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Furanoeremophilane derivatives from *Senecio flavus* ☆

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Abstract

The aerial parts of *Senecio flavus* contain besides known eremophilane derivatives, four new furanoeremophilanes oxidized at C-3 and a new eremophilenone lactam. The rhizomes of the plant also contain the same ketoeremophilenes found in the aerial parts and a new epoxyeremophilanolide. The structure of these compounds has been established by spectroscopic methods. © 1999 Elsevier Science Ltd. All rights reserved.

Keywords: *Senecio flavus*; Compositae; Sesquiterpenes; Furanoeremophilanes; Eremophilenolide; Eremophilenone lactam

1. Introduction

For some time we have been interested in the phytochemistry of the Spanish *Senecio* species (Torres, Ayala, Grande, Macías & Grande, 1998; Torres, Chinchilla, Asensi & Grande, 1989; Torres, Chinchilla & Grande, 1992; Torres, Mancheño, Chinchilla, Asensi & Grande, 1988) and we would like to report here the results of our studies on the composition of *S. flavus* (Decne) Schultz Bip. This species is an annual plant whose distribution in Europe is restricted to the province of Almería (Spain) (Fernández Casas & Ceballos Jiménez, 1982) for which we have not found any reference to its chemical composition.

In this paper, we report the identification of some new furanoeremophilanes (**1a**, **1c**, **2** and **4**), one eremophilenone lactam (**8**) and one eremophilenolide (**9**) besides some known compounds (**1b**, **3**, **5**, **6** and **7**) found in the aerial parts and the rhizomes of the plant.

2. Results and discussion

The *n*-hexane–Et_2O–MeOH (1:1:1) extract from the aerial parts of *Senecio flavus* afforded the compounds **1**–**8** after column chromatography on silica gel.

The least polar component **1** was in fact a mixture of three esters as revealed by NMR spectra. The hydrolysis of this ester mixture (KOH/MeOH) gave the pure alcohol **1d** (MS: $[M]^+$ 232 amu; $C_{15}H_{20}O_2$) which showed in ^{13}C NMR signals for three methyl groups, three methylenes, six C^2_{sp} atoms characteristic of a trisubstituted furane ring and a trisubstituted ethylene, two methynes — one of them deshielded by an hydroxyl group — and one saturated quaternary carbon. The presence in ^1H NMR of a methyl group at δ 1.89 (d, J = 1.2 Hz) coupled with a vinyl proton at δ 7.05 as well as a methyl singlet and a methyl doublet (J = 7 Hz) let us conclude that the alcohol **1d** is a furanoeremophilane. The multiplicity of the vinyl proton at δ 5.47 (*quintet*, $J \approx 2.4$ Hz), suggests the $\Delta^{1(10)}$ position for the trisubstituted double bond by comparison with other euryopsin derivatives (Torres et al., 1998). Finally, the hydroxyl group was placed at C-3 because of the multiplicity of its geminal proton (δ 4.04, ddd, J = 7.9, 5.1 and 3.2 Hz). These coupling constants are in agreement with the β-configuration for the hydroxyl group at C-3 with the A ring adopting a half-chair

☆ Dedicated to the late Professor Joaquín de Pascual Teresa who introduced us to the natural products chemistry.

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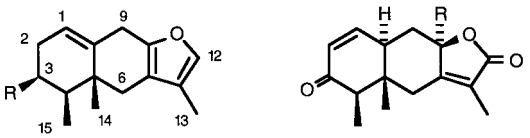
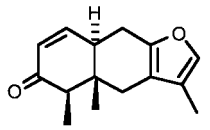


R	
1a	OMeBu
1b	OAng
1c	OSen
1d	OH
2	=O

R	
5	OMe
6	OH
7	H



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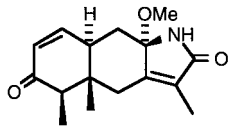

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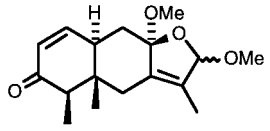
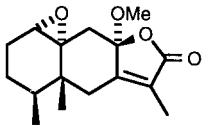


4a 12αOMe
4b 12βOMe



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conformation $^4H_3$ in which the 3β-OH is equatorial and the 3α-H has dihedral angles 3α,2β > 3α,4α > 3α,2α. The carboxylic acids present in the natural esters **1a**–**c** were identified as 2-methylbutyric, angelic and senecioic acid respectively according to the GC–MS analysis and their characteristic ^{1}H NMR signals (see Table 1). As we know, only **1b**, 3β-angeloyloxyeuryopsin, has been reported previously from *Euryops pectinatus* (Bohlmann & Zdero, 1978).

