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SESQUITERPENE LACTONES AND OTHER CONSTITUENTS OF *SESELI VAYREDANUM*

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Key Word Index—*Seseli vayredanum*; Umbelliferae; sesquiterpenes; phenylpropanoids; acetylene derivatives; sterols; triterpenes; diterpenes.

Abstract—Twelve sesquiterpenes, seven phenylpropanoids, two sterols, one triterpene, one diterpene and one polyacetylenic compound were identified from the most polar fractions of the hexane extract of the aerial parts of *Seseli vayredanum*. Twelve of them are new natural products: 1β-senecioyloxy-5βH,6αH,7αH,10αMe,11αH-eudesm-3-en-6,12-olide, 1β-senecioyloxy-5βH,6αH,7αH,10αMe,11αH-eudesma-2,4(15)-dien-6,12-olide, 2α-angeloyloxy-5β-hydroxy-7αH,10βMe-eudesm-3-en-1-one, 8α-angeloyloxy-10β-hydroxy-slov-3-en-6,12-olide, 10β-hydroxy-8α-senecioyloxy-slov-3-en-6,12-olide, 2-oxo-8α-senecioyloxy-5βH,6αH-guai-1(10),3,7(11)-trien-6,12-olide, 8β-angeloyloxy-2-oxo-5βH,6αH-guai-1(10),3,7(11)-trien-6,12-olide, 2-oxo-8β-senecioyloxy-5βH,6αH-guai-1(10),3,7(11)-trien-6,12-olide, 10β-acetoxy-8α-angeloyloxy-3β-hydroxy-1βH,6αH,7αH,11αH-guai-4-en-6,12-olide, *erythro*-1-hydroxy-2-angeloyloxy-3',4'-methylenedioxy-5'-methoxy-1-phenylpropane, *threo*-1-hydroxy-2-angeloyloxy-3',4'-methylenedioxy-5'-methoxy-1-phenylpropane and 1-hydroxy-3',4'-methylenedioxy-2',5'-dimethoxy-1-phenylpropane. Their structures were established by spectroscopic methods and chemical correlations.

INTRODUCTION

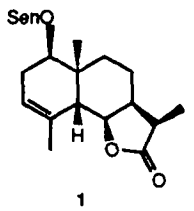
Several sesquiterpenes and phenylpropanoids were reported [1] to occur in the aerial parts of *Seseli vayredanum* (*Athamanta vayredana*) species endemic to southern Spain. Here, we report the results obtained from the study of the components not previously identified. Twenty-four compounds were characterized including 12 new natural products and the known compounds β-eudesmol [2], 2-angeloyloxylatifolone [3], 2'-methoxylatifolone [4], lupeol [5], phytol [6], stigmasta-4,22-dien-3-one [7], sitosterol [8] and falcarindiol [9].

RESULTS AND DISCUSSION

Compounds **1** and **2** were identified as components of a 3:1 mixture which could not be resolved by the usual chromatographic techniques. In the IR spectrum the mixture showed bands of a γ-lactone (1760 cm^{-1}) and an α,β-unsaturated ester (1706 cm^{-1}). The ^1H NMR and ^{13}C NMR spectra (Tables 1 and 2) indicated the presence of a senecioyl group in both compounds. The GC–mass spectral analysis of the mixture did not mark the molecular peak of either of the compounds. The highest peak in **1** appeared at *m/z* 232 as a result of the loss of senecioic acid $[M-HOSen]^+$, which suggested a molecular formula $C_{20}H_{28}O_4$. Analysis of the NMR spectra (Tables 1 and 2) led us to assign to **1** the structure of 1-senecioyloxy-eudesm-3-en-6,12-olide. The stereochemistry represented in **1** was determined on the basis of the $^3J_{HH}$ values and the chemical shifts observed, in agreement with those described for similar compounds [10–13]. So the β disposition of the methyl Me-13 was determined on the basis of both the $J_{7,11}$ (7.4 Hz) and the chemical shifts of C-13 (δ10.3) and C-8 (δ18.8), which appeared shielded due to mutual γ interaction [14].

The hydrolysis of the mixture **1** plus **2** with 5% KOH–methanol and its subsequent relactonization in acid medium led to the formation of senecioic acid and the isolation of the hydroxylactone **3**. Epimerization of Me-13 was revealed by means of the $J_{7,11}$ value (12.7 Hz) and the chemical shift of C-13 (δ13.5). Another remarkable change observed in the ^{13}C NMR spectrum was the upfield shift experienced by Me-14 (δ15.5) with respect to the chemical shift in **1** ($\Delta\delta = -7.0$ ppm). These differences could be explained by a conformational change in the B ring of $B^{5,8} - T^{5,8}$ in **1** (structure A) to $^5C_8$ in **3** (structure B) [12].

The mass spectrum of **2** showed the highest peak at *m/z* 230 corresponding to the loss of senecioic acid $[M-HOSen]^+$ which suggests a molecular formula $C_{20}H_{26}O_4$. The ^1H (Table 1) and ^{13}C NMR (Table 2) spectra were very similar to those of **1**. However, the spectroscopic analysis of **2** revealed the presence of a diene system (C-2/C-3 and C-4/C-15) instead of the double bond on C-3/C-4. The $^3J_{HH}$ observed allowed us to propose the same relative stereochemistry as in **1**. On the other hand, the similarity found between **2** and the



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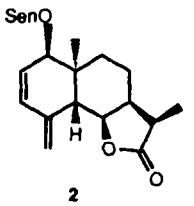

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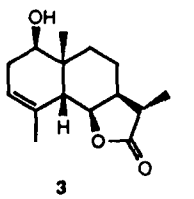

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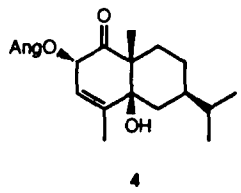

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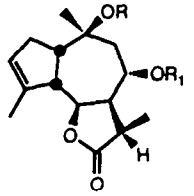
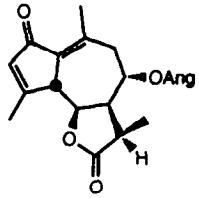


