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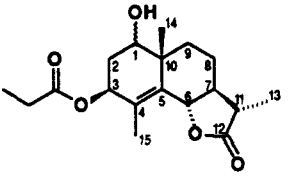
FURTHER NEW SESQUITERPENE LACTONES FROM *ARTEMISIA HERBA-ALBA* SUBSP. *VALENTINA*

JUAN F. SANZ, ENRIQUE FALCÓ, and J. ALBERTO MARCO*

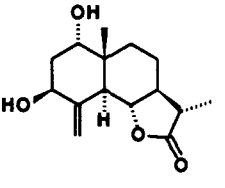
Departamento de Química Orgánica, Facultad de Química, E-46100, Burjassot, Valencia, Spain

ABSTRACT.—From a new chemotype of *Artemisia herba-alba* subsp. *valentina* we have isolated four new eudesmanolides **1–4** and a new eudesmane acid **5**, together with other known compounds.

Artemisia herba-alba Asso subsp. *valentina* Lam. (= *Artemisia valentina* Lam.) is one of the two Spanish subspecies of *A. herba-alba* (1). Eleven years ago we investigated one chemotype of this plant and determined the composition of its waxes and essential oils. Three sesquiterpene lactones with eudesmane framework were also found in the plant. One of these, torrentin, was a new compound (2), the initially proposed structure of which has been recently revised (3). Even more recently we investigated another chemotype of the same subspecies and were able to isolate seven new sesquiterpene lactones with eudesmane and germacrane frameworks and a new eudesmane ester (4). In the present paper, we report the results of our investigation of a third chemotype of *A. herba-alba* subsp. *valentina*, which has yielded four new eudesmanolides **1–4** and a new eudesmane acid **5**, as well as other known compounds: the acids **6–8** (5–7); torrentin (3); the two epimers at C-11 of 11,13-dihydrocostunolide, 11,13-dihydroreynosin, and 11,13-dihydrosantamarin (4,8); artesin, taurin, and their respective epimers at C-11 (4,8); gallicin (8); 8α-hydroxytaurin (9); artapshin (10); ilicic acid methyl ester (4); 4-(*p*-hydroxyphenyl)butan-2-one (11); *p*-hydroxyacetophenone; and methyl trans-*p*-



1 1β-OH
2 1α-OH



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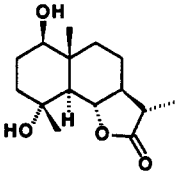

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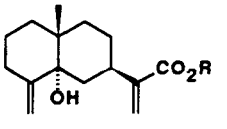
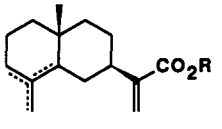


5 R=H
9 R=Me



6 R=H (Δ^3, 5α-H)
7 R=H (Δ^4)
8 R=H ($\Delta^{4(15)}$, 5α-H)
10 R=Me (Δ^3, 5α-H)
11 R=Me (Δ^4)
12 R=Me ($\Delta^{4(15)}$, 5α-H)

coumarate. Some of these products were not found in the previously studied chemotypes.

RESULTS AND DISCUSSION

Compounds **1** and **2** are clearly two isomers with close structural similarity. Both have the same molecular formula ($C_{18}H_{26}O_5$), and both display hydroxyl, lactone, and ester bands in their ir spectra. The presence of a propionyl residue was deduced from nmr and mass spectral features. The base peak in the mass spectrum, for instance, is visible at $[M-74]^+$ (*m/z* 248), this fragment obviously corresponding to the loss of propionic acid from the parent ion. Furthermore, characteristic ^{1}H-nmr signals from the propionic acid chain appear at δ 1.16 (t, $J=7.5$ Hz) and δ 2.36 (apparent dq, $J=7.5$ and 2.5 Hz).

