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FURANOEREMOPHILANES AND A BAKKENOLIDE FROM *SENECIO AURICULA* VAR. *MAJOR*

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Key Word Index—*Senecio auricula* var. *major*; Compositae; sesquiterpenes; furanoeremophilanes; bakkenolide; senauricolide; triterpenoid fatty esters; Transannular hydride shift.

Abstract—The roots of *Senecio auricula* var. *major* yielded, in addition to known compounds, four new eremophilane derivatives: the furanoeremophilanes 6β-(2-methylbutyryloxy)-10α*H*-furanoeremophilan-1-one, 6β-isobutyryloxysenberginone, 6β-(2-methylbutyryloxy)-senberginone and the bakkenolide 11β,12β-epoxy-6β-(2-methylbutyryloxy)-$\Delta^{1(10)}$-7-epidihydrobakkenolide A (senauricolide). Alkaline hydrolysis of senberginone esters gave, apart from the expected alcohols, the isomeric new 1β-hydroxy-10β*H*-furanoremophilan-6-one. The aerial parts contained α-tocopherol, fatty esters of β-amyrin, fatty esters of 20(29)-lupene-3β,16β-diol and sitosterol. © 1997 Elsevier Science Ltd

INTRODUCTION

In continuation of our studies on members of the large genus *Senecio* [1–3], we have investigated the constituents of *Senecio auricula* Bourg. var. *major* WK., an endemic plant of Alicante, Spain [4].

Senecio species, some of which have been used in folk medicine, usually contain metabolites different from those present in other species of Compositae: the main components of *Senecio* sp. are usually pyrrolizidine alkaloids and sesquiterpenoids with the furanoeremophilane skeleton [5].

The only article we have found on the metabolites of *Senecio auricula* reports the isolation of two alkaloids [6]. This paper describes our isolation and structural identification of the known furanoeremophilanes **1a** [7], **1b** [8], **2a** [9, 10], **2b** [11], **2c** [10, 12] and **3a** [13], as well as three new natural furanoeremophilanes, **3b**, **3c** and **3d**, and a new bakkenolide A derivative, **4**, for which the name senauricolide is proposed.

RESULTS AND DISCUSSION

The hexane-diethyl ether extract of the air dried roots of the plant afforded after silica gel chromatography compounds **1(a+b)**, **2(a+b)**, **2c**, **3(a–d)** and **4**. Saponification of the mixture of esters **1(a+b)** with methanolic potassium hydroxide gave the known alcohol **1c** [14] and **1d**. The structure of **1d** was deduced from the ^{1}H and ^{13}C NMR spectral data (Tables 1 and 2) quite similar to those of **1a–1c** [7, 8 and 14]. A singlet at δ 3.19 (3H) in the ^{1}H NMR spectrum and the absence of signals assigned to an ester group, clearly indicate the presence of one methoxyl group at C-6 in **1d**. The α-orientation of the methoxyl group can explain the observed shielding of H-14 in ^{1}H NMR as well as the deshielding of C-15 in ^{13}C NMR (γ-gauche effect). This compound should arise from nucleophilic displacement of the ester group by the solvent. Similarly the furanoeremophilane **2c**, described as a natural produce elsewhere [10, 12], could be an artefact produced during the extraction process.

Compounds **3a–3d** could not be isolated as pure compounds. A sample enriched in **3b** was analysed by GC/MS and showed an $[M]^+$ ion at *m/z* 332 ($C_{20}H_{28}O_4$), a base peak ion at *m/z* 125 and identical fragments to those of **3a** [14]. The identification of the ester group in **3b** as 2-methylbutyrate was deduced from the ^{13}C NMR data (Table 2) and confirmed by the presence of a fragment ion at *m/z* 85 in the mass spectrum.