Compound **2** (MS: $[M]^+$ 230; $C_{15}H_{18}O_2$) has a carbonyl group (^{13}C NMR, δ 210.5 ppm) and shows similar NMR signals than **1d**. The deshielding $\Delta\delta = 0.95$ ppm of the signal assigned to the proton H-4, geminal to the Me-15 doublet, and the absence of the C-3 hydroxylated carbon signal, suggests for the carbonyl group the C-3 position. The deshielding effect is also observed for the C-2 hydrogen atoms ($\Delta\delta = 0.6$–0.8 ppm) and for the carbon atoms C-2 and C-4, while the remaining NMR signals are quite similar to those of the alcohol **1d**. Consequently, it is proposed for **2** the structure of euryopsin-3-one. As this ketone was isolated in a small quantity we tried to synthesize it by oxidation of **1d** with PDC, but we did not succeed because the oxidation product recovered was identical (spectral and other physical data) to the conjugated ketone **3**. This chemical correlation between **1d** and **3** implies that both substances have the same absolute configuration at C-4 and C-5.

Compound **3** is the most abundant component in the extract of the aerial parts and was identified by spectroscopic methods, including HMQC, HMBC and NOE 1D experiments, as furanoligularenone (Patil, Ourisson, Tanahashi, Wada & Takahashi, 1968). The absolute configuration of **3** was deduced from the CD curve as 4*R*, 5*S*, 10*R*, (Gawronski, 1989) also in agreement with the configuration reported for furanoligularenone (Jizba, Samek, Novotny, Najdenova & Boeva, 1978).

We also tried to transform the conjugated enone **3** into the less abundant ketone **2**. The deconjugation was attempted with acids (pTsOH/$HOCH_2CH_2OH$) and with bases (DBU/Benzene, NaMeO/MeOH, LDA/THF) but under the tested conditions we only obtained mixtures of products resulting from the attack to the furane ring and/or conjugate addition to the enone.

Compound **4** (MS: $[M]^+$ 292; $C_{17}H_{24}O_3$), retains the enone system present in **3** as conclude from the IR (1670 cm^{-1}) and UV ($\lambda = 226$ nm; ϵ 13400) absorptions and also from the ABX system displayed by the hydrogen atoms H-1, H-2 and H-10 (see Table 1). The aliphatic methyl groups Me-14 (s) and Me-15 (d, J = 6.8 Hz) absorb nearly at the same field as in **3** but the vinylic methyl is slightly shielded (ca. 0.2 ppm). However, the ^{1}H NMR spectrum of **4** shows two strong methoxyl singlets and the ^{13}C NMR signal for C-8 and C-12 are shielded at 109.9 and 108.8 ppm, characteristic chemical shifts for acetalic carbon atoms and this suggests a 8,12-dimethoxyketal structure for this enone. Compound **4** was in fact accompanied by an epimeric dimethoxy acetal as evidenced in the ^{1}H and ^{13}C NMR spectra: two smaller methoxyl signals are evident in the pmr spectrum and some ^{13}C signals are splitted in the cmr spectrum (Tables 1 and 2). The configuration of the methoxyl groups was assigned according to NOE 1D experiments. Irradiation on the methoxyl signal at δ 3.16 ppm resulted in a NOE on the H-6α, H-9α, H-10 and H-12 signals while the irradiation on the methoxyl at δ 3.53 gave NOE only with its geminal proton H-12 (Fig. 1). This experiment let us conclude that the configuration of the methoxyl group at C-8 should be α and *trans* to the C-12 methoxyl in the major isomer **4b** and the minor isomer **4a** should have the *cis*-8α,12α configuration.