5 R = H R_1 = Ang

6 R = H R_1 = Sen

24 R = Ac R_1 = Ang



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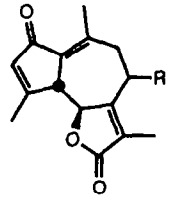
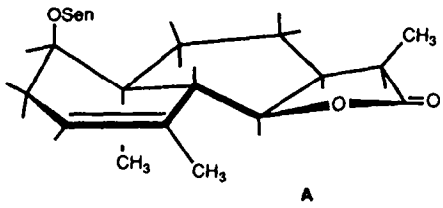


8 R = α-OAng

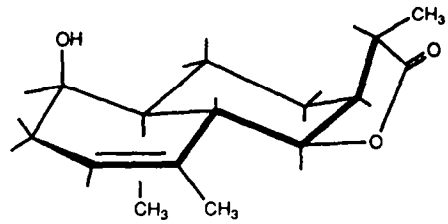
9 R = α-OSen

10 R = β-OAng

11 R = β-OSen



A



B

Table 1. ^{1}H NMR spectral data of **1**–**3** (300 MHz, TMS, $CDCl_3$)

H	1	2	3
1	4.63 *br d* (4.0)	4.78 *d* (5.8)	3.36 *br d* (4.4)
2α	2.37 *m*		
		5.80 *dd* (5.3, 9.6)	
2β	2.70 *m*		2.01 *m*
3	5.29 *m*	6.27 *d* (9.7)	5.31 *m*
5	2.49 *br dd* (1.3, 9.9)	2.67 *m*	
6	4.56 *dd* (6.1, 9.4)	4.76 *dd* (9.3, 7.2)	4.56 *dd* (7.3, 11.1)
7	2.70 *m*	2.67 *m*	1.95 *m*
9α		1.95 *dt* (5.4, 13.9)	
9β			1.95 *m*
11	2.83 *dq* (7.4, 7.4)	2.81 *dq* (7.4, 7.4)	2.56 *dq* (6.8, 12.7)
13	1.15 *d* (7.3)	1.22 *d* (7.4)	1.20 *d* (6.9)
14	0.94 *s*	0.86 *s*	0.77 *s*
15		5.37 *br s*	
	1.53 *d* (1.4)		1.83 *ddt* (1.6, 1.6, 1.6)
15'		5.21 *d* (2.6)	
OSen	5.63 *m*	5.63 *m*	
	2.12 *d* (1.3)	2.14 *d* (1.2)	
	1.93 *d* (1.3)	1.86 *d* (1.2)	

Values in parentheses are coupling constants in Hz.

Table 2. ^{13}C NMR spectral data of **1**–**3** (75 MHz, TMS, $CDCl_3$)

C	1	2	3
1	73.6 *d*	73.2 *d*	73.2 *d*
2	28.6 *t*	134.3 *d*	32.3 *t*
3	119.0 *d*	123.2 *d*	119.6 *d*
4	133.5 *s*	142.0 *s*	133.7 *s*
5	41.4 *d*	41.5 *d*	42.8 *d*
6	79.5 *d*	79.6 *d*	79.1 *d*
7	37.9 *d*[a]	38.0 *d*[a]	41.2 *d*
8	18.9 *t*	19.2 *t*	20.2 *t*
9	30.3 *t*	30.9 *t*	28.3 *t*
10	34.7 *s*	34.7 *s*	38.3 *s*
11	38.0 *d*[a]	37.8 *d*[a]	36.2 *d*
12	179.4 *s*	179.5 *s*	179.2 *s*
13	10.3 *q*	11.4 *q*	13.5 *q*
14	22.5 *q*[b]	22.3 *q*	15.5 *q*
15	22.1 *q*[b]	117.2 *t*	23.2 *q*
OSen	168.5 *s*	166.4 *s*	
	116.3 *d*	116.3 *d*	
	157.1 *s*	157.0 *s*	
	27.5 *q*	27.4 *q*	
	20.3 *q*	20.2 *q*	

[a,b]Signals may be interchanged within each column.

eudesmanolide oopodin [15] confirmed the structure and stereochemistry proposed.

The mass spectrum of **4** showed $[M]^+$ at *m/z* 334 in agreement with a molecular formula $C_{20}H_{30}O_4$. Its IR spectrum showed absorption bands due to a hydroxyl group (3531 cm^{-1}), a ketone (1739 cm^{-1}) and an α,β-unsaturated ester (1710 and 1644 cm^{-1}). The ^1H and ^{13}C NMR (Table 3) spectra indicated that **4** presented a structure of 2-angeloyloxy-eudesm-3-en-1-one, bearing a tertiary hydroxyl group on C-5 or C-7. Once the assignment of the signals of the ^{13}C NMR spectrum was completed (2D COSY and hetero-COSY experiments), the hydroxyl group was located on C-5, since C-4 appeared at δ 146.2, unshielded approximately 10 ppm with respect to other 3-eudesmenes as a result of the β-effect of the hydroxyl group. As to the relative stereochemistry of **4**, the existence of a NOE effect between Me-14 and H-2 led us to establish a *cis* disposition between them. The decalin system presented a *cis* fusion since the ^1H NMR spectrum in pyridine-d_5 showed strong unshieldings for Me-14 and H-2 ($\Delta\delta = \delta pyridine\text{-}d_5 - \delta_{CDCl_3} = 0.35$ and 0.54 ppm, respectively) which could be explained only if the hydroxyl group and those protons were disposed towards the same side of the molecule. Although there was no evidence for the configuration at C-7, a *cis* disposition between the isopropyl group and the Me-14 was proposed according to the biogenetic precedence given by the existence of other non-lactonic eudesmanes in *Seseli vayredanum* (β-eudesmol and α-selinene [1]) with the same stereochemistry.

