Phytochemistry, Vol. 29, No. 9, pp. 2913–2917, 1990.
Printed in Great Britain.

0031-9422/90 $3.00+0.00

SESQUITERPENE LACTONES FROM *ARTEMISIA CAERULESCENS* SUBSP. *GARGANTAE*

JUAN F. SANZ and J. ALBERTO MARCO

Departamento de Química Orgánica, Universidad de Valencia, E-46100 Burjasot, Valencia, Spain

(*Received in revised form* 19 *January* 1990)

Key Word Index—*Artemisia caerulescens* subsp. *gargantae*; Compositae; Anthemideae; sesquiterpenes; sesquiterpene lactones; germacranolides; eudesmanolides, shonachalin B.

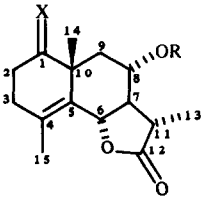
Abstract—Extraction of aerial parts of *Artemisia caerulescens* subsp. *gargantae* and chromatographic separation yielded two new eudesmane ketones and a new eudesmanolide, in addition to several known compounds. Chemical and spectroscopic evidence shows that the structure of shonachalin B has to be corrected.

INTRODUCTION

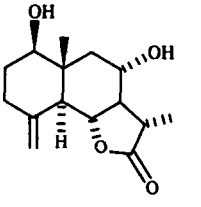
We recently reported the isolation of two new eudesmanolides, gargantolide (**1**) and 1-epigargantolide (**2**), from the aerial parts of *A. caerulescens* L. subsp. *gargantae* Vallès-Xirau et Seoane-Camba [1]. Because small amounts of further sesquiterpenes were indicated by some of the ^{1}H NMR spectra of crude fractions, we have now reinvestigated the plant to isolate these minor terpenoid metabolites. In the present work, we wish to report the isolation of the new eudesmane ketones 1β-hydroxy-α-cyperone (**8**) and the endoperoxide **9**, as well as the new eudesmanolide **10**. Furthermore, we have isolated the known sesquiterpene lactones 8α-hydroxytaurin (**3**) [2], artapshin (**4**) [3, 4], gallicin (**5**) [5], shonachalin A (**6**) [4, 6, 7], its 1-dehydroderivative (**7**) [4, 7] and phloroacetophenone 2,4-dimethyl ether (brevifolin, xanthoxylin) [8].

RESULTS AND DISCUSSION

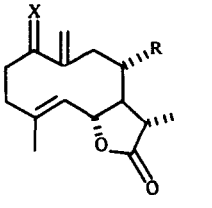
Compound **8** displayed a strong IR band at 1640 cm^{-1}, which suggests the presence of a conjugated ketone, this being confirmed by the UV band at 250 nm. The mass spectrum (EI) showed a molecular peak at *m/z* 234.1619, which agrees with a molecular formula $C_{15}H_{22}O_2$. This formula accounts for one carbonyl group, one C=C and two further unsaturations, possibly two rings. The ^{1}H NMR spectrum (Table 1) was very similar to that of the eudesmane ketone α-cyperone [9]. The multiplet at δ4.78 is the signal from the olefinic protons of the isopropenyl residue, which also gives rise to the methyl double doublet at δ1.78 ($J = ca$ 1 Hz). Irradiation of the multiplet at δ4.78 transforms, as expected, the latter signal into a sharp singlet. The other olefinic methyl group appears at δ1.73 (*d*, $J = 1.5$ Hz), whereas the singlet of the angular methyl group in the eudesmane framework is located at δ1.18. An additional signal is visible at δ3.83 as a double doublet ($J = 13$, 5.5 Hz). The position and shape of this signal are typical of an axial proton geminal to a hydroxyl group at either C-1 or C-9 of the eudesmane system. Irradiation of this signal produces the collapse of two double doublets at δ2.64 and 2.56 to two doublets with $J = 16.5$ Hz. Because these signals obviously origin-