Compound **3d**, showed a parent ion at *m/z* 332 ($C_{20}H_{28}O_4$) and ^{1}H NMR and ^{13}C NMR signals quite similar to those of the 6β-acetoxysenberginone [7]. The only significant difference observed were the sig-

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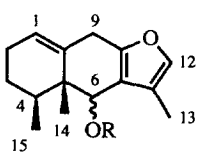
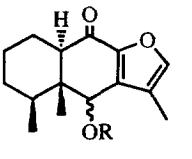
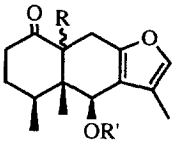


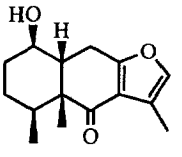
	R
1a	β-*i*Bu
1b	β-MeBu
1c	β-H
1d	α-Me



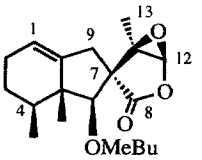
	R
2a	β-*i*Bu
2b	β-MeBu
2c	α-Me



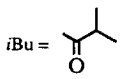
	R	R'
3a	α-H	*i*Bu
3b	α-H	MeBu
3c	β-H	*i*Bu
3d	β-H	MeBu
3e	α-H	H
3f	β-H	H

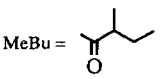


3g



4





nals of the ester group, which was identified as 2-methylbutyrate (Table 2).

The minor component **3c** was detected by GC-mass spectrometry. This substance showed an $[M]^+$ ion at *m/z* 318 ($C_{19}H_{26}O_4$), a base peak ion at *m/z* 146 and identical mass spectral fragments to those given by **3d**. These spectral data for **3c** suggest the structure of 6β-isobutyryloxysenberginone.

Alkaline hydrolysis of the ester mixture **3a–3d** gave the new alcohols **3e**, **3f** and **3g**. Compound **3e** showed a molecular ion $[M]^+$ at *m/z* 248 in agreement with the molecular formula $C_{15}H_{20}O_3$. The ^1H NMR spectrum was quite similar to those of compounds **3a** and **3b** (Table 1), but the H-6 signal was shielded in this case at δ 4.75 (*br s*), characteristic of an allylic proton geminal to a hydroxyl group. These data allowed us to identify **3e** as 6β-hydroxy-10α*H*-furanoeremophilan-1-one.

The mass spectrum of compound **3f** showed a molecular ion $[M]^+$ at *m/z* 248 ($C_{15}H_{20}O_3$) and its ^1H NMR and ^{13}C NMR spectra (Tables 1 and 2) were quite similar to those of **3d**, except for the H-6 ^1H NMR signal which absorbed in this case at δ 4.55 (*br s*). These data support the structure of 6β-hydroxy-10β*H*-furanoeremophilan-1-one for **3f**.

Compound **3g** ($[M]^+$ at *m/z* 248, $C_{15}H_{20}O_3$), displayed in the ^1H NMR spectrum typical signals of a furanoeremophilane: one methyl group and one proton on a furan ring [δ 2.19 (3H, *br s*) and δ 7.08 (1H, *br s*)], one quaternary methyl group [δ 1.13 (*s*)] and a secondary methyl group [δ 1.00 (3H, *d*, $J = 7.4$ Hz)] coupled with one proton [δ 2.58 (*m*)] (see Table 1). The IR spectrum indicated the presence of a hydroxyl (3300 cm^{-1}) and conjugated carbonyl groups (1655 cm^{-1}). Its UV spectrum showed absorptions at λ_{max}^{EtOH} 270 and 224.5 nm characteristic of a 6-oxofuranoeremophilane [15]. These data allowed us to propose for **3g** the structure of 1β-hydroxy-10β*H*-furanoeremophilan-6-one. This structure is also in agreement with the ^{13}C NMR data (Table 2) and with the mass spectral fragmentation pattern.