The spectral data for the compounds **5**, **6** and **7** (UV and NMR spectra; Tables 1 and 2) prove that they should have for the A ring the same structure as the preceding enones **3** and **4**. Their IR spectra show in addition strong bands at ca. 1740 and 1665 cm^{-1} which can be assigned to a α-β unsaturated γ-lactone. These three furanoeremophilanolides differ in the C-8 substitution: compound **5** has a methoxyl group ($[M]^+$ 276 amu; δ_H 3.17 s; δ_C 105.4 ppm), while **6** has a hydroxyl group ($[M]^+$ 262 amu; ν 3240 cm^{-1}; δ_C 103.2 ppm) and **7** has a hydrogen atom at C-8 ($[M]^+$ 246

Table 1
^{1}H NMR spectral data for compounds **1a–9** (300 MHz, $CDCl_3$. Coupling constants in Hz are given in parentheses)[a]

H	1a–c	1d	2	3	4b	5	6	7	8	9
1	5.48 br s	5.47 qnt (2.4)	5.60 br s	6.62 dd (10.0, 1.7)	6.52 dd (10.0, 1.9)	6.55 dd (10.0, 2.0)	6.58 dd (10.0, 2.0)	6.58 dd (10.0, 2.0)	6.53 dd (10.0, 1.9)	3.17 br t (2.4)
2	2.24 m	2.16 m	2.80 br d (17.9), 3.05 br d (17.9)	6.08 dd (10.0, 2.9)	6.01 dd (10.0, 3.2)	6.06 dd (10.0, 3.3)	6.07 dd (10.0, 3.3)	6.08 dd (10.0, 3.2)	6.05 dd (10.0, 3.3)	1.88 m, 2.05 m
3	5.15 ddd, 5.21 ddd	4.04 ddd, (7.9, 5.1, 3.2)								1.41 m
4	1.96 m	1.79 dq (7.0, 3.2)	2.76 q (6.7)	2.43 q (6.8)	2.43 q (6.8)	2.52 q (6.8)	2.54 q (6.8)	2.52 q (6.5)	2.49 q (6.8)	1.41 m
6	2.28 d (14.0), 2.53 d (14.0)	2.24 d (15.0), 2.42 br d (15.0)	2.40 br d (15.3), 2.50 d (15.3)	2.33 m	1.87 d (12.8), 2.38 d (12.8)	2.18 br d (13.1), 2.68 d (13.1)	2.64 d (13.2), 2.40 br d (13.2)	2.25 br d (13.5), 2.79 d (13.5)	2.04 br d (12.9), 2.60 d (12.9)	2.31 br d (13.6), 2.61 d (13.6)
8								4.83 br t		
9	3.11 d (17.2), 3.35 br d (17.2)	3.11 d (17.0), 3.35 br d (17.0)	3.34 d (19.3), 3.44 br d (19.3)	2.47 m, 2.82 br dd (14.4, 5.6)	2.21 dd (13.0, 3.4), 1.60 t (13.6)	1.72 t (13.5), 2.46 dd (13.5, 3.4)	1.77 t (13.6), 2.48 dd (13.6, 3.4)	1.52 ddd (13.8, 12.5, 10.9), 2.52 ddd (12.5, 6.5, 3.0)	1.67 t (13.4), 2.30 dd (13.4, 3.4)	1.88 d, 2.22 d (14.0)
10				2.73 ddd, (5.2, 3.0, 2.0)	2.96 br dd (13.6, 2.4)	3.03 dddd, (13.5, 3.4, 3.3, 2.0)	3.12 br dd (13.6, 2.0)	2.80 m	3.07 br d	
12	7.04 br s	7.05 d (0.6)	7.08 br s	7.09 br s	5.24 s					
13	1.89 d (1.1)	1.89 d (1.2)	1.92 s	1.93 d (1.2)	1.72 s	1.89 d (1.9)	1.81 d (1.4)	1.84 t (1.6)	1.84 d (1.4)	1.90 d (1.7)
14	1.06 s	1.07 s	0.90 s	0.68 s	0.59 s (0.66 s)	0.65 s	0.63 s	0.64 s	0.61 s	0.93 s
15	1.02 d (7.0)	1.03 d (7.0)	1.16 d (6.7)	1.16 d (6.8)	1.11 d (6.8)	1.15 d (6.8)	1.15 d (6.8)	1.16 d (6.8)	1.15 d (6.8)	0.97 d (6.5)

[a] Other signals: **1a**: OMeBu: 2.42 m; 1.81 ddq; 1.22 d; 0.96 t; **1b**: OAng: 6.06 br q, 1.99 m; **1c**: OSen: 5.69 br s, 2.18 br s, 1.90 br s; **1c**: OH: 1.7 br s; **4a**: OMe-8: 3.08 s; OMe-12: 3.40 s; **4b**: OMe-8: 3.16 s; OMe-12: 3.53 s; **5**: OMe-8: 3.17 s; **6**: OH: 4.8 br s; **8**: OMe-8: 3.05 s; NH: 6.0 br s; **9**: OMe-8: 3.13 s.