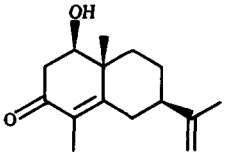
1 X = H,βOH, R = Ac
2 X = H,αOH, R = Ac
3 X = O, R = H



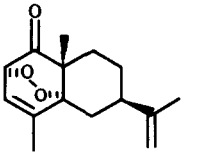
4



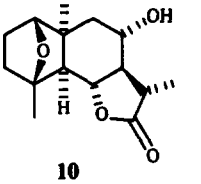
5 X = H,βOH, R = H
6 X = H,βOH, R = OH
7 X = O, R = OH



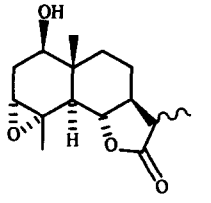
8



9



10



11a 11αH
11b 11βH

ate in the α-ketonic methylene group (C-2), we conclude that the hydroxyl is at C-1β. Further decoupling and NOE experiments allow the definitive establishment of the carbon framework and the assignment of all signals in the spectrum, as well as the complete stereochemistry. The ^{13}C NMR spectrum (Table 2) is in good agreement with the proposed structure. The signals were assigned by two-dimensional, heteronuclear shift correlation.

A few years ago structure **8** was assigned to a compound isolated from roots of *Senecio bracteolatus* [10].

Table 1. ^{1}H NMR data of compounds **8–10**, **11a** and **11b***

H	8	9	10	11a	11b
1	3.83 *dd*	—	3.72 *br d*	3.41 *dd*	3.42 *dd*
2α	2.64 *dd*	—	1.59 *m*	2.43 *ddd*	2.44 *ddd*
2β	2.56 *dd*	4.50 *d*	1.71 *dddd*	1.75 *ddd*	1.78 *ddd*
3α	—	6.28 *dq*	1.99 *ddd*	—	—
3β	—		1.59 *m*	3.00 *dd*	3.01 *dd*
5	—	—	1.53 *d*	1.79 *d*	1.77 *d*
6α	2.79 *ddd*	1.90 *m*†	—	—	—
6β	2.08 *ddd*	1.90 *m*†	3.82 *dd*	4.13 *dd*	3.92 *dd*
7	2.02 *br dddd*	2.48 *br dddd*	1.90 *ddd*	2.02 *dddd*	1.56 *dddd*
8α	1.75 *m*	1.90 *m*†	—	1.71 *dddd*	1.90 *m*
8β	1.59 *dddd*	1.50 *m*	4.17 *br dd*	1.55 *dddd*	1.50 *m*
9α	1.35 *ddd*	1.90 *m*†	1.38 *br d*	1.16 *ddd*	1.14 *ddd*
9β	2.16 *ddd*	1.90 *m*†	2.15 *br dd*	1.88 *ddd*	1.90 *m*
11	—	—	2.37 *dq*	2.63 *dq*	2.30 *dq*
12	4.78 *m*	4.77 *m*	—	—	—
13	1.78 *dd*	1.75 *br s*	1.36 *d*	1.19 *d*	1.22 *d*
14	1.18 *s*	1.13 *s*	1.31 *s*	0.90 *s*	0.92 *s*
15	1.73 *d*	1.93 *d*	1.45 *s*	1.46 *s*	1.46 *s*

*At 400 MHz in $CDCl_3$ (27°).

†Strong signal overlapping in the range δ2.00–1.70.