In both compounds, the ^{1}H-nmr spectrum (Table 1) suggests an 11,13-dihydroeudesmanolide structure: the singlet of the angular methyl (H-14) appears at δ 1.19 in **1** and at δ 1.26 in **2**, whereas the doublet ($J=7$ Hz) from the lactonic methyl (H-13) is located at δ 1.24 and 1.23, respectively. In fact, both ^{1}H-nmr spectra markedly

TABLE 1. ^{1}H-nmr Data of Compounds **1–4** and **9**.[a]

Hydrogen	Compound				
	1[b]	**2**[b]	**3**	**4**[c]	**9**[d]
H-1	3.57 dd	3.70 dd	3.58 br t	3.41 dd	
H-2α	2.19 ddd	1.90 ddd	2.12 ddd		1.70–1.50 m[e]
H-2β	1.78 ddd	2.05 ddd	1.78 ddd	1.80–1.50 m[e]	
H-3α	5.35 br dd	5.30 br dd	4.40 br dd		2.62 ddtt
H-3β			—		2.10 br dd
H-5	—	—	2.67 br d	1.72 d	—
H-6α	—	—	—	—	1.88 dd
H-6β	4.63 ddq	4.65 ddq	4.09 dd	4.13 dd	1.76 dd
H-7	1.75 ddd	1.75 ddd	1.65 dddd	1.80–1.50 m[e]	3.08 br ttt
H-8α	1.97 dddd	2.01 dddd	1.91 dddd	1.91 dddd	
H-8β	1.55 dddd	1.55 dddd	1.51 dddd	1.80–1.50 m[e]	1.70–1.50 m[e]
H-9α	1.29 ddd	1.75 ddd	1.97 ddd	1.30 dddd[e]	
H-9β	2.07 ddd	1.55 ddd	1.37 ddd	1.98 dddd	
H-11	2.29 dq	2.30 dq	2.33 dq	2.30 dq	—
H-13	1.24 d	1.23 d	1.23 d	1.22 d	6.17 br s
					5.58 br s
H-14	1.19 s	1.26 s	0.85 s	0.98 s	0.89 s
H-15	1.80 d	1.85 d	5.25 br t	1.34 s	4.80 t
			4.98 br t		4.63 t

[a]At 400 MHz in $CDCl_3$ (25°), unless otherwise stated. Coupling constants in Hz: **1**: $J_{1,2\alpha}=3.5$, $J_{1,2\beta}=J_{2\alpha,2\beta}=12$, $J_{2\alpha,3}=7$, $J_{2\beta,3}=10$, $J_{6,7}=11.5$, $J_{3,6}=J_{6,15}=1.5$, $J_{7,8\alpha}=3$, $J_{7,8\beta}=J_{8\alpha,8\beta}=J_{8\beta,9\alpha}=J_{9\alpha,9\beta}=13.5$, $J_{8\alpha,9\alpha}=J_{8\alpha,9\beta}=4$, $J_{8\beta,9\beta}=3.5$, $J_{7,11}=12$, $J_{11,13}=7$. **2**: $J_{1,2\alpha}=3$, $J_{1,2\beta}=9$, $J_{2\alpha,2\beta}=13$, $J_{2\alpha,3}=5.5$, $J_{2\beta,3}=5$, $J_{6,7}=11$, $J_{3,6}=J_{6,15}=1$, $J_{7,8\beta}=J_{8\alpha,8\beta}=J_{9\alpha,9\beta}=J_{8\beta,9\alpha}=13$, $J_{7,8\alpha}=J_{8\alpha,9\alpha}=J_{8\alpha,9\beta}=J_{8\beta,9\beta}=3.5$, $J_{7,11}=12$, $J_{11,13}=7$. **3**: $J_{1,2\alpha}=J_{1,2\beta}=3$, $J_{2\alpha,2\beta}=14$, $J_{2\alpha,3}=5.5$, $J_{2\beta,3}=12$, $J_{3,15(15')}=J_{5,15(15')}=1.5$, $J_{5,6}=J_{6,7}=11$, $J_{7,8\alpha}=3.5$, $J_{7,8\beta}=J_{8\alpha,8\beta}=J_{8\beta,9\alpha}=12$, $J_{9\alpha,9\beta}=13$, $J_{8\alpha,9\alpha}=J_{8\beta,9\beta}=4$, $J_{8\alpha,9\beta}=2.5$, $J_{7,11}=12$, $J_{11,13}=7$. **4**: $J_{1,2\alpha}=5$, $J_{1,2\beta}=10$, $J_{5,6}=11.5$, $J_{6,7}=10$, $J_{8\alpha,8\beta}=J_{9\alpha,9\beta}=12.5$, $J_{7,8\alpha}=J_{8\alpha,9\alpha}=J_{8\alpha,9\beta}=J_{8\beta,9\beta}=3.5$, $J_{7,11}=12$, $J_{11,13}=7$. **9**: $J_{2\alpha,3\alpha}=6$, $J_{2\alpha,3\beta}=1.5$, $J_{2\beta,3\alpha}=J_{3\alpha,3\beta}=13$, $J_{2\beta,3\beta}=4$, $J_{3\alpha,15(15')}=1.5$, $J_{6\alpha,7}=J_{7,8\alpha}=4$, $J_{6\alpha,6\beta}=13$, $J_{6\beta,7}=J_{7,8\beta}=12.5$.