amu; δ_H 4.83 br t; δ_C 79.3 ppm). The α configuration assigned to the methoxyl group was deduced from the NOE observed between this group and the hydrogen atoms H-10, H-9α and H-6α. The ^{13}C NMR signals for **5**, **6** and **7** are nearly the same, except for the absence of the methoxyl carbon signal in the last two compounds and the shielding of C-8 in compound **7**. Consequently, we propose for these lactones **6** and **7** the 8α-OH and 8α-H configuration respectively. These three eremophilanolides have been previously described in *Senecio nemorensis* var. *bulgaricus* (Jizba et al., 1978) and *S. pseudoorientalis* (Bohlmann & Ziesche, 1980).

We have also isolated a small amount of compound **8** which showed nearly the same ^{1}H NMR spectra as **5**. Only small shift differences (ca. 0.1 ppm) of some protons (OMe, C-9, C-6) were observed in the ^{1}H NMR spectrum however, the ^{13}C NMR spectrum of **8** showed a strong shielding for C-8 ($\Delta\delta$ 17 ppm) and smaller but significant effects on other contiguous carbon atoms were also observed (Table 2). This behavior could be explained if C-8 is attached to a less electronegative atom than oxygen, for instance a nitrogen atom. The mass spectrum confirmed the presence of a nitrogen atom and consequently, **8** should have a lactame instead of the lactone ring. The molecular ion and the first fragments maintain the nitrogen atom in the structure: m/z (%) = 275 (52), $[M]^+$, $C_{16}H_{21}NO_3$; 260 (30), $[M–Me]^+$; 244 (90), $[M–OMe]^+$; 228 (18), $[M–Me–OMe]^+$. According to these data we propose for this compound the structure of the eremophilenone amide **8** which to our knowledge, this is the second time that an eremophilene lactame has been isolated from natural sources. The first compound described, $\Delta^{7(11)}$-eremophilene lactam, was isolated from the rhizomes of *Petasites hybridus* (Jizba, Samek & Novotny, 1977).

Compond **9** (MS: $[M]^+ = 278$ amu, $C_{16}H_{22}O_4$) is present in the rhizomes of the plant from which the compounds **3**, **4**, **5** and **6** were also isolated. It is also an unsaturated γ-lactone as deduced from the IR spectrum (ν 1760, 1698 cm^{-1}). The skeleton of this substance was deduced from the NMR data. The ^{13}C NMR showed the presence of four methyl groups, one of them highly deshielded (OMe group), three C^2_{sp} (C=C and C=O), three carbon atoms geminal to oxygen (two quaternary and one tertiary), four CH_2, one CH and one tetrasubstituted C atom. The four methyl groups were also clearly observed in the ^{1}H NMR at δ 3.13 (s, -OMe), 1.90 (d, J = 1.7, vinylic Me-13), 0.97 (d, J = 6.5, Me-15) and 0.93 (s, Me-14). The methoxyl and lactone groups account for three of the oxygen atoms and the fourth should correspond to an epoxide function according to the IR and ^{13}C NMR data. This functional group should be placed at the 1,10 position because the ^{1}H NMR spectra present two independent

Table 2
^{13}C NMR spectral data for compounds **1a**–**9** (75 MHz, $CDCl_3$)

C	1[a]	1d	2	3	4a	4b	5	6	7	8	9
1	118.4	118.6	118.6	149.7	151.1	151.1	149.2	149.7	148.9	149.9	63.6
2	31.0	31.6	40.2	128.9	129.0	129.1	129.4	129.5	129.6	129.6	24.1
3	70.4	68.8	210.5	201.0	200.8	200.8	199.6	200.3	199.6	200.3	23.6
4	40.9	43.4	53.5	53.4	43.9	43.9	42.8	43.1	43.0	42.6	40.1
5	30.1	39.1	43.7	40.7	43.3	43.2	44.1	44.4	43.5	44.1	38.6
6	28.4	31.0	29.2	25.6	35.0	35.0	36.2	36.0	34.0	35.7	36.5
7	116.7	116.7	117.8	116.5	133.3[b]	132.8[b]	155.0	157.4	158.5	149.4	156.1
8	148.1	148.3	147.5	147.6	111.5	109.9	105.4	103.2	79.3	88.4	105.5
9	35.8	35.9	35.1	33.6	39.2	39.5	37.9	38.6	37.1	39.5	43.3
10	137.8	137.8	139.1	42.9	54.2	54.0	53.9	54.0	53.8	54.2	61.4
11	120.1	120.0	119.6	120.0	132.4[b]	131.9[b]	127.1	124.7	123.0	131.1	125.7
12	137.3	137.4	137.6	137.6	109.8	108.8	170.9	172.4	174.0	172.3	171.5
13	8.1	8.0	8.0	8.0	9.2	9.6	8.1	8.1	8.0	8.0	8.2
14	20.1	21.3	20.0	10.5	10.9	10.6	10.8	10.8	11.1	10.8	17.6
15	10.3	9.6	8.1	7.1	7.19	7.19	7.1	7.3	7.1	7.2	15.9
OMe-8					49.0	49.5	50.0			49.5	50.2
OMe-12					56.3	56.3					