Table 3. ^1H NMR and ^{13}C NMR spectral data of **4**

C	δ_H	δ_C
1		220.2 *s*
2	5.23 *d* (7.6)	75.7 *d*
3	5.66 *br d* (7.7)	119.7 *d*
4		146.2 *s*
5		82.3 *s*
6α	2.36 *m*	
		38.5 *t*
6β	2.05 *m*	
7	2.23 *m*	50.6 *d*
8α	2.36 *m*	
		29.1 *t*
8β	2.23 *m*	
9α	2.36 *m*	
		37.1 *t*
9β	2.05 *m*	
10		60.1 *s*
11	2.05 *m*	26.3 *d*
12	0.96 *d* (6.7)	21.1 *q*
13	1.03 *d* (6.7)	18.3 *q*
14	1.02 *s*	24.6 *q*
15	1.72 *d* (1.2)	26.1 *q*
OAng		166.1 *s*
		126.9 *s*
	5.98 *qq* (1.4, 7.1)	139.4 *d*
	1.94 *dq* (1.5, 7.1)	15.7 *q*
	1.86 *dq* (1.4)	20.8 *q*

Values in parentheses are coupling constants in Hz.

Compounds **5** and **6** were identified as a 1:2 mixture whose IR spectrum showed absorption bands of a hydroxyl group (3517 cm^{-1}). The ^1H NMR spectrum (Table 4) established the presence of a senecioyloxy group in the major compound and an angeloyloxy group in the minor one. The GC–mass spectral analysis revealed that it was a mixture of isomers, whose mass spectrum did not show the $[M]^+$ and whose highest peak appeared at *m/z* 248 corresponding to loss of angelic acid $[M - HOAng]^+$ for **5** and of senecioic acid $[M - HOSen]^+$ for **6**. The analysis of the ^1H NMR spectrum let us to establish that the minor component corresponded to **5** and the major one to **6**. This conclusion was achieved by comparing their spectroscopic data with those of 8α-angeloyloxy-10β-hydroxy-slov-3-en-6,12-olide, obtained by smooth saponification of the corresponding 10β-acetoxy derivative **24** [1].

The spectroscopic data of **7** were in accordance with those described for badkhysin isolated from *Ferula oopoda* [16, 17]. The structure of **7** was correlated with that compound by oxidation of **24** with *t*-butyl chromate.

The compounds **8** and **9** were isolated as a 4:1 mixture, whose GC–MS analysis indicated the $[M]^+$ at *m/z* 342 for both substances, in agreement with a molecular formula $C_{20}H_{22}O_5$. Their UV, IR and ^1H NMR spectra indicated that both molecules contained an α,β-unsaturated ester and a conjugated dienone system similar to **7**. In addition, the ^1H (Table 4) and ^{13}C NMR (Table 5) spectra of the mixture indicated the presence of angelate and senecioate esters for **8** and **9**, respectively. On the other hand, the main differences in the ^1H NMR spectrum of major compounds **8** and **7** lay in the absence in **8** of signals corresponding to H-7 and H-11, and in the unshielding of the signal corresponding to methyl Me-13 from δ 1.28 at 2.48 ppm. These data allowed us to identify **8** as shairidin isolated from *Ferula varia* [18]. The rest of the ^1H NMR signals corresponding to the minor compound were similar to those of **8**, except for the presence of a senecioate group on C-8, which led us to assign it the structure **9**.

Compounds **10** and **11** were also isolated as a 1:1 mixture with spectroscopic data very similar to those of a mixture of **8** and **9**, which led us to the conclusion that they were stereoisomers. The configurational change was located at the chiral centre C-8, whose acylating group now had the β-orientation, due to the differences observed both in the chemical shift in the ^1H NMR spectrum for H-8 (δ6.05 vs 5.50 for **10** and 6.00 vs 5.44 for **11**) and in the coupling constant $J_{8,9\alpha}$ (6.4 Hz vs 11.8 Hz for **10** and 6.0 Hz vs 11.8 Hz for **11**).

The IR, ^1H and ^{13}C NMR (Tables 4 and 5) spectra of **12** determined the presence of γ-lactonic, hydroxyl, acetoxy and angeloyloxy groups. The mass spectrum did not reveal the $[M]^+$, but showed peaks at *m/z* 246 and 228 corresponding to the loss of angelic and acetic acids $[M - HOAng - HOAc]^+$ and of angelic and acetic acids and water $[M - HOAng - HOAc - H_2O]^+$, respectively.

Table 4. ^{1}H NMR spectral data of **5–14** (300 MHz, TMS, $CDCl_3$)

H	5	6	7	8	9
1	2.37 *m*	2.37 *m*			
2	2.15 *m*	2.15 *m*			
3	5.46 *m*	5.46 *m*	6.09 *m*	6.24 *m*	6.24 *m*
5	2.56 *dd* (5.6, 11.4)	2.54 *dd* (5.6, 11.4)	3.54 *br d* (10.9)	3.09 *br d* (10.4)	3.09 *br d* (10.4)
6	4.53 *dd* (9.1, 11.5)	4.51 *dd* (9.0, 11.5)	4.39 *dd* (8.2, 10.6)	4.45 *dq* (1.5, 10.5)	4.42 *dq* (1.5, 10.5)
7	3.06 *dt* (9.2, 11.0)	2.99 *dt* (9.2, 11.0)	3.04 *dt* (8.4, 10.5)		
8	5.42 *t* (11.0)	5.37 *t* (11.0)	5.43 *ddd* (3.7, 9.5, 10.5)	5.50 *br d* (11.8)	5.44 *br d* (11.8)
9α	2.05 *dd* (9.5, 14.6)	2.05 *dd* (9.5, 14.6)	2.46 *dd* (9.4, 18.3)	2.43 *dd* (2.1, 13.3)	2.40 *dd* (2.1, 13.3)
9β	2.37 *m*	2.37 *m*	2.87 *dd* (3.7, 18.4)	2.85 *dd* (11.7, 13.1)	2.78 *dd* (11.7, 13.7)
11	2.66 *dq* (7.9, 9.2)	2.64 *dq* (7.9, 9.2)	2.78 *dq* (7.8, 8.4)		
13	1.26 *d* (7.9)	1.24 *d* (7.9)	1.28 *d* (7.7)	2.48 *br s*	2.46 *br s*
14	1.18 *s*	1.16 *s*	2.21 *br s*	2.31 *br s*	2.31 *br s*
15	1.81 *m*	1.85 *d* (1.4)	2.19 *br s*	2.31 *br s*	2.31 *br s*
OAng	6.08 *qq* (1.5, 7.3)		6.10 *qq* (1.5, 7.3)	6.28 *qq* (1.4, 7.5)	
	1.92 *dq* (1.5, 7.3)		1.93 *dq* (1.5, 7.3)	2.03 *dq* (1.4, 7.5)	
	1.81 *m*		1.82 *dq* (1.5)	1.95 *m*	
OSen		5.59 *qq* (1.2)			5.73 *m*
		2.11 *d* (1.2)			2.19 *d* (1.2)
		1.81 *m*			1.95 *m*
OAc					

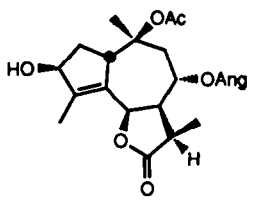
Values in parentheses are coupling constants in Hz.