Coupling constants in Hz: **8** $J_{1,2\alpha}=5.5$; $J_{1,2\beta}=13$; $J_{2\alpha,2\beta}=16.5$; $J_{6\alpha,6\beta}=14$; $J_{6\beta,15}=1.5$; $J_{6\alpha,7}=2.5$; $J_{6\beta,7}=12$; $J_{7,8\alpha}=3.5$; $J_{7,8\beta}=J_{8\beta,9\alpha}=J_{8\alpha,8\beta}=J_{9\alpha,9\beta}=13.5$; $J_{8\alpha,9\alpha}=4$; $J_{8\alpha,9\beta}=3$; $J_{8\beta,9\beta}=3.5$; $J_{12(12'),13}=ca$ 1. **9** $J_{2,3}=6.5$; $J_{3,15}=2$; $J_{6\alpha,7}=J_{7,8\alpha}=4$; $J_{6\beta,7}=J_{7,8\beta}=13$; $J_{7,12(12')}<1$. **10** $J_{1,2\alpha}=ca$ 0; $J_{1,2\beta}=5$; $J_{2\alpha,2\beta}=J_{3\alpha,3\beta}=13$; $J_{2\alpha,3\alpha}=8.5$; $J_{2\beta,3\beta}=12$; $J_{2\beta,3\alpha}=4.5$; $J_{5,6}=10$; $J_{6,7}=J_{7,11}=12$; $J_{7,8}=8$; $J_{8,9\alpha}=ca$ 0; $J_{8,9\beta}=7$; $J_{9\alpha,9\beta}=15$; $J_{11,13}=7$. **11a** $J_{1,2\alpha}=6.5$; $J_{1,2\beta}=10$; $J_{2\alpha,2\beta}=15.5$; $J_{2\alpha,3}<1$; $J_{2\beta,3}=3$; $J_{5,6}=11.5$; $J_{6,7}=11$; $J_{7,8\alpha}=J_{8\beta,9\beta}=3.5$; $J_{8\alpha,9\alpha}=4$; $J_{7,8\beta}=J_{8\alpha,8\beta}=J_{8\beta,9\alpha}=J_{9\alpha,9\beta}=13$; $J_{8\alpha,9\beta}=3$; $J_{7,11}=J_{11,13}=7.5$. **11b** $J_{1,2\alpha}=6.5$; $J_{1,2\beta}=10.5$; $J_{2\alpha,2\beta}=15.5$; $J_{2\alpha,3}<1$; $J_{2\beta,3}=3$; $J_{5,6}=11.5$; $J_{6,7}=10$; $J_{7,8\alpha}=3$; $J_{8\alpha,9\alpha}=4$; $J_{8\beta,9\alpha}=J_{9\alpha,9\beta}=13$; $J_{7,11}=J_{7,8\beta}=12$; $J_{11,13}=7$.

Table 2. ^{13}C NMR data of compounds **3**, **6–10**, **11a** and **11b***

C	3	6†	7†	8	9	10	11a	11b
1	212.41	78.15	203.75	74.44	206.29	84.96	73.67	73.63
2	35.56	32.81	37.14	42.35	78.42	25.64	30.94	30.89
3	33.14	36.06	35.88	197.47	119.71	36.31	60.86	60.79
4	128.03	145.56‡	141.57	129.53	151.64[b]	86.03	57.56	57.47
5	128.03	122.44	126.08	161.87	85.28	58.96	52.62	52.02
6	78.48	76.60	77.04	32.81	29.73[a]	76.35	79.58	80.53
7	58.75	57.66‡	57.69	45.06	38.53	52.21	48.97	53.05
8	69.59	73.74	71.97	26.50	24.84	70.78	20.01	22.59
9	44.42	42.74‡	41.17	37.68	29.47[a]	41.59	34.45	34.42
10.	47.66	148.11	146.75	41.26	44.74	46.87	39.98	40.09
11	40.82	41.85	40.27	148.92	148.73[b]	41.64	38.15	40.66
12	178.34	178.90	178.67	109.40	109.49	179.24	179.82	179.16
13	14.29	16.20	16.36	20.63	19.97[c]	14.00	9.63	12.40
14	24.87	111.66	123.92	16.25	20.91[c]	25.58	11.77	11.74
15	19.72	17.85	17.08	11.00	17.72[c]	18.32	21.65	21.52

*At 50.32 MHz in $CDCl_3$ (27°), unless otherwise stated.

†At 57°.

‡Broadened signal.

[a,b,c] The signals with these superscripts may be interchanged within the same column.