[a] **1a**: OMeBu: 176.6 s, 41.3 d, 25.8 t, 15.9 q, 12.0 q. **1b**: OAng: 167.3 s, 137.5 d, 128.2 s, 20.7 q, 15.7 q. **1c**: OSen: 166.4 s, 156.4 s, 116.4 d, 27.3 q, 21.0 q.
[b] Signals that may be interchanged within the same column.

AB systems for the methylene protons at C-6 and C-9 and the Me-15 signal is a doublet.

The stereochemistry proposed for this furanoeremophilanolide is in agreement with the NOE shown in Fig. 1. The signal at δ 2.61 was assigned to the H-6β, a proton that should be almost in the deshielding plane of the $\Delta^{7(11)}$ double bond. That signal showed NOE with the geminal H-6α and with the three methyl groups. Moreover, the singlet of Me-14 (δ 0.93) showed NOE with the doublets at δ 2.61 (H-6β) and δ 2.22. This last signal was assigned to H-9β, while a doublet at δ 1.88 (d, J = 14.0 Hz) was assigned to H-9α, shielded by the 8α-OMe group (Bohlmann et al., 1986). These NOE correlations can be explained assuming a $^7C_{10}$ chair conformation for ring B and a half-chair $^3H_4$ (or envelop E_4) for ring A with the methyl groups Me-14 axial and Me-15 equatorial (Fig. 1). Some 1(10)β-epoxy-8β-hydroxylated eremophilenolides have been reported (Zhao, Jia & Yang, 1994) but in our case a β-configuration for the 8-OMe group would not explain neither the deshielding of H-9β nor the observed NOE between the δ 2.22 signal and Me-14. Further data supporting the 8α-OMe configuration is the sign of the optical rotation of **9** which is negative as expected according to the von Awers-Skita rule (Naya, Matsuura, Makiyama & Tsumura, 1978).

The α-configuration of the epoxide was assigned by comparison of the NMR data of **9** with other α- and β-epoxyeremphilanes. Two articles dealing with these substances report that the angular β-methyl group is shielded at δ 0.93 ppm in the 1(10)α-epoxyfuranoeremophilane (Bohlmann et al., 1979) and in 1(10)α-epoxy-6β-hydroxyeremophil-7(11)-enolide (Kitagawa, Shibuya & Kawai, 1977) in contrast to the β-epoxides which absorb at lower fields: δ 1.13 and 1.07, respectively (see also Bohlmann et al., 1986). The ^{13}C NMR spectra of **9** is also in agreement with the α-configuration given to the epoxide. According to Bohlmann et al. (1979) the most significant differences between the isomeric 1(10)-epoxyfuranoeremophilanes are the

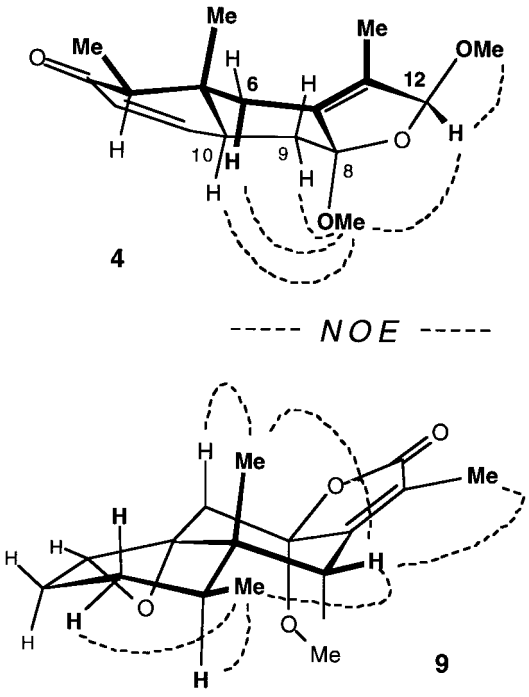

Fig. 1. NOE in compounds **4** and **9**.