[b]Propionate group: Me, 1.16 t ($J=7.5$ Hz); CH_2, 2.36 dq ($J=7.5$, 2.5 Hz).

[c]At 200 MHz.

[d]OMe: 3.75 s.

[e]Overlapped signals.

resemble that of torrentin (3). The signal from the proton geminal to the acetoxy group (H-3) in the latter compound almost has the same position (δ ca. 5.3 ppm) and shape as one of the signals in the spectra of both **1** and **2**. Moreover, a counterpart having practically the identical position and shape of H-6 in the ^{1}H-nmr spectrum of torrentin (δ ca. 4.6 ppm) is visible in the spectra of **1** and **2**. In the case of **1**, the similarity with torrentin further extends to the signal of the hydrogen atom geminal to the free hydroxyl group, which appears as a double doublet (J = 12, 3.5 Hz) at δ 3.57. In view of these data, it is possible to conclude that compound **1** is the propionyl analogue of torrentin, i.e., it has the same structure as this lactone, except that a propionyl residue replaces the acetyl group. Decoupling experiments starting from the signals at δ 3.57, 4.63, and 5.35 not only confirmed the proposed structure, but also led to the assignment of all ^{1}H-nmr signals. The ^{13}C-nmr spectrum (Table 2), which shows similarities to that of torrentin (3), supplies additional verification of the structure.

TABLE 2. ^{13}C-nmr Data of Compounds **1–4** and **9**.[a]

Carbon	Compound				
	1	**2**	**3**	**4**	**9**[b]
C-1	74.08	72.96	75.18	77.69	34.91[c]
C-2	32.96	32.44[c]	39.36	28.33	22.27
C-3	72.60	72.00	68.78	38.16[c]	31.71
C-4	133.79[c]	137.48[d]	147.28	71.24	151.90
C-5	125.08[c]	123.65[d]	45.84	55.98	75.47
C-6	82.55	82.27	79.59	80.78	36.06
C-7	52.52	54.04	51.94	53.19	34.77
C-8	24.47	24.70	22.96	23.39	26.28
C-9	38.10	31.48[c]	33.02	39.30[c]	34.28[c]
C-10	42.64	42.42	42.73	41.84	37.93
C-11	41.16	41.22	41.16	40.56	145.78
C-12	178.47	178.39	179.46	178.37	167.87
C-13	12.40	12.43	12.52	12.50	122.96
C-14	18.39	23.97	18.35	13.69	19.96
C-15	14.48	16.05	105.87	24.30	107.59
OProp	174.28 (CO)	174.32 (CO)	—	—	—
	27.82 (CH_2)	27.89 (CH_2)	—	—	—
	9.20 (CH_3)	9.25 (CH_3)	—	—	—

[a]At 50.32 MHz in $CDCl_3$ (27°).
[b]OMe: 51.78.
[c,d]The signals with these superscripts may be interchanged within the same column.