The published ^{1}H NMR data, however, do not agree with those of our compound. More specifically, in our opinion, the position of the *gem*-hydroxylic signal at δ4.30 in the ^{1}H NMR spectrum of the mentioned compound [10] is at too low a field. Because in view of the available spectral data, our structure can now be taken for granted, we believe that the structure of the compound from *Senecio bracteolatus* should be revised. This latter product may be an isomer closely related to **8**, possibly the 2α-hydroxy derivative of α-cyperone (see Acknowledgements).

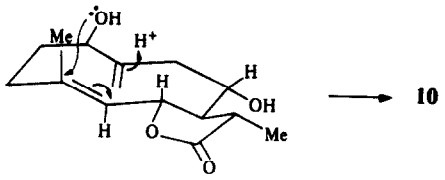
Compound **9**, isolated in a small amount, is also a ketone, as deduced from the IR band at 1730 cm^{-1}. The mass spectrum showed a molecular peak at *m/z* 248.1412, consistent with a molecular formula $C_{15}H_{20}O_3$. The multiplet at δ4.77 and the olefinic methyl signal (*br s*) at δ1.75 again suggest an eudesmane derivative with an isopropenyl residue at C-7, as in compound **8**. The idea of an eudesmane skeleton is further supported by the methyl singlet at δ1.13. In the olefinic region, a distinct double quadruplet (J = 6.5, 2 Hz) appeared at δ6.28. On irradiation at an olefinic methyl doublet (J = 2 Hz) at δ1.93, the former signal collapsed to a doublet with J = 6.5 Hz. Moreover, saturation of a doublet (J = 6.5 Hz) at δ4.50 transformed the signal at δ6.28 into a quadruplet with J = 2 Hz. These experiments prove the presence of the fragment –CO–CH(OR)–CH=C–Me. In the ^{13}C NMR spectrum (Table 2), two signals are assignable to oxygenated carbon atoms. One of them (δ78.42) correlates precisely with the ^{1}H doublet at δ4.50, as established via selective decoupling, and is thus assigned to C-2 of the eudesmane system. The other one (δ85.28) originates from a quaternary carbon atom and is thus assigned to C-5. In view of the molecular formula with three oxygen atoms, the existence of a peroxide bridge between C-2 and C-5 seems reasonable. The strong overlapping of absorptions in the range 2.00–1.70 ppm, however, prevents a complete assignment of all signals. Inspection of molecular models reveals that H-15 would be in spatial proximity to H-6 only when the peroxide bridge is located on the α-side of the eudesmane framework, as expressed by structure **9**, whereas a β-peroxide bridge would situate H-15 close to H-7. Although a NOE experiment was performed in order to answer this question, it did not yield reliable results due to the mentioned overlapping of signals. The proposed α-peroxide stereochemistry is based on the similarity of the position and shape of several signals (H-2, H-3 and H-15) to those observed in structurally related 2,5-peroxyeudesmanolides of unambiguous stereochemistry, which we recently isolated from other plant sources (unpublished results from our group).

Compound **10**, mp 131–132°, is a hydroxylactone, IR ν cm^{-1}: 3450, 1760, MS *m/z* 266.1524 ($C_{15}H_{22}O_4$), and it has an ^{1}H NMR spectrum which also suggests an eudesmane framework (Table 1). No olefinic signals are visible, but rather three absorptions from hydrogens geminal to oxygen functions. One of these is assumed to originate in the lactonic hydrogen (δ3.82, *dd*, J = 12, 10 Hz) and is assigned to H-6 (*trans*-diaxial relationship to H-5 and H-7). The other two are a broad double doublet at δ4.17 (J = 8, 7 Hz) and a slightly broadened doublet at δ3.72 (J = 5 Hz). Taking the chemical shift into account, this last signal was first thought to come from an epoxide group, and the structure of an epoxydihydrosantamarin (**11a** or **11b**) was thus proposed for the compound.