chemical shifts of C-1 and C-14: 63.4 and 14.5 for the α-epoxide and 59.0 and 20.8 for the β-epoxide, respectively. In the case of **9**, the chemical shifts for C-1 and C-14 are 63.6 and 17.6 and would fit better with an α-epoxide. The multiplicity of the H-1 signal (br t, $J = 2.4$ Hz) also supports the α-configuration: H-1 in 1(10)β-epoxyeremophilanolides and 1(10)β-epoxyfuranoeremophilanes is described as a doublet ($J \approx 4$-5 Hz) while in the α-isomers appears as a triplet ($J \approx 2.5$ Hz) (Bohlmann et al., 1979; Kitagawa et al., 1977).

The eremophilanolide **9** is a new natural compound although the same constitution has been proposed for a compound isolated from *Senecio gallicus* (Urones et al., 1987) for which the configuration is not specified and the physical data were different from those of **9**.

As mentioned above, the most abundant furanoeremophilane is **3**. This enone could be biosynthesized from the esters **1** via enzymatic hydrolysis followed by oxidation and double bond isomerization. However, as furanoeremophilane derivatives are easily oxydized to the γ-lactones, as pointed out before (Novotny & Kotva, 1974; Ulubelen & Öksüz, 1984), 8-methoxy ketals are presumably artefacts originated from the enone **3** during the extraction and work up processes.

3. Experimental

3.1. General

Mp: uncorr. ^{1}H and ^{13}C NMR: 300 and 75 MHz, respectively, with TMS as int. standard, δ in ppm. 2D (HMQC and HMBC) and NOE 1D were recorded in a 400 MHz instrument. EIMS (GC) were carried out at 70 eV.

3.2. Material, extraction and isolation

Plant material was collected in April 1992 near Tabernas (Almería, Spain). A voucher specimen is deposited at the Herbarium of the Department of Botany, University of Salamanca (SALA 57183). The air-dried plant material was extracted with hexane–Et_2O–MeOH (1:1:1). The resulting extract was defatted (MeOH, −30°C) and chromatographed on silica gel (Merck, 7734) with a hexane–Et_2O gradient (0–100% Et_2O) and Et_2O–AcOEt (2:1, 1:1). TLC: silica gel 0.2 cm Schleicher & Schuell F 1500/LS 254. The already known compounds were identified by spectra comparison with those of authentic material.

The aerial parts (1100 g) afforded **1a–c** (730 mg. R_f 0.64; hexane–Et_2O 9:1), **2** (15 mg. R_f 0.51; hexane–Et_2O 8:2), **3** (4.5 g. R_f 0.39; hexane–Et_2O 9:1), **4** (35 mg. R_f 0.51; hexane–Et_2O 6:4), **5** (150 mg. R_f 0.41; hexane–Et_2O 3:7), **6** (276 mg. R_f 0.35; Et_2O), **7** (60 mg. R_f 0.31; Et_2O), **8** (15 mg. R_f 0.50; $CHCl_3$–EtOH 95:5), the roots (82 g) give **3** (50 mg), **4** (5 mg), **5** (15 mg), **6** (25 mg) and **9** (10 mg. R_f 0.42; hexane–Et_2O 6:4).

3.3. 3β-Methylbutyryloxyeuryopsin (*1a*), 3β-angeloyloxyeuryopsin (*1b*) and 3β-senecioyloxyeuryopsin (*1c*)