Table 4. *Continued*

H	10	11	12	13	14
1			3.19 *br d* (8.7)	3.02 *m*	3.83 *br dt* (2.2, 10.5)
2α			1.67 *ddd* (6.4, 8.7, 13.6)	4.74 *m*	5.74 *dd* (2.4, 10.5)
2β			2.53 *dd* (6.4, 13.6)		
3	6.18 *dq* (1.3)	6.18 *dq* (1.3)	4.71 *br t* (6.4)	5.60 *dq* (1.7, 1.7)	5.81 *dd* (2.0, 5.9)
5	3.09 *br d* (10.5)	3.08 *br d* (10.6)		2.73 *m*	2.63 *dd* (10.5, 12.7)
6	4.51 *ddq* (1.8, 1.8, 10.6)	4.51 *ddq* (1.8, 1.8, 10.6)	5.31 *d* (6.2)	4.59 *dd* (8.5, 11.0)	4.87 *dd* (9.0, 12.8)
7			2.78 *ddd* (6.2, 7.8, 10.1)	3.02 *m*	3.10 *dt* (9.1, 9.1, 11.1)
8	6.05 *dd* (1.1, 6.4)	6.00 *dd* (1.0, 6.2)	5.18 *t* (9.6)	5.49 *ddd* (2.5, 10.9, 10.9)	5.43 *ddd* (2.6, 11.2, 11.2)
9α	2.61 *br d* (14.4)	2.58 *br d* (14.4)	1.69 *dd* (9.6, 15.4)		
9β	2.77 *dd* (6.3, 14.5)	2.73 *dd* (6.3, 14.5)	2.58 *d* (15.4)		
11			2.95 *dq* (7.6)	2.73 *m*	2.76 *m*
13	1.99 *d* (2.0)	1.97 *d* (1.8)	1.16 *d* (7.6)	1.31 *d* (7.9)	1.31 *d* (7.9)
14	2.39 *s*	2.39 *s*	1.34 *s*	1.57 *s*	1.40 *s*
15	2.29 *s*	2.29 *s*	1.80 *m*	1.89 *br d* (1.0)	1.49 *s*
OAng	6.09 *qq* (1.5, 7.3)		6.02 *qq* (1.4, 7.3)	6.10 *qq* (1.5, 7.3)	6.09 *qq* (1.5, 7.2)
	1.88 *dq* (1.5, 7.3)		1.91 *dq* (1.4, 7.3)	1.95 *dq* (1.5, 7.2)	1.95 *dq* (1.5, 7.2)
	1.76 *dq* (1.5)		1.80 *m*	1.83 *dq* (1.5)	1.83 *dq* (1.5)
OSen		5.55 *qq* (1.3)			
		2.09 *d* (1.3)			
		1.85 *d* (1.3)			
OAc			2.04 *s*	2.06 *s*	2.00 *s*

Values in parentheses are coupling constants in Hz.

These data allowed the assignment of a molecular formula $C_{22}H_{30}O_7$ corresponding to a sesquiterpenic lactone whose structure was established as 10-acetoxy-8-angeloyloxy-3-hydroxy-guai-4-en-6,12-olide by the NMR spectra (Tables 4 and 5) and by comparison with those of **24** [1]. The oxidation of **24** by singlet oxygen in *i*-PrOH afforded the corresponding hydroperoxides, which by reduction with dimethyl sulphide yielded **12** together with **13** and **14**. In **12** the β-orientation of the hydroxyl group at C-3 was established from the same disposition of



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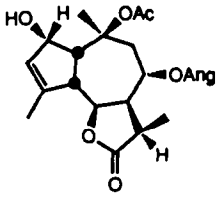
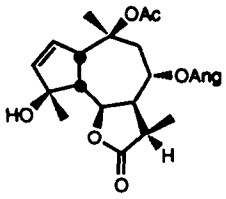
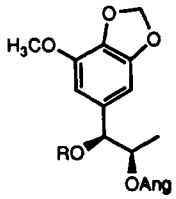


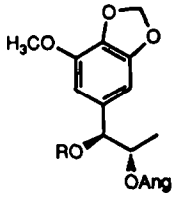
13



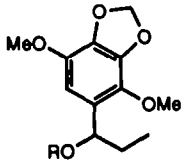
14



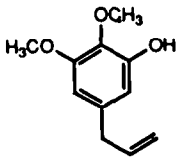
15 R = H
17 R = Ac



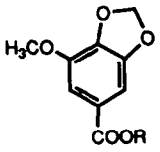
16 R = H
18 R = Ac



19 R = H
20 R = Ac



21



22 R = H
23 R = Me

Table 5. ^{13}C NMR spectral data of **5–14** (75 MHz, TMS, $CDCl_3$)