The structure of lactone **2** is closely related to that of **1**, as mentioned above. The main difference in the ^{1}H-nmr spectra is the signal geminal to the hydroxyl group, which in lactone **2** appears at a somewhat lower field, δ 3.70 (dd, J = 9, 3 Hz). A plausible explanation is that **2** and **1** are epimers at C-1. This is confirmed by the nOe observed in the former compound between the signals of H-1 and H-14, which indicates that H-1 has a β orientation. This nOe is not observed in the spectrum of **1**, as expected. Note also the shifts in some ^{13}C-nmr signals, especially the marked low-field shift of C-14 and the high-field shift of C-9 (Table 2). These changes are undoubtedly related to the configurational inversion at C-1.

Compound **3** displays hydroxyl and lactone bands in its ir spectrum, as in **1** and **2**. The molecular formula $C_{15}H_{22}O_4$, with five unsaturations, points to the presence of two hydroxyl groups, one lactone ring, and three double bonds/rings. Here again, the

^{1}H-nmr spectrum (Table 1) suggests a *trans*-eudesman-12,6-olide structure, as in compound **1** and **2**. The two hydroxyl groups correspond to secondary alcohols, as deduced from the observation of three signals of protons geminal to oxygen functions at δ 3.58, 4.09, and 4.40, one of which must be due to the lactone hydrogen H-6. This conclusion is further supported by the ^{13}C-nmr spectrum (Table 2), which shows three methine peaks from oxygenated carbon atoms. The presence of an exocyclic methylene follows from the two narrow multiplets at δ 4.98 and 5.25 in the ^{1}H-nmr spectrum, and from the two peaks at δ 105.87 (t) and 147.28 (s) in the ^{13}C-nmr spectrum. Because no other olefinic signals are observed, the molecule must therefore contain two rings.

Diverse decoupling experiments permitted us to trace the complete hydrogen connectivity and, together with the ^{13}C-nmr data, to confirm the presence of an eudesmane framework. Evidence of the stereochemistry of the molecule was offered by nOe measurements. Saturation of the signal of H-14 at δ 0.85 gave rise to significant nOe at the signals of H-1 and H-6. Moreover, irradiation of the signal of H-3 caused nOe's at the signals of H-2α and H-5, as expected, but not at H-1. This clearly indicates the presence of one axial hydroxyl group at C-1 and another equatorial one at C-3, as expressed by structure **3**. We have named this compound 3-*epi*-erivanin because it is the epimer at C-3 of the known eudesmanolide erivanin, isolated from *Artemisia fragrans* var. *erivanica* (12).

The ir spectrum of compound **4** also shows the presence of hydroxyl and lactone functions. The molecular formula $C_{15}H_{24}O_4$ contains one unsaturation less than that of **3** and is thus compatible with the presence of two hydroxyl groups, two carbocyclic rings, and one lactone ring. No carbon-carbon double bonds are present, as deduced from the absence of olefinic absorptions in either the ^{1}H- or the ^{13}C-nmr spectrum (Tables 1 and 2). Methyl singlets are visible at δ 0.98 and 1.34, as is the typical lactone methyl doublet ($J = 7$ Hz) at δ 1.22. The ^{13}C-nmr spectral data indicate that the molecule contains a secondary and a tertiary hydroxyl group. Indeed, the nmr spectral features are reminiscent of those observed in 1β-hydroxy-11-*epi*-colartin, already isolated from another chemotype of *A. herba-alba* subsp. *valentina* by us (4). Judging from the nmr data, this latter product differs from the compound under study only in the configuration of C-11, which is unequivocally H-11β in the present case (value of the coupling constant $J_{7,11} = 12$ Hz). Structure **4**, 1β-hydroxycolartin is thus proposed for the compound. A search of the literature revealed that this product had already been described as a synthetic intermediate (13).