A careful review of the literature showed that one of these two latter structures had already been proposed for shonachalin B, a sesquiterpene lactone isolated from *Artemisia fragrans* [11]. In fact, the physical and spectral constants given in this last paper for shonachalin B (mp 127–129°) are almost coincident with those of our compound, though the identity of both products was not completely sure, due to the unavailability of an authentic sample of shonachalin B. When we synthesized lactones **11a** and **11b**, however, by peracid epoxidation of the corresponding C-11 epimeric dihydrosantamarins [4, 12], none of the obtained products was identical with the natural product (see Tables 1 and 2 and the physical constants in the Experimental). We then carefully re-examined the ^{1}H and ^{13}C NMR spectral data of our compound and performed NOE experiments in order to clarify the stereochemical aspects of its structure. Subsequently, we propose structure **10** with a 1,4-ether bridge for the compound. The hydrogen connectivity is easily deduced from decoupling experiments. Irradiation of the signal at δ4.17 transformed a double triplet (J = 12, 8 Hz) at δ1.90 into a triplet (J = 12 Hz). Saturation of the signal at δ3.82 transformed it to a double doublet (J = 12, 8 Hz). This unambiguously establishes the fragment C-6 to C-8 as –CH(OR)–CH–CH(OH)–. Furthermore, irradiation at δ3.72 affected a complex signal at δ1.71. This signal is part of a methylene group because it correlates, together with another complex multiplet at δ1.59, with a methylene carbon signal at δ25.66, as established by two-dimensional, heteronuclear shift correlation. This signal is thus assigned to C-2 in the eudesmane framework.

Nonlactonic eudesmanes with similar 1,4-ether bridges have been isolated before from *Verbesina glabrata* [13] and from *Ambrosia artemisioides* [14]. The stereochemical results deduced from NOE experiments pointed, however, to compound **10** having a different ring fusion stereochemistry. For instance, H-14, gave clear NOE effects with H-1, H-3α, H-5 and H-7. This cannot be explained when we assume the usual eudesmane stereochemistry with a β-oriented angular methyl group. Other significant NOE effects were observed between H-6, H-8, and H-11, between H-6 and H-15, and between H-6 and H-9β. This last effect implies that the corresponding six-membered ring adopts a boat conformation. Molecular models reveal that this is indeed the case and that the dihedral angle H-8–C–C–H-9α has a value of about 90°, as expected from $J_{8,9\alpha}$ being practically zero. Moreover, inspection of the models further reveals that the epimer at C-10 (β-oriented methyl group) can be expected to be appreciably tense.

The synthesis of compound **10** by acid-catalysed cyclization of shonachalin A(**6**) (Experimental), as described for the structurally related compound **5** [5], confirmed the structure. Interestingly, eudesmanes like artapshin (**4**), which could also be expected to arise in the reaction [5], were formed only in trace amounts. In order to explain the observed stereochemical course, it must be assumed that the molecule of shonachalin A adopts a double-boat conformation during the cyclization (see Scheme 1). Similar double boat geometries have been proposed to explain the cyclization of 4,5-epoxygermacranolides to give *trans*-guaianolides [15]. The result we have observed, however, is in a marked contrast with that published for the structurally related compound **5**, in which a 1,4β-epoxyeudesmanolide with a β-angular



10

methyl group is reported to be formed [5].

Artemisia caerulescens is included in sect. *Seriphidium* of the genus *Artemisia* [16]. Two subspecies have been already investigated, which yielded diverse 11,13-didhydroeudesman-12,6-olides [17, 18], as is usual in members of the mentioned section [16, 19]. In addition to the lactones with this framework, we have now found 11,13-dihydrogermacran-12,6-olides for the first time in this species. Furthermore, it is the first time that eudesmanes with a 10α-angular methyl group are reported in the genus *Artemisia*.

EXPERIMENTAL

NMR spectra were measured at the frequencies indicated in the Tables. IR spectra were recorded as KBr pellets or liquid films. Mass spectra were run at 70 eV on the EI mode. Optical rotations were determined in $CHCl_3$ solution. Column chromatography (CC) was made on silica gel Merck. HPLC was performed in the reverse phase mode (detection by refractive index, LiChrosorb RP-8 or RP-18, 250 × 8 mm).