Colorless oil; $[\alpha]_D = +45.9$ (*c*, 1, $CHCl_3$); IR ν cm^{-1}: 2940, 2900, 1710, 1640, 1440, 1380, 1350, 1230, 1150, 1090, 1080, 990, 850, 780, 730; ^{1}H NMR: Table 1; ^{13}C NMR: Table 2. **1a** — EIMS *m/z* (rel. int.): 316 $[M]^+$ (31), 215 (25), 214 (90), 199 (100), 185 (35), 172 (14), 171 (21), 159 (42), 146 (97), 145 (26), 128 (17), 118 (51), 108 (61), 105 (13), 91 (28), 85 (16), 79 (22), 57 (59), 43 (45), 41 (49). **1b** — EIMS *m/z* (rel. int.): 314 $[M]^+$ (22), 214 (100), 199 (95), 185 (24), 171 (18), 159 (37), 146 (75), 145 (24), 128 (16), 118 (53), 115 (15), 108 (68), 105 (11), 91 (27), 83 (38), 79 (22), 77 (17), 55 (91), 53 (18), 43 (25), 41 (18). **1c** — EIMS *m/z* (rel. int.): 314 $[M]^+$ (20), 214 (99), 199 (100), 185 (24), 171 (17), 159 (54), 146 (76), 145 (26), 128 (16), 118 (45), 115 (17), 108 (64), 105 (12), 91 (23), 83 (92), 79 (19), 77 (17), 55 (64), 53 (18), 43 (24), 41 (16).

3.4. 3β-Hydroxyeuryopsin (*1d*)

A methanolic solution of compounds **1a–c** (150 mg) was hydrolyzed with 5% methanolic KOH for 60 h at room temperature, to give the alcohol **1d** (80 mg). Colorless oil; R_f 0.37 (hexane–Et_2O 6:4). $[\alpha]_D = +41$ (*c*, 1, $CHCl_3$); IR ν cm^{-1}: 3360, 1650, 1630, 1550, 1430, 1400, 1370, 1340, 1080, 1030, 1000, 820, 800, 770, 725; ^{1}H NMR: Table 1; ^{13}C NMR: Table 2; EIMS *m/z* (rel. int.): 232 $[M]^+$ (81), 214 (40), 199 (100), 185 (29), 173 (22), 171 (24), 159 (96), 145 (70), 132 (15), 131 (20), 129 (25), 128 (30), 115 (37), 105 (22), 91 (46), 79 (28), 77 (34), 43 (30).

3.5. Euryopsin-3-one (*2*)

Colorless oil; ^{1}H NMR: Table 1; ^{13}C NMR: Table 2; EIMS *m/z* (rel. int.): 230 $[M]^+$ (26), 215 (3), 201 (2), 187 (7), 183 (8), 174 (11), 173 (16), 159 (100), 145 (32), 131 (13), 128 (15), 117 (10), 115 (17), 91 (31), 79 (19), 77 (30), 65 (15), 43 (14).

3.6. Furanoligularenone (*3*)

Colorless crystals, mp 91–92°C (hexane/Et_2O 9:1); $[\alpha]_D = +3.25$ (*c*, 1, $CHCl_3$); UV λ nm: 226 (ϵ 12500); IR ν cm^{-1}: 3138, 3100, 3027, 1680, 1645, 1564, 1537, 1460, 1260, 1213, 1086, 970, 822, 770; ^{1}H NMR: Table 1; ^{13}C NMR: Table 2; EIMS *m/z* (rel. int.): 230 $[M]^+$ (99), 215 (3), 201 (3), 187 (5), 173 (7), 159 (7), 145

(11), 122 (11), 119 (7), 115 (14), 108 (100), 105 (10), 94 (26), 91 (19), 79 (50), 77 (31), 65 (12), 53 (14); CD (*c* 0,2 mg/ml, EtOH): $\Delta\epsilon_{218}$ −1,8, $\Delta\epsilon_{256}$ +0,1, $\Delta\epsilon_{338}$ −0,5.

3.7. 3-Oxo-8α,12α-dimethoxy-8,12-dihydro-10αH-furanoeremophil-1-ene (*4*)

Colorless oil; UV λ nm: 226 (ϵ 13400); IR ν cm^{-1}: 2910, 1670, 1440, 1370, 1330, 1160, 1080, 1050, 980, 920, 860, 820, 770, 730; ^{1}H NMR: Table 1; ^{13}C NMR: Table 2; EIMS *m/z* (rel. int.): 292 $[M]^+$ (11), 277 (4), 261 (40), 260 (26), 245 (22), 233 (100), 229 (8), 201 (13), 173 (17), 159 (11), 157 (35), 156 (34), 145 (14), 135 (14), 131 (10), 128 (11), 109 (17), 97 (27), 91 (36), 79 (33), 77 (34), 53 (36), 43 (16), 41 (26).