C	5	6	7	8	9	10	11	12	13	14
1	55.5 *d*	55.5 *d*	129.7 *s*	131.3 *s*	131.3 *s*	130.7 *s*	130.6 *s*	49.8 *d*	57.9 *d*	53.0 *d*[a]
2	32.2 *t*	32.2 *t*	195.1 *s*	195.0 *s*	195.0 *s*	194.9 *s*	195.2 *s*	37.7 *t*	80.1 *d*	130.4 *d*
3	125.2 *d*	125.2 *d*	139.8 *d*	136.0 *d*	136.0 *d*	135.9 *d*	135.9 *d*	75.2 *d*	130.0 *d*	139.2 *d*[b]
4	146.9 *s*	146.9 *s*	169.7 *s*	170.1 *s*	170.1 *s*	169.9 *s*	170.0 *s*	148.5 *s*	147.1 *s*	82.3 *s*
5	50.0 *d*	50.0 *d*	48.9 *d*	52.1 *d*	52.0 *d*	52.5 *d*	52.5 *d*	131.2 *s*	50.9 *d*	54.2 *d*[a]
6	90.7 *d*	90.7 *d*	80.6 *d*	82.2 *d*	82.2 *d*	81.3 *d*	81.3 *d*	79.1 *d*	77.3 *d*	77.3 *d*
7	45.5 *d*	45.5 *d*	37.1 *d*	158.2 *s*	158.4 *s*	156.8 *s*	157.1 *s*	48.4 *d*	46.8 *d*	46.3 *d*
8	67.2 *d*	66.3 *d*	67.0 *d*	68.5 *d*	67.8 *d*	65.0 *d*	64.2 *d*	66.3 *d*	65.8 *d*	66.4 *d*
9	43.1 *t*	43.2 *t*	43.4 *t*	42.5 *t*	42.5 *t*	39.2 *t*	39.2 *t*	43.9 *t*	43.7 *t*	43.9 *t*
10	71.3 *s*	71.3 *s*	145.1 *s*	145.9 *s*	146.0 *s*	147.1 *s*	147.3 *s*	84.1 *s*	82.3 *s*	85.5 *s*
11	36.2 *d*	36.1 *d*	45.0 *d*	122.5 *s*	122.8 *s*	126.5 *s*[a]	126.3 *s*	39.8 *d*	36.8 *d*	36.4 *d*
12	179.2 *s*	179.4 *s*	177.9 *s*	172.9 *s*	173.0 *s*	172.6 *s*	172.7 *s*	178.2 *s*	178.7 *s*	178.6 *s*
13	13.4 *q*	13.4 *q*	13.1 *q*	9.6 *q*	9.7 *q*	8.9 *q*	8.9 *q*	11.2 *q*	13.6 *q*	13.8 *q*
14	30.9 *q*	30.9 *q*	19.5 *q*[a]	20.7 *q*[a]	20.7 *q*[a]	22.3 *q*	22.3 *q*	21.8 *q*	26.2 *q*	24.8 *q*
15	18.6 *q*	18.6 *q*	20.3 *q*[a]	20.6 *q*[a]	20.6 *q*[a]	20.4 *q*[b]	20.4 *q*[a]	20.3 *q*	17.6 *q*	25.7 *q*
OAng	166.6 *s*		166.5 *s*	166.0 *s*		166.3 *s*		166.1 *s*	166.4 *s*	166.4 *s*
	127.2 *s*		126.9 *s*	126.4 *s*		126.6 *s*[a]		127.3 *s*	127.3 *s*	127.2 *s*
	139.3 *d*		135.2 *d*	141.3 *d*		140.6 *d*		138.9 *d*	138.8 *d*	139.0 *d*[b]
	15.7 *q*		15.7 *q*	16.0 *q*		15.8 *q*		15.8 *q*	15.8 *q*	15.8 *q*
	20.3 *q*		20.0 *q*[a]	20.0 *q*[a]		19.8 *q*[b]		20.3 *q*	20.4 *q*	20.4 *q*
Osen		168.0 *s*			164.6 *s*		165.0 *s*			
		115.4 *d*			114.5 *d*		114.6 *s*			
		158.8 *s*			160.7 *s*		159.6 *s*			
		27.4 *q*			27.7 *q*		27.4 *q*			
		20.3 *q*			20.0 *q*[a]		19.8 *q*[a]			
OAc								171.1 *s*	170.2 *s*	170.1 *s*
								22.8 *q*	22.5 *q*	22.4 *q*

[a,b]Signals may be interchanged within each column.

Table 6. ^{1}H NMR spectral data of **17** and **18** (300 MHz, TMS, $CDCl_3$)

H	17	18	Laserine*	Epilaserine*
1	5.82 *d* (4.8)	5.68 *d* (7.6)	5.75 *d* (7.3)	5.90 *d* (4.4)
2	5.23 *dq* (4.7, 6.4)	5.27 *dq* (6.4, 7.5)	5.32 *dq* (6.5, 7.1)	5.26 *dq* (6.5, 4.5)
3	1.22 *d* (6.5)	1.23 *d* (6.5)	1.24 *d* (6.5)	1.24 *d* (6.5)

Values in parentheses are coupling constants in Hz.
*See ref. [1].

H-5 in **24** on the basis of the mechanism of the reaction [19]. In **13** the α-orientation of the hydroxyl group at C-2 was determined by the $J_{1,2}$ value (< 2 Hz), that showed a *syn*-relationship between H-1 and H-2. The C-2 configuration was confirmed by the unshielding methyl Me-14 in deuteropyridine ($\Delta\delta = \delta_{\text{pyridine-}d_5} - \delta_{CDCl_3} = 0.27$ ppm). The C-4 configuration in **14** was established on the basis of the chemical shift of H-1 (δ 3.83), which appeared strongly unshielded if compared with that in **24**, due to the *cis* disposition between that proton and the hydroxyl group.

Compounds **15** and **16** were isolated as acetyl derivatives (**17** and **18**) and obtained as a 2:1 mixture. The ^{1}H NMR spectrum compared closely with that of the diastereoisomers laserine–epilaserine [1], differing in the signals of the side chain due to the presence of an acetoxyl group on C-1 (Table 6).

The phenylpropanoid **19** was identified as acetyl derivative **20**. The mass spectrum of **20** showed $[M]^+$ at *m/z* 282, which allowed the establishment of the molecular formula $C_{14}H_{18}O_6$. The ^{1}H NMR spectrum showed signals of one aromatic proton at δ 6.54, a methylenedioxy group at δ 5.95 and two aromatic methoxyl groups at δ 3.90 and 3.85. In addition, signals attributable to a 1-acetoxy-1-propyl group were observed, where the proton of the oxygenated carbon appeared at δ 5.95 as a triplet in agreement with structure **20**.

Compounds **21** and **22** were isolated as a 2:1 mixture whose structure was established easily by GC–MS, IR and ^{1}H NMR spectra, being molecules previously described in the literature [20, 21].