Plant material. The plant material was collected in the same geographical location mentioned in our former paper [1].

Extraction and chromatography. The air-dried plant material (aerial parts, 600 g) was finely ground and extracted twice at room temp. with hexane–Et_2O–MeOH (1:1:1) (2 × 6 l, 5 days). The extract was defatted by pptn from cold MeOH (−15°). After filtration and elimination of MeOH *in vacuo*, the residue (15 g) was prefractionated by coarse CC on silica gel, A, hexane–Et_2O (9:1); B, hexane–Et_2O (1:1); C, hexane–Et_2O (1:3); D, Et_2O and E, Et_2O–MeOH (9:1).

Fraction A (0.42 g) consisted mainly of waxes and volatile terpenes. Repeated CC on silica gel (hexane–Et_2O, 2:1) yielded brevifolin (35 mg). Fraction B (1.80 g) contained a high percentage of sterols and other unpolar, less relevant components. After extensive CC on silica gel (first toluene–Et_2O, 9:1; then hexane–EtOAc, 9:1), compound **9** (5 mg) was isolated.

Fraction C (0.78 g) was fractionated by CC on silica gel ($CHCl_3$–Et_2O mixtures). This gave three intermediate fractions, C-1 to C-3 (in order of increasing polarity), which were further purified by prep. TLC (hexane–Et_2O mixtures) and HPLC (MeOH–H_2O, 13:7; *ca* 130 bar). This yielded compounds **2** (12 mg) from C-1, **1** (40 mg) from C-2 and **8** (14 mg) from C-3.

Fraction D (0.33 g) was submitted to CC on silica gel ($CHCl_3$–Et_2O, 1:1). After inspection by TLC, three main fractions, D-1 to D-3, were selected and further purified as with fraction C. These fractions yielded, respectively, compounds **5** (8 mg), **3** (10 mg) and **7** (9 mg).

Fraction E (2.30 g) was subjected to repeated CC on silica gel (Et_2O–MeOH, 30:1, then CH_2Cl_2–Et_2O–MeOH, 7:7:1). The intermediate fractions were further purified by HPLC (MeOH–H_2O, 1:1; *ca* 200 bar). This gave compounds **10** (6 mg), **6** (40 mg) and **4** (8 mg).

1β-Hydroxy-α-cyperone (*1β-hydroxyeudesma-4,11-dien-3-one*) (**8**). Needles, mp 121–123° (pentane–Et_2O); $[\alpha]_D^{23}$ −75°, $[\alpha]_{578}^{23}$ −78°, $[\alpha]_{546}^{23}$ −87°, $[\alpha]_{435}^{23}$ −105° ($CHCl_3$; *c* 0.94). IR ν_{max}^{KBr} cm^{-1}: 3350 (OH), 1640 (ketone C=O), 1601 (conj. C=C), 1145, 1078, 1025, 865. UV λ_{max}^{MeOH} nm: 250. EIMS (probe) *m/z* (rel. int.): 234.1619 ($[M]^+$ (54), 219 $[M-Me]^+$ (10), 216 $[M-H_2O]^+$ (8), 206 $[M-CO]^+$ (8), 191 $[M-Me-CO]^+$ (38), 190 (39), 175 (25), 147 (62), 137 (84), 122 (50), 109 (55), 69 (86), 55 (100). Calc. for $C_{15}H_{22}O_2$. [M] 234.1619. For NMR data, see Tables 1 and 2.