Compound **5** occurred as free acid but, like **6–8**, was best isolated as its methyl ester **9**. The ir spectrum of **9** gives evidence supporting the presence of a hydroxy group. The ^{1}H-nmr spectrum (Table 1) is very similar to that of costic acid methyl ester **12**, the main differences being low-field shifts of the signals of H-3β, H-7, and H-15. These shifts can be explained by assuming the presence of an axial tertiary OH at C-5. In correspondence with this, one signal from a tertiary oxygenated carbon atom appears at δ 75.47 in the ^{13}C-nmr spectrum (Table 2). In addition, the signals of C-1, C-3, C-7, and C-9 appear at a higher field than those of **12**, as expected from the shielding τ effect produced on these carbon atoms by the axial 5-OH. The downfield shift in the signal of C-14, a feature not easy to explain, has also been observed in structurally related cases (14). Therefore, compound **5** is 5α-hydroxycostic acid.

As usually observed in members of the section *Seriphidium* (15), 11,13-dihydrogermacranolides and 11,13-dihydroeudesmanolides are the most abundant lactone types in *A. herba-alba* subsp. *valentina*. The configuration of these lactones at C-11 is especially worth mentioning due to the fact that in the previously studied chemotypes of *A. herba-alba* subsp. *valentina* (2,4) and *A. herba-alba* subsp. *herba-alba* (8), they had pre-

dominantly an H-11α stereochemistry, whereas the opposite configuration is the most frequent one in the lactones from the present chemotype. Such differences in the chemical composition might be expected in view of the precedent of *A. herba-alba* subspecies from Israel and Egypt (16). A noteworthy difference with these is that the Spanish subspecies investigated up to now have not yielded lactones oxygenated at C-9. It is also noteworthy that ilicic acid occurs in the plant as the methyl ester, whereas the closely related **5–8** are found as free acids.

EXPERIMENTAL

GENERAL EXPERIMENTAL PROCEDURES.—Ir spectra were recorded as KBr pellets or liquid films in a Perkin-Elmer spectrophotometer model 281. Nmr spectra were measured in Bruker spectrometers WM-400 and AC-200 at the frequencies indicated in the tables. Mass spectra were run in a Varian MAT 711 system. Si gel for medium pressure column chromatography (mpcc) was from Merck (40–63 μ). In each case, solvent mixtures were utilized with gradient elution starting from the first mentioned eluent towards the second one. Hplc was performed in the reversed-phase mode (LiChrosorb RP-8, length 250 mm, i.d. 8 mm) with elution by MeOH/H_2O mixtures (flow 3 ml/min) and detection by refractive index. Melting points were determined in a Reichert apparatus and are not corrected.

PLANT MATERIAL.—*A. herba-alba* subsp. *valentina* was collected in November 1987 at the border between the provinces of Valencia and Teruel, Spain. Voucher specimens can be found in the Herbarium of the Department of Botany at the Faculty of Biology, University of Valencia (Prof. A. Aguilella).

EXTRACTION AND CHROMATOGRAPHY.—Air-dried parts of the plant (600 g) were finely ground and extracted at room temperature with hexane-Et_2O-MeOH (1:1:1) (2 × 5 liters, 4 days). The obtained extract (ca. 50 g) was defatted by dissolving in hot MeOH (500 ml) and then cooling at −15° for 3 h. After elimination of the waxy precipitate, the extract was prefractionated by cc on Si gel (column length, 70 cm, i.d. 5 cm, 5 liters of each solvent mixture). Five fractions were collected corresponding to elution with hexane-Et_2O (3:1) (A), hexane-Et_2O (1:1) (B), hexane-Et_2O (1:3) (C), Et_2O (D), and Et_2O-MeOH (9:1) (E). In every step of the separation process described below, individual fractions were examined as to their complexity by tlc and ^{1}H-nmr. Further processing or rejection of the fractions was decided according to these criteria and the weight of the fractions.

