66	26.41

^{a,b} Assignments may be reversed in each vertical column but those given here are considered most likely.

obtained and after repeated CC with petrol–EtOAc mixtures, yielded in order of elution: lupeol (11 mg), germanicol (6 mg), 3β-hydroxyglutin-5-ene (**10**) (63 mg), β-amyrin (8 mg), 3β-hydroxyole/,9(11), 12-diene (**7**) (6 mg), 3-oxo-olean-9(11),12-diene (**8**) (28 mg), 3β,11α-dihydroxyolean-18-ene (15 mg), 3β,11α-diacetoxyolean-12-ene (**6**) (18 mg) and 1β,3β,11α-trihydroxy-olean-12-ene (**1**) (15 mg).

1β,3β,11α-*Trihydroxyolean*-12-*ene* (**1**). Obtained as a gum. ^{1}H NMR (200 MHz) C_6D_5N: δ0.92 (6H, *s*), 1.15, 1.16, 1.28, 1.31, 1.38, 1.40 (each 3H, *s*), 3.68 (1H, *m*), 4.20 (2H, *m*), 5.60 (1H, *d*). EIMS (rel. int.): *m/z* 458 $[M]^+$ (6.9), 440 (32.7), 422 (3.8), 404 (1.0), 287 (10.0), 255(18.2).

Acetylation of **1**. Compound **1** (7.5 mg) was dissolved in pyridine (8 drops) and 4 drops of Ac_2O were then added. The soln was kept at room temp. for 24 hr and then extracted as usual yielding, after chromatography on silica gel, compounds **2** (3.5 mg) and **3** (2 mg). When the same process was followed for 6 days **2** (2.5 mg), **3** (1.5 mg) and **4** (1.5 mg) were obtained.

3β-acetoxy-1β,11α-*dihydroxyolean*-12-*ene* (**2**). Mp 222–226°. $[M]^+$ at *m/z* 500.3855. (Calc. for $C_{32}H_{52}O_4$, 500. 3865). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3680, 3590, 2950, 1720, 1595, 1452, 1377, 1369, 1250. ^{1}H NMR (200 MHz): δ0.77 (3H, *s*), 0.83 (9H, *s*), 0.91, 1.01, 1.08, 1.14, 1.03 (each 3H, *s*), 3.54, 3.59 (1H, *dd*, *J* = 11.0, 5.0 Hz), 4.29, 4.33 (1H, *dd*, *J* = 8.0, 3.5 Hz), 4.51, 4.57 (1H, *dd*, *J* = 12.0, 5.0 Hz), 5.21 (1H, *d*, *J* = 3.5 Hz). EIMS: *m/z* 500 $[M]^+$, 482, 422, 329, 255. (rel. int. not measured).

3β,11α-*diacetoxy*-1α-*hydroxyolean*-12-*ene* (**3**) Amorphous powder. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3640, 2970, 1719, 1596, 1452, 1366, 1255, 1025. ^{1}H NMR (200 MHz): δ0.76, 0.82 (each 3H, *s*), 0.84 (6H, *s*), 0.89 1.01, 1.04, 1.15, 1.92, 2.03 (each 3H, *s*), 3.64 (1H, *m*, $W_{1/2}$ = 19.7 Hz), 4.45, 4.51 (1H, *dd*, *J* = 12.0, 4.0 Hz) 5.38 (2H, *m*, $W_{1/2}$ = 5.0 Hz). EIMS: *m/z* 542 $[M]^+$, 500, 482, 422, 329, 255. (rel. int. not measured).

1β,3β,11α-*triacetoxyolean*-12-*ene* (**4**). Obtained as a gum. $[M-Me-COOH]^+$ at 524.3883. (Calc. for $C_{34}H_{52}O_4$, 524.3863). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3012, 2944, 1724, 1598, 1460, 1452, 1369, 1255. ^{1}H NMR (200 MHz): 0.76 (3H, *s*), 0.84 (9H, *s*), 0.88, 1.01, 1.14, 1.86, 1.92, 2.01 (each 3H, *s*), 4.57, 4.63 (1H, *dd*, *J* = 12.0, J = 4.0 Hz), 4.71, 4.77 (1H, *dd*, *J* = 11.0, 5.0 Hz), 5.30, 5.33 (1H, *dd*, *J* = 7.0, 4.4 Hz), 5.50 (1H, *d*, *J* = 4 Hz), EIMS (rel. int.): *m/z* 524 $[M-Me-COOH]^+$ (3.4), 482 (7.5), 456(4.1), 371(2.3), 255(18.7).

Dehydration of **1**. *Compound* **1** (20 mg), dissolved in dry C_6H_6 (20 ml), was taken to dryness in a rotavapor at 50° and 20 mm pressure and gave a mixture of three products separated by chromatography: **1** (10.4 mg); **5** (7,3 mg) and a third substance (1.3 mg) which could not be purified.

1β,3β-*dihydroxyolean*-9(11),12-*diene* (**5**). Amorphous powder. $[M]^+$ at *m/z* 440.3602. (Calc. for $C_{30}H_{48}O_2$, 440.3654). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3598, 3000, 1459, 1450, 1324, 1237, 1046, 986. UV λ_{max}^{EtOH} nm: 202, 283. ^{1}H NMR (200 MHz): δ0.76 (3H, *s*), 0.79 (6H, *s*), 0.82, 0.88, 0.90, 0.96, 1.14 (each 3H, *s*), 3.26, 3.32 (1H, *dd*, *J* = 12.0, 4.3 Hz), 3.81, 3.86 (1H, *dd*, *J* = 11.5, 4.5 Hz), 5.45, 6.51 (each 1H, *d*, *J* = 6.0 Hz). EIMS (rel. int.): *m/z* 440 $[M]^+$ (31.0), 422 (2.4), 407 (3.0), 287 (28.3), 255 (44.9).

3β,29-*dihydroxyglutin*-5-*ene* (**9**). Mp 270–272°. $[M]^+$ at *m/z* 442.3838. (Calc. for $C_{30}H_{50}O_2$, 442.3811). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3680, 3615, 3000, 1595, 1470, 1380, 1024, 1014. ^{1}H NMR (200 MHz): δ0.85, 1.00, 1.02, 1.05, 1.13, 1.14, 1.21 (each 3H, *s*), 3.27 (2H, *d*, *J* = 3.8 Hz), 3.47 (1H, *br s*), 5.66 (1H, *d*, *J* = 7.0 Hz). ^{13}C NMR (50 MHz): see Table 1. EIMS (rel. int.): *m/z* $[M]^+$ 442 (1.0), 427 (1.4), 424 (2.6), 290 (51.7), 274 (51.6), 221 (19.9), 141 (5.3).

3β,29-*diacetoxyglutin*-5-*ene* (**11**). Amorphous powder. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3020, 1718, 1595, 1468, 1380, 1253, 1030. ^{1}H NMR (200 MHz): δ0.83, 0.95 (each 3H, *s*), 1.01 (6H, *s*), 1.05, 1.10, 1.18, 1.99, 1.06 (each 3H, *s*), 3.73 (2H, *s*), 4.67 (1H, *t*, *J* = 2.8 Hz), 5.53 (1H, *d*, *J* = 7.0 Hz). ^{13}C NMR (50 MHz): see Table 1. EIMS (rel. int.) *m/z* $[M]^+$ 526 (0.5), 496 (0.5), 480 (5.4), 465 (23.9), 332 (30.1), 316 (0.5), 243 (4.3), 183 (7.6).

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