2α,5α-Peroxyeudesma-3,11-dien-1-one (**9**). Gum, $[\alpha]_D^{23}$ +239°, $[\alpha]_{578}^{23}$ +258°, $[\alpha]_{546}^{23}$ +309°, $[\alpha]_{435}^{23}$ +752° (*c* 0.22; $CHCl_3$). IR ν_{max}^{Film} cm^{-1}: 1730 (ketone C=O). EIMS (probe) *m/z* (rel. int.): 248.1412 $[M]^+$ (6), 233 $[M-Me]^+$ (5), 232 $[M-O]^+$ (18), 220 $[M-CO]^+$ (7), 214 (9), 205 (17), 189 (95), 111 (100), 95 (88), 69 (70), 55 (71). Calc. for $C_{15}H_2O_3$, [M] 248.1412. For NMR data, see Tables 1 and 2.

8α-Hydroxy-1,4β-epoxy-10-epieudesman-5α,6β,7α,11βH-12,6-olide (**10**). Needles, mp 131–132° (pentane–Et_2O), $[\alpha]_D^{23}$ +3.8°, $[\alpha]_{578}^{23}$ +3.8°, $[\alpha]_{546}^{23}$ +4.2°, $[\alpha]_{435}^{23}$ +7.9° ($CHCl_3$; *c* 0.4). IR ν_{max}^{KBr} cm^{-1}: 3450 (OH), 1760 (lactone C=O), 1125, 1025, 975, 726. EIMS (probe) *m/z* (rel. int.): 266.1524 $[M]^+$ (10), 251 $[M-Me]^+$ (1), 248 $[M-H_2O]^+$ (6), 230 $[M-2H_2O]^+$ (2), 222 $[M-CO_2]^+$ (12), 208 (18), 194 (10), 181 (12), 175 (11), 163 (18), 135 (19), 107 (26), 95 (39), 71 (50), 55 (46), 43 (100). Calc. for $C_{15}H_{22}O_4$, [M] 266.1518. For NMR data, see Tables 1 and 2.

Acid-catalysed cyclization of **6** *to give* **10**. Compound **6** (30 mg) was dissolved in CH_2Cl_2 (3 ml) and treated at room temp. with camphorsulphonic acid (15 mg). After standing for 4 hr, the mixture was directly subjected to CC on silica gel (Et_2O–MeOH, 50:1), yielding compound **10** (9 mg) as the main product, together with minor impurities.

2,4-Dimethoxy-6-hydroxyacetophenone (*brevifolin, xanthoxylin*). Needles, mp 80–81° (hexane), lit. [8] mp 82–83° (dil. EtOH). ^1H NMR ($CDCl_3$): δ 14.00 (*s*, OH), 6.03 (*d*, *J* = 2.4 Hz), 5.90 (*d*, *J* = 2.4 Hz), 3.83 (*s*, 3H, OMe), 3.80 (*s*, 3H, OMe), 2.58 (*s*, 3H, COMe). ^{13}C NMR ($CDCl_3$): δ 203.13 (*s*), 167.56 (*s*), 166.07 (*s*), 162.88 (*s*), 105.95 (*s*), 93.45 (*d*), 90.68 (*d*), 55.51 (2 × *q*), 32.90 (*q*).

11α,13-Dihydrosantamarin 3,4α-epoxyde (**11a**). Obtained by peracid oxidation of 11α,13-dihydrosantamarin [4] in CH_2Cl_2 at room temp. White solid, mp 194–196° (EtOAc), $[\alpha]_D^{23}$ +119°, $[\alpha]_{578}^{23}$ +125°, $[\alpha]_{546}^{23}$ +141°, $[\alpha]_{435}^{23}$ +241°, ($CHCl_3$; *c* 2). IR ν_{max}^{KBr} cm^{-1}: 3460 (OH), 1760 (lactone C=O), 1260, 1200, 1165, 1035, 995, 965, 785. EIMS (probe) *m/z* (rel. int.): 266.1518 $[M]^+$ (6), 251 $[M-Me]^+$ (5), 248 $[M-H_2O]^+$ (3), 222 (2), 193 (42), 163 (20), 135 (17), 121 (12), 95 (100), 55 (32), Calc. for $C_{15}H_{22}O_4$, [M] 266.1518. For NMR data, see Tables 1 and 2.