Fraction A (3.3 g) consisted mainly of waxes and essential oils. Mpcc on Si gel [hexane-Et_2O (5:1) to (1:1)] gave only one relevant fraction (210 mg), which contained a ca. 1:2 mixture of 11α,13- and 11β,13-dihydrocostunolide (4).

Fraction B (3.5 g) was subjected to mpcc on Si gel [hexane-Et_2O (3:1) to Et_2O]. Three relevant fractions, B-1 to B-3, were selected. Fraction B-1 was subjected to mpcc [$CHCl_3$-MeOH (100:1) to (20:1)]. This yielded a mixture of taurin and 11-*epi*-taurin (14 mg), methyl *trans*-*p*-coumarate (30 mg), and a crude fraction containing the acid **7**. Methylation of this fraction and subsequent preparative tlc gave **11** (30 mg). Fraction B-2 yielded 4-(*p*-hydroxyphenyl)butan-2-one (25 mg) and ilicic acid methyl ester (40 mg), without prior methylation, after mpcc on Si gel [$CHCl_3$-Et_2O (19:1)]. Finally, mpcc of fraction B-3 on Si gel [hexane-Et_2O (1:1) to Et_2O] gave more ilicic acid methyl ester (175 mg), *p*-hydroxyacetophenone (10 mg), and a fraction containing free acids. Methylation of this fraction gave a 5:1 mixture (35 mg) of **10** and **12**, which were separated by hplc [MeOH-H_2O (6:4)].

Fraction C (4.7 g) was fractionated by mpcc [hexane-Et_2O (1:1) to Et_2O]. This gave three relevant fractions, C-1 to C-3. Fraction C-1 was further fractionated by mpcc to fractions C-11 and C-12. Fraction C-11 contained the two epimeric 11,13-dihydrosantamarins (110 mg) while fraction C-12 (45 mg) was a mixture of artesin and its 11-epimer. Fraction C-2 was a mixture of propionates **1** and **2**. Separation by hplc [MeOH-H_2O (1:1)] gave **1** (9 mg), Rt = 32 min, and **2** (3 mg), Rt = 28.5 min. Fraction C-3 was further fractionated by repeated preparative tlc [hexane-Et_2O (1:1)]. This gave the two epimeric eudesmanolides 11α,13-dihydroreynosin (7 mg) and 11β,13-dihydroreynosin (37 mg).

Fraction D (5.8 g) contained mainly flavonoids. Mpcc [hexane-Et_2O (1:3) to Et_2O] gave two relevant fractions, D-1 and D-2. Fraction D-1 was methylated with ethereal CH_2N_2 and fractionated by preparative tlc [hexane-Et_2O (1:4)]. This gave **9** (9 mg). Fraction D-2 was further fractionated by preparative tlc [hexane-Et_2O (1:4)]. This gave 8α-hydroxytaurin (2 mg) and gallicin (9 mg).

Fraction E (5.9 g) was fractionated by mpcc on Si gel [Et_2O to Et_2O-MeOH (5:1)]. This gave two relevant fractions E-1 and E-2. Fraction E-1 was purified by preparative tlc [Et_2O-MeOH (25:1)], yielding **4** (25 mg). Fraction E-2 was subjected to mpcc again [Et_2O-MeOH (15:1)] and then hplc [MeOH-H_2O (1:1)], yielding **3** (8 mg) and artapshin (6 mg).