EXPERIMENTAL

Plant material. Aerial parts of *Seseli vayredanum* were collected in the Castillejos ravine (Lujan sierra, Granada) in June 1989 and identified by Professor J. Molero, Professor of the Department of Vegetable Biology, University of Granada. A voucher specimen (GDA 6811) is available for inspection at the herbarium of the Faculty of Pharmacy of the University of Granada.

Extraction and purification. Air-dried and powdered aerial parts (2.80 kg) of *Seseli vayredanum* were extracted and worked-up as described previously [1], yielding 25.93 g of defatted extract. The defatted extract was chromatographed on a silica gel column with hexane–Et_2O mixts of increasing polarity, Et_2O, and Et_2O–MeOH mixts of increasing polarity, affording 2-angeloyloxylatifolone (97 mg), **21** plus **22** (65 mg), phytol (20 mg), 2′-methoxylatifolone (32 mg), stigmasta-4,22-dien-3-one (66 mg), β-eudesmol (10 mg), sitosterol (711 mg), **1** plus **2** (696 mg), **4** (361 mg), falcarindiol (259 mg), **5** plus **6** (1128 mg), **15** plus **16** (47 mg), lupeol (39 mg), **19** (45 mg), **8** plus **9** (574 mg), **10** plus **11** (1319 mg), **7** (2736 mg) and **12** (180 mg). Fractions were monitored by TLC on silica gel, hexane–Et_2O (1:1) and Et_2O as eluent and visualized with phosphomolybdic acid in EtOH. The *acetyl derivatives* were obtained by acetylation with Ac_2O in pyridine.

GC-MS analysis. Analyses were carried out in a Hewlett-Packard 5890-A using an ionization voltage of 70 eV. The GC conditions were: capillary column (30 m), packed with methyl silicone, temp. programmed 120–320° at 10° min^{-1}, injector temp. 260°, detector temp. 280°, He at 1 ml min^{-1}.

1β-Senecioyloxy-5βH,6αH,7αH,10αMe,11αH-eudesm-3-en-6,12-olide (**1**) *and 1β-senecioyloxy-5βH,6αH,7αH,10αMe,11αH-eudesma-2,4(15)-dien-6,12-olide* **2**. Crystalline mixt. $[\alpha]_D^{25}$ −10.26° ($CHCl_3$; *c* 1). UV λ_{max}^{MeOH} (ε) nm: 206.7 (11 406). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 2944, 2874, 1760, 1706, 1645, 1447, 1380, 1354, 1212, 1185, 1149, 1077, 1016, 972.

Compound **1**. GC-MS (70 eV) *m/z* (rel. int.): 232 [M − HOSen]$^+$ (36), 217 (9), 188 (2.5), 159 (31), 158 (50), 143 (50), 119 (21), 105 (28), 91 (28), 83 (100), 55 (46).

Compound **2**. GC-MS (70 eV) *m/z* (rel. int.): 230 [M − HOSen]$^+$ (6), 185 (3), 157 (43), 119 (24), 91 (20), 83 (100), 55 (31.5).

Hydrolysis of **1** *plus* **2**. A soln of **1** plus **2** (50 mg), enriched in **1**, in 2 M KOH–MeOH (3 ml) was refluxed for 2 hr. Water (50 ml) was added and the soln extracted with Et_2O. THF (3 ml) was added to the aq. residual soln acidified with 2 M HCl (pH 2) and stirred at room temp. for 12 hr. The THF was evapd and the soln extracted with Et_2O. The ethereal soln was washed with 10% NaOH (3 × 5 ml), yielding 16 mg **3**.

Compound **3**. Syrup. $[\alpha]_D^{25}$ −54.1° ($CHCl_3$; *c* 1). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3507, 2931, 1762, 1690, 1453, 1381, 1229, 1172, 1040, 1000, 973. EI-MS (probe) 70 eV, *m/z* (rel. int.): 250 $[M]^+$ (3), 232 (42), 217 (21), 188 (2), 177 (18.5), 159 (100), 158 (28.5), 143 (67), 119 (36), 105 (54), 91 (59).

2α-Angeloyloxy-5β-hydroxy-7αH,10βMe-eudesm-3-en-1-one (**4**). Syrup. $[\alpha]_D^{25}$ −18.8° ($CHCl_3$; *c* 1), UV λ_{max}^{MeOH} (ε) nm: 212.5 (24 242). IR ν_{max}^{film} cm^{-1}: 3531, 2954, 1739, 1710, 1644, 1380, 1352, 1229, 1148, 1084, 1039, 1014. EI-MS (probe) 70 eV, *m/z* (rel. int.): 334 $[M]^+$ (1), 316 (1), 291 (1), 251 (31), 234 (5), 233 (9), 205 (3), 191 (10), 177 (9.5), 119 (29), 83 (90), 55 (100).

8α-*Angeloyloxy*-10β-*hydroxy-slov*-3-*en*-6,12-*olide* (**5**) *and* 10β-*hydroxy*-8α-*senecioyloxy-slov*-3-*en*-6,12-*olide* (**6**). Crystalline mixt. $[\alpha]_D^{25}$ + 37.15 ($CHCl_3$; *c* 1). UV λ_{max}^{MeOH} (ε) nm: 218.3 (7597). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3517, 2977, 2950, 2855, 1764, 1695, 1645, 1454, 1379, 1353, 1265, 1231, 1213, 1186, 1150, 1106, 1083, 1039, 1020, 1000, 964.

Compound **5**. GC-MS (70 eV) *m/z* (rel. int.): 248 [M − HOAng]$^+$ (3), 230 (3), 174 (3), 159 (3), 132 (5.5), 107 (4), 83 (100), 55 (31).

Compound **6**. GC-MS (70 eV) *m/z* (rel. int.): 248 [M − HOSen]$^+$ (7), 230 (5), 215 (2), 174 (5.5), 159 (7.5), 132 (12), 107 (11), 83 (91), 55 (100).