3.8. 3-Oxo-8α-methoxy-10αH-eremophila-1,7(11)-dien-12,8β-olide (*5*)

Pink crystals, mp 214°C (EtOAc); $[\alpha]_D = +253.5$ (*c*, 0.6, EtOH); UV λ nm: 224 (ϵ 13400); IR ν cm^{-1}: 2940, 2920, 2810, 1730, 1660, 1440, 1420, 1370, 1320, 1200, 1170, 1150, 990, 960, 940, 920, 810, 760; ^{1}H NMR: Table 1; ^{13}C NMR: Table 2; EIMS *m/z* (rel. int.): 276 $[M]^+$ (84), 248 (49), 245 (30), 244 (54), 233 (13), 229 (20), 217 (34), 216 (34), 201 (43), 195 (12), 189 (25), 188 (51), 187 (10), 173 (17), 163 (25), 161 (24), 160 (15), 140 (35), 135 (36), 121 (23), 112 (17), 107 (21), 93 (52), 91 (72), 81 (32), 79 (51), 77 (53), 67 (27), 65 (25), 53 (100); CD (*c* 0.9 mg/ml, EtOH): $\Delta\epsilon_{220}$ −4.0, $\Delta\epsilon_{325}$ −0.5.

3.9. 3-Oxo-8α-hydroxy-10αH-eremophila-1,7(11)-dien-12,8β-olide (*6*)

Colorless crystals, mp 206°C (EtOAc); UV λ nm: 224 (ϵ 13900); IR ν cm^{-1}: 3240, 2950, 2920, 2840, 2820, 1730, 1660, 1420, 1380, 1330, 1290, 1270, 1210, 1160, 1140, 1130, 1070, 990, 980, 950, 930, 820, 760; ^{1}H NMR: Table 1; ^{13}C NMR: Table 2; EIMS *m/z* (rel. int.): 262 $[M]^+$ (23), 244 (48), 229 (6), 201 (20), 188 (100), 173 (31), 160 (49), 145 (27), 135 (23), 115 (20), 93 (16), 91 (44), 79 (22), 77 (30), 65 (15), 53 (42).

3.10. 3-Oxoeremophila-1,7(11)-dien-12,8β-olide (*7*)

Colorless crystals, mp 186°C (EtOAc); UV λ nm: 224 (ϵ 13000); FTIR ν cm^{-1}: 3035, 2972, 2954, 2921, 2873, 2855, 1743, 1671, 1440, 1387, 1336, 1220, 1212, 1153, 1099, 1067, 1054, 1030, 854, 818, 768, 754, 566, 558, 465; ^{1}H NMR: Table 1; ^{13}C NMR: Table 2; EIMS *m/z* (rel. int.): 246 $[M]^+$ (33), 231 (2), 201 (6), 185 (3), 173 (6), 148 (3), 135 (100), 121 (6), 110 (21), 107 (9), 105 (5), 93 (8), 91 (13), 81 (42), 77 (17), 55 (10), 53 (30), 41 (9).

3.11. 3-Oxo-8α-methoxy-10αH-eremophila-1,7(11)-dien-12,8β-lactam (*8*)

Colorless oil; ^{1}H NMR: Table 1; ^{13}C NMR: Table 2; EIMS *m/z* (rel. int.): 275 $[M]^+$ (52), 260 (30), 244 (90), 243 (56), 228 (18), 200 (26), 187 (100), 172 (47), 140 (20), 139 (84), 138 (22), 123 (26), 122 (21), 93 (27), 91 (32), 81 (30), 79 (32), 77 (37), 69 (20), 67 (20), 55 (34), 53 (41), 41 (23).

3.12. 1β,10β-Epoxy-8α-methoxyeremophil-7(11)-en-12,8β-olide (*9*)

Colorless crystals, mp 102–103°C (hexane); $[\alpha]_D = -87.5$ (*c* 1; $CHCl_3$); FTIR ν cm^{-1}: 2975, 2958, 2934, 2878, 1760, 1698, 1452, 1437, 1385, 1293, 1171, 1104, 964, 816, 733, 562; ^{1}H NMR: Table 1; ^{13}C NMR: Table 2; EIMS *m/z* (rel. int.): 278 $[M]^+$ (23), 263 (4), 250 (8), 235 (4), 218 (14), 203 (10), 193 (21), 192 (18), 191 (10), 177 (11), 175 (18), 161 (15), 149 (13), 147 (13), 140 (53), 135 (13), 133 (24), 123 (18), 112 (26), 107 (23), 105 (29), 95 (39), 91 (44), 81 (24), 79 (42), 77 (39), 67 (45), 55 (53), 53 (81), 43 (71), 41 (100).

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