1β-Hydroxy-3β-propionyloxy-6β,7α,11βH-eudesm-4-en-12,6-olide [**1**].—Colorless needles: mp 151–152° (pentane/EtOAc); $[\alpha]^{24}_D$ + 18°, $[\alpha]^{24}_{578}$ + 19°, $[\alpha]^{24}_{546}$ + 21°, $[\alpha]^{24}_{435}$ + 31° (*c* = 0.62, $CHCl_3$); ir

ν max 3480 (OH), 1770 (lactone C=O), 1720 (ester C=O), 1330, 1190, 1080, 1020, 980, 955, 895, 805 cm^{-1}; eims *m/z* (% rel. int.) $[M]^+$ 322 (13), $[M-C_3H_4O]^+$ 266 (9), $[M-C_3H_6O_2]^+$ 248 (100), $[M-C_3H_6O_2-Me]^+$ 233 (43), 219 (9), 205 (32), 193 (23), 175 (52), 165 (42), 159 (58), 145 (43), 133 (37), 121 (38), 107 (42), 91 (40), 74 (37), 57 (82), 55 (62); hrms found 322.1785, calcd for $C_{18}H_{26}O_5$, 322.1780; ^1H nmr see Table 1; ^{13}C nmr see Table 2.

1α-Hydroxy-3β-propionyloxy-6β,7α,11βH-eudesm-4-en-12,6-olide [**2**].—Colorless gum: $[\alpha]^{24}D$ −25°, $[\alpha]^{24}_{578}$ −26°, $[\alpha]^{24}_{546}$ −30°, $[\alpha]^{24}_{435}$ −57° (*c* = 0.3, $CHCl_3$); ir ν max 3480 (OH), 1765 (lactone C=O), 1725 (ester C=O), 1330, 1180, 1025, 980, 730 cm^{-1}; eims *m/z* (% rel. int.) $[M]^+$ 322 (6), $[M-H_2O]^+$ 304 (2), $[M-C_3H_4O]^+$ 266 (50), $[M-C_3H_6O_2]^+$ 248 (100), $[M-C_3H_6O_2-Me]^+$ 233 (53), 215 (19), 205 (36), 193 (23), 175 (50), 165 (32), 159 (55), 147 (43), 133 (40), 121 (44), 107 (52), 91 (43), 74 (27), 69 (45), 57 (79), 55 (58); hrms found 322.1789, calcd for $C_{18}H_{26}O_5$, 322.1780; ^1H nmr see Table 1; ^{13}C nmr see Table 2.

1α,3β-Dihydroxy-5α,6β,7α11βH-eudesm-4(15)-en-12,6-olide, 3-epi-*erivanin* [**3**].—Colorless gum: $[\alpha]^{24}D$ +124°, $[\alpha]^{24}_{578}$ +130°, $[\alpha]^{24}_{546}$ +148°, $[\alpha]^{24}_{435}$ +253° (*c* = 0.7, $CHCl_3$); ir ν max 3420 (OH), 1765 (lactone C=O), 1190, 1145, 1040, 1015, 990, 965, 730 cm^{-1}; eims *m/z* $[M]^+$ 266 (30), $[M-H_2O]^+$ 248 (69), $[M-H_2O-Me]^+$ 233 (41), $[M-2H_2O]^+$ 230 (8), 219 (10), 205 (12), 191 (23), 175 (38), 167 (41), 159 (50), 133 (44), 123 (58), 107 (57), 93 (55), 81 (57), 69 (56), 55 (100); hrms found 266.1523, calcd for $C_{15}H_{22}O_4$, 266.1519; ^1H nmr see Table 1; ^{13}C nmr see Table 2.