Oxidation of **24** *with t-butyl chromate: synthesis of* **7**. Compound **24** (100 mg, 0.28 mmol) in 3.5 ml CCl_4 was refluxed for 8 hr under N_2 with 4.9 ml HOAc, 0.25 ml Ac_2O and 2 ml of 1.0 M *t*-butyl chromate soln (prepd by dissolving 1.36 g of CrO_3 in 4 ml *t*-BuOH with cooling, diluting with 12 ml CCl_4, washing well with H_2O and drying over $MgSO_4$). The resulting mixt. was cooled and then stirred for 1 hr with 389 mg oxalic acid in 3.3 ml H_2O. The almost colourless organic layer was sepd, washed with H_2O, dried and the solvent removed. The resulting compound was identified as **7**.

Shairidin **8** *and* 2-*oxo*-8α-*senecioyloxy*-5βH,6αH-*guai*-1(10),3,7(11)-*trien*-6,12-*olide* (**9**). Crystalline mixt.; $[\alpha]_D^{25}$ + 1.3° ($CHCl_3$; *c* 1). UV λ_{max}^{MeOH} (ε) nm: 253.8 (5612), 220 (8012). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3006, 2961, 2928, 2861, 1759, 1717, 1687, 1644, 1617, 1438, 1323, 1306, 1290, 1254, 1212, 1195, 1143, 1123, 1099, 1070, 1031.

Compound **8**. GC-MS (70 eV), *m/z* (rel. int.): 342 [M]$^+$ (6), 259 (1), 242 (78), 227 (59), 199 (84), 186 (54), 171 (32), 159 (6), 158 (6), 128 (18), 115 (13), 83 (100), 55 (69).

Compound **9**. GC-MS (70 eV), *m/z* (rel. int.): 342 [M]$^+$ (3), 242 (50), 227 (30), 199 (39.5), 186 (26), 171 (17), 159 (2.5), 158 (4), 128 (9), 115 (8), 83 (100), 55 (27).

8β-*Angeloyloxy*-2-*oxo*-5βH,6αH-*guai*-1(10),3,7(11)-*trien*-6,12-*olide* (**10**) and 2-*oxo*-8β-*senecioyloxy*-5βH,6αH-*guai*-1(10),3,7(11)-*trien*-6,12-*olide* (**11**). Crystalline mixt. $[\alpha]_D^{25}$ + 29.7° ($CHCl_3$; *c* 1). UV λ_{max}^{MeOH} (ε) nm: 252 (3486), 220 (4811). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 2956, 2926, 1766, 1717, 1688, 1644, 1438, 1378, 1317, 1255, 1141, 1096, 1046, 1015, 861.

Compound **10**. GC-MS (70 eV), *m/z* (rel. int.): 342 [M]$^+$ (18), 242 (41), 199 (34), 186 (19), 185 (11), 171 (17), 141 (13), 128 (16), 115 (16), 91 (23), 83 (100), 55 (23).

Compound **11**. GC-MS (70 eV), *m/z* (rel. int.): 342 [M]$^+$ (21), 281 (0.6), 243 (61), 242 (92), 199 (82), 186 (44), 171 (45.5), 141 (40), 128 (50), 115 (43), 91 (49.5), 83 (98), 55 (100).

10β-*Acetoxy*-8α-*angeloyloxy*-3β-*hydroxy*-1βH,6αH, 7αH,11αH-*guai*-4-*en*-6,12-*olide* (**12**). Crystals from hexane–*t*-BuMeO–MeOH (8:2:1), mp 171°. [α] −31.7° ($CHCl_3$; *c* 1, Hg 405). UV λ_{max}^{MeOH} (ε) nm: 208.8 (13 648). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3457, 2982, 2927, 1767, 1719, 1646, 1452, 1378, 1256, 1152, 1075, 1043, 1020, 849. EI-MS (prove) 70 eV, *m/z* (rel. int.): 281 [M − C_5H_7O − C_2H_2O]$^+$ (2), 263 (5), 246 (24), 231 (14), 228 (17), 173 (34), 148 (82), 83 (95), 55 (100).

Photooxidation of **24**: *synthesis of* **12**. To a soln of **24** (300 mg, 0.77 mmol) in *i*PrOH (31 ml), Rose Bengal (5 mg) was added and the soln exposed to sunshine for 8 hr. The solvent was removed, yielding a solid, which was dissolved in Me_2S (12 ml). The soln was kept at room temp. for 1 hr. After the usual work-up, **12** (187 mg), **13** plus **14** (30 mg) and **14** (92 mg) were isolated by silica gel CC.

Compounds **13** plus **14**. Syrup mixt.; $[\alpha]_D^{25}$ + 46.3° ($CHCl_3$; *c* 1). UV λ_{max}^{MeOH} (ε) nm: 218.8 (12 129). IR ν_{max}^{film} cm^{-1}: 3460, 2927, 1773, 1715, 1646, 1454, 1378, 1258, 1150, 1086, 1017, 805, 756.

Compound **13**. GC-MS (70 eV), *m/z* (rel. int.): 328 [M − HOAc − H_2O]$^+$ (3.5), 228 (12), 213 (4), 199 (7), 171 (7.5), 155 (8), 143 (9.5), 129 (11), 128 (10), 115 (10), 91 (12), 83 (100), 55 (57), 43 (6).

Compound **14**. Syrup. $[\alpha]_D^{25}$ + 60.3° ($CHCl_3$; *c* 0.53). UV λ_{max}^{MeOH} (ε) nm: 218.8 (4368). IR ν_{max}^{film} cm^{-1}: 3590, 1770, 1724, 1645, 1255, 1176, 1148, 1085, 1044, 1016, 694. EI-MS (probe) 70 eV, *m/z* (rel. int.): 281 [M − C_5H_7O − C_2H_2O]$^+$ (4.5), 251 (25), 228 (56), 184 (9), 155 (33), 83 (49), 55 (100), 43 (18).