11β,13-Dihydrosantamarin 3,4α-epoxyde (**11b**). Obtained by peracid oxidation of 11β,13-dihydrosantamarin [12] in CH_2Cl_2 at room temp. White needles, mp 188–190° (EtOAc), lit. [12] mp 195° (EtOH); $[\alpha]_D^{23}$ +60°, $[\alpha]_{578}^{23}$ +63°, $[\alpha]_{546}^{23}$ +72°, $[\alpha]_{435}^{23}$ +122° ($CHCl_3$; *c* 1.4). IR ν_{max}^{KBr} cm^{-1}: 3470 (OH), 1765 (lactone C=O), 1155, 1135, 1065, 1040, 990, 790 cm^{-1}. EIMS (probe) *m/z* (rel. int.): 266.1518 $[M]^+$ (5), 251 $[M-Me]^+$ (4), 248 $[M-H_2O]^+$ (4), 223 (3), 193 (30), 163 (21), 135 (21), 121 (11), 71 (59), 57 (100). Calc. for $C_{15}H_{22}O_4$, [M] 266.1518. For NMR data, see Tables 1 and 2.

All known compounds were compared with authentic samples from our collection.

Acknowledgements—The authors wish to express their gratitude to Dr J. Jakupovic (Technical University, Berlin), for helpful discussions in relation to the structure of compounds **8** and **10** and for the measurement of the 400 MHz ^1H NMR spectra.

REFERENCES

1. Sanz, J. F. and Marco, J. A. (1990) *Planta Med.* **56**, (in press).
2. Meriçli, A. H., Jakupovic, J., Bohlmann, F., Damadyan, B., Ozhatay, N. Çubukcu, B. (1988) *Planta Med.* **54**, 447.

3. Serkerov, S. V. and Aleskerova, A. N. (1983) *Khim. Prir. Soedin.* 578.
4. Marco, J. A. (1989) *Phytochemistry* **28**, 3121.
5. González, A. G., Bermejo, J., Mansilla, H., Galindo, A., Amaro, J. M. and Massanet, G. M. (1978) *J. Chem. Soc., Perkin Trans I* 1243.
6. Serkerov, S. V. and Aleskerova, A. N. (1985) *Khim. Prir. Soedin.* 196.
7. Rustaiyan, A., Zare, K., Ganji, T. M. and Sadri, H. A. (1989) *Phytochemistry* **28**, 1535.
8. Karrer, W. (1958) *Konstitution und Vorkommen der organischen Pflanzenstoffe*, p. 181. Birkhäuser, Basel.
9. Devon, T. K. and Scott, A. I. (1972) *Handbook of Naturally Occurring Compounds* Vol. II. Academic Press, New York.
10. Bohlmann, F., Jakupovic, J., Warning U., Grenz, M., Chau-Thi, T. V., King, R. M. and Robinson, H. (1986) *Bull. Soc. Chim. Belg.* **95**, 707.
11. Serkerov, S. V. and Aleskerova, A. N. (1985) *Khim. Prir. Soedin.* 636.
12. Ando, M. and Takase, K. (1977) *Tetrahedron* **33**, 2785.
13. Jakupovic, J., Ellmauerer, E., Jia, Y., Bohlmann, F., Dominguez, X. A. and Schmeda-Hirschmann, G. (1987) *Planta Med.* **53**, 39.
14. Jakupovic, J., Jaensch, M., Bohlmann, F. and Dillon, M. O. (1988) *Phytochemistry* **27**, 3551.
15. González, A. G., Galindo, A. and Mansilla, H. (1989) *Heterocycles* **28**, 529.
16. Kelsey, R. G. and Shafizadeh, F. (1979) *Phytochemistry* **18**, 1591.
17. Greger, H., Zdero, C. and Bohlmann, F. (1986) *Phytochemistry* **25**, 891.
18. San Feliciano, A., Medarde, M., Poza, M. T. and Miguel del Corral, J. M. (1986) *Phytochemistry* **25**, 1757.
19. Seaman, F. C. (1982) *Bot. Rev.* **48**, 121.