1β,4α-Dihydroxy-5α,6β,7α,11βH-eudesman-12,6-olide, 1β-hydroxycolartin [**4**].—Colorless needles: mp 185–190° (EtOAc) [lit. (13) mp 197–199°]; $[\alpha]^{24}D$ +7°, $[\alpha]^{24}_{578}$ +7°, $[\alpha]^{24}_{546}$ +8°, $[\alpha]^{24}_{435}$ +15° (*c* = 0.2; $CHCl_3$); ir ν max 3400 (OH), 1770 (lactone C=O), 1446, 1165, 1148, 1060, 1035, 969, 900 cm^{-1}; eims *m/z* $[M-Me]^+$ 253 (40), $[M-H_2O]^+$ 250 (5), $[M-H_2O-Me]^+$ 235 (5), $[M-2H_2O]^+$ 232 (6), 101 (100), 43 (60); ^1H nmr see Table 1; ^{13}C nmr see Table 2.

5α-Hydroxy-7αH-eudesma-4(15),11(13)-dien-12-oic acid [**5**].—Isolated as the methyl ester **9**: colorless oil, $[\alpha]^{24}D$ +66°, $[\alpha]^{24}_{578}$ +67°, $[\alpha]^{24}_{546}$ +82°, $[\alpha]^{24}_{435}$ +140° (*c* = 0.09, $CHCl_3$); ir ν max 3450 (OH), 1712 (ester C=O), 1690, 1635, 1618, 1430, 1230, 1140, 960, 900 cm^{-1}; eims *m/z* $[M]^+$ 264 (41), $[M-Me]^+$ 249 (8), $[M-H_2O]^+$ 246 (4), $[M-MeOH]^+$ 232 (100), 217 (26), 204 (37), 189 (30), 161 (22), 137 (52), 109 (49), 95 (69), 91 (56), 67 (43), 55 (35); hrms found 264.1730, calcd for $C_{16}H_{24}O_3$, 264.1725; ^1H nmr see Table 1; ^{13}C nmr see Table 2.

All known compounds were identified by comparison (nmr, tlc) with authentic samples from our collection.

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LITERATURE CITED

1. J. Vallès Xirau, *Bol. Soc. Broteriana, Sér. 2*, **60**, 5 (1987).
2. J. Delgado Gomis, J.A. Marco, J.R. Pedro, E. Seoane, J. Sánchez Parareda, and J.M. Sendra, *Phytochemistry*, **18**, 1523 (1979).
3. J.A. Marco, J.F. Sanz, and M. Carda, *Phytochemistry*, **28**, 2505 (1989).
4. J.F. Sanz, G. Castellano, and J.A. Marco, *Phytochemistry*, **29**, 541 (1990).
5. G. Shtacher and Y. Kashman, *J. Med. Chem.*, **13**, 1221 (1970).
6. F. Bohlmann, J. Jakupovic, and M. Lonitz, *Chem. Ber.*, **110**, 301 (1977).
7. W. Herz, H. Chikamatsu, and L.R. Tether, *J. Org. Chem.*, **31**, 1632 (1966).
8. J.A. Marco, *Phytochemistry*, **28**, 3121 (1989).
9. A.H. Meriçli, J. Jakupovic, F. Bohlmann, B. Damadyan, N. Ozhatay, and B. Çubukçu, *Planta Med.*, **54**, 447 (1988).
10. I. Fernández, B. García, and J.R. Pedro, *Tetrahedron*, **43**, 805 (1987).
11. J.A. Marco, O. Barberá, S. Rodríguez, C. Domingo, and J. Adell, *Phytochemistry*, **27**, 3155 (1988).
12. R.S. Harapanhalli, *J. Chem. Soc., Perkin Trans. 1*, 2633 (1988), and references therein.
13. M. Ando and K. Takase, *Tetrahedron*, **33**, 2785 (1977).
14. F.S. El-Feraly, D.A. Benigni, and A.T. McPhail, *J. Chem. Soc., Perkin Trans. 1*, 355 (1983).
15. R.G. Kelsey and F. Shafizadeh, *Phytochemistry*, **18**, 1591 (1979).
16. R. Segal, I. Feuerstein, and A. Danin, *Biochem. Syst. Ecol.*, **15**, 411 (1987), and references therein.

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