Erythro-1-*acetoxy*-2-*angeloyloxy*-3′,4′-*methylenedioxy*-5′-*methoxy*-1-*phenylpropane* (**17**) *and threo*-1-*acetoxy*-2-*angeloyloxy*-3′,4′-*methylenedioxy*-5′-*methoxy*-1-*phenylpropane* (**18**). Syrup; $[\alpha]_D^{25}$ −2.7° ($CHCl_3$; *c* 1). UV λ_{max}^{MeOH} (ε) nm: 208 (16 557). IR ν_{max}^{film} cm^{-1}: 2959, 2931, 2874, 1726, 1634, 1509, 1454, 1376, 1274, 1232, 1135, 1073, 1041, 981. EI-MS (probe) 70 eV, *m/z* (rel. int.): 350 [M]$^+$ (2), 290 (0.3), 250 (20), 208 (45), 181 (100), 179 (10), 153 (8), 123 (9), 83 (36), 55 (27), 43 (30).

Compound **17**. ^{1}H NMR (300 MHz, $CDCl_3$): δ6.56 (1H, *d*, *J* = 1.5 Hz, H-6′), 6.53 (1H, *d*, *J* = 1.5 Hz, H-2′), 6.03 (1H, *qq*, J_1 = 1.5 Hz, J_2 = 7.4 Hz, H-3″Ang), 5.95 (2H, *s*, OCH_2O), 5.82 (1H, *d*, *J* = 4.8 Hz, H-1), 5.23 (1H, *dq*, J_1 = 4.7 Hz, J_2 = 6.4 Hz, H-2), 3.88 (3H, *s*, OMe), 2.11 (3H, *s*, COMe), 1.91 (3H, *dq*, J_1 = 1.5 Hz, J_2 = 7.3 Hz, H-4″Ang), 1.82 (3H, *dq*, *J* = 1.5 Hz, H-5″Ang), 1.22 (3H, *d*, *J* = 6.5 Hz, H-3).

Compound **18**. ^{1}H NMR (300 MHz, $CDCl_3$): δ6.55 (1H, *d*, *J* = 1.5Hz, H-6′), 6.52 (1H, *d*, *J* = 1.5 Hz, H-2′), 6.03 (1H, *qq*, J_1 = 1.5 Hz, J_2 = 7.4 Hz, H-3″Ang), 5.96 (2H, *s*, OCH_2O), 5.68 (1H, *d*, *J* = 7.6 Hz, H-1), 5.27 (1H, *dq*, J_1 = 6.4 Hz, J_2 = 7.5 Hz, H-2), 3.88 (3H, *s*, OMe), 2.03 (3H, *s*, COMe), 1.95 (3H, *dq*, J_1 = 1.5 Hz, J_2 = 7.3 Hz, H-4″Ang), 1.85 (3H, *dq*, *J* = 1.5 Hz, H-5″Ang), 1.23 (3H, *d*, *J* = 6.5 Hz, H-3).

1-*Hydroxy*-3′,4′-*methylenedioxy*-2′,5′-*dimethoxy*-1-*phenyl propane* (**19**). White syrup; $[\alpha]_D^{25}$ + 2.86° ($CHCl_3$; *c* 1). IR ν_{max}^{film} cm^{-1}: 3403, 2935, 1638, 1494, 1452, 1376, 1222, 1187, 1139, 1047. ^{1}H NMR (80 MHz, $CDCl_3$): δ6.50 (1H, *s*, H-6′), 5.95 (2H, OCH_2O), 4.75 (1H, *t*, *J* = 7 Hz, H-1), 3.90 (3H, *s*, OMe), 3.85 (3H, *s*, OMe).

1-*Acetoxy*-3′,4′-*methylenedioxy*-2′,5′-*dimethoxy*-1-*phenyl propane* (**20**). White syrup. IR ν_{max}^{film} cm^{-1}: 2933, 2871, 1734, 1641, 1611, 1497, 1452, 1431, 1370, 1243, 1143, 1050, 980, 885, 804. EI-MS (probe) 70 eV, *m/z* (rel. int.) : 282 [M]$^+$ (43), 253 (6), 223 (42), 211 (100), 195 (12), 193 (15.5), 163 (9), 153 (8), 125 (9), 77 (6.5), 43 (25.5). ^{1}H NMR (80 MHz, $CDCl_3$): δ6.45 (1H, *s*, H-6′), 5.95 (2H, *s*, OCH_2O), 5.95 (1H, *t*, *J* = 7 Hz, H-1), 3.90 (3H, *s*, OMe), 3.85 (3H, *s*, OMe), 2.00 (3H, *s*, COMe).

5-Allyl-2,3-dimethoxy phenol (**21**) and *myristićinic acid* (**22**). Syrup mixt. IR ν_{max}^{film} cm^{-1}: 3418, 1706, 1632, 1593, 1506, 1235, 1199, 1167, 1110, 1042, 1002, 916.

Compound **21**. ^1H NMR (300 MHz, $CDCl_3$): δ6.41 (1H, *d*, $J = 1.8$ Hz, H-4), 6.26 (1H, *d*, $J = 1.8$ Hz, H-6), 5.76 (1H, *ddt*, $J_1 = 6.7$ Hz, $J_2 = 8.3$ Hz, $J_3 = 16.9$ Hz, H-2'), 5.06 (1H, *dq*, $J_1 = 1.5$ Hz, $J_2 = 16.9$ Hz, H-3'a), 5.02 (1H, *dq*, $J_1 = 1.5$ Hz, $J_2 = 8.3$ Hz, H-3'b), 3.82 (3H, *s*, OMe), 3.81 (3H, *s*, OMe), 3.25 (2H, *da*, $J = 6.7$ Hz, H-1').

Compound **22**. ^1H NMR (300 MHz, $CDCl_3$): δ7.34 (1H, *d*, $J = 1.3$ Hz, H-6), 7.22 (1H, *d*, $J = 1.3$ Hz, H-2), 6.03 (2H, *s*, OCH_2O), 3.90 (3H, *s*, OMe).

The methylation of **21** plus **22** with CH_2N_2 yielded a mixt. of **21** and **23**.

Compound **21**. GC-MS (70 eV), *m/z* (rel. int.): 194 $[M]^+$ (100), 179 (46), 163 (9), 147 (15), 136 (7), 119 (46), 107 (14), 91 (78), 77 (43).

Compound **23**. GC-MS (70 eV), *m/z* (rel. int.): 210 $[M]^+$ (68), 179 (100), 151 (20), 135 (8), 107 (4), 78 (12), 50 (18).

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