The formation of enone **3g** during the hydrolysis can be explained by a transannular hydride shift from C-6 to C-1 in compounds **3c** and **3d**.These substances

Table 1. ^1H NMR spectral data for compounds **1d**, **3a–3g** and **4** (300 MHz, $CDCl_3$, coupling constants (Hz) were given in parenthesis)

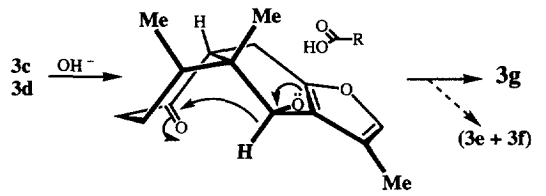
H	1d	3a–3b	3c–3d	3e	3f	3g	4*
1	5.68 *br d*					3.41 *ddd* (5.1, 9.7, 10.5)	5.51 *br s*
2					2.40 *m*	1.69 *m*	α 2.18 *m*
					2.50 *m*		β 2.05 *br d* (16)
3						1.48 *m*	1.50 *m*
4						2.58 *m*	1.72 *m*
6	4.10 *s*	6.16 *br s*	6.02 *br s*	4.72 *br s*	4.55 *br s*		5.34 *s*
9					2.64 *dd* (6.1, 16.9)	α 3.35 *d* (18.3)	α 2.38 *br d* (15)
					2.91 *dd* (6.1, 16.9)	β 2.90 *dd* (5.2, 18.3)	β 2.89 *dq* (15, 3)
10					2.82 *t* (6.1)	2.10 *dd* (5.2, 10.5)	
12	7.07 *br s*	7.03 *br s*	7.07 *br s*	7.05 *br s*	7.08 *br s*	7.08 *br s*	5.31 *s*
13	2.03 *s*	1.80 *br s*	1.80 *br s*	2.06 *br s*	2.03 *d* (0.7)	2.19 *br s*	1.64 *s*
14	0.76 *s*	0.86 *s*	0.97 *s*	0.73 *s*	1.03 *s*	1.13 *s*	1.07 *s*
15	0.99 *d* (6.7)	0.98 *d* (7.5)	0.98 *d* (7.5)	1.25 *d* (6.8)	1.05 *d* (7.6)	1.00 *d* (7.4)	0.86 *d* (6.5)
OMe	3.19 *s*						

*OMeBu: 2.42 *m*; 1.81 *ddq*; 1.22 *d*; 0.96 *t*.

Table 2. ^{13}C NMR spectral data for compounds **1a–1d**, **2b/2c**, **3a/3b**, **3d–3g** and **4** (75 MHz, $CDCl_3$)

C	1a	1b	1c	1d	2b	2c	3a	3b	3d	3e	3f	3g	4
1	124.3	124.1	123.8	125.9	32.2	29.9	209.0	209.0	209.0	208.0	208.4	69.3	121.9
2	21.3	21.1	22.1	25.9[a]	20.7	20.6	39.8	41.0	36.0	41.2	36.2	29.6	26.1[a]
3	31.3[a]	31.3[a]	31.2[a]	27.7[a]	25.0	25.1	31.4	31.4	29.8	31.3	30.0	27.7	27.0[a]
4	31.9	31.6	33.2	31.7	42.5	50.0	41.2	42.0	30.3	42.8	30.2	30.4	41.2
5	42.5	42.6	43.1	43.1	50.0	47.2	45.2	45.3	44.1	45.7	45.1	50.2	46.7
6	72.1	71.8	73.3	75.6	75.3	75.2	74.7	74.5	67.9	75.0	67.3	199.2	82.8
7	119.7	119.7	120.4	120.6	134.3	135.6	115.8	116.0	116.0	118.5	118.9	118.0	61.5
8	151.3	151.4	150.4	152.1	145.0	147.5	150.7	150.8	149.8	149.7	148.9	163.8	174.3
9	26.3[a]	26.1[a]	26.9[a]	29.5[a]	186.7	188.4	20.3	20.3	22.3	20.2	21.8	21.5	37.9
10	135.3	135.3	136.7	136.3	55.1	57.3	55.3	55.4	51.1	55.4	50.3	45.6	139.8
11	117.4	117.4	119.7	117.9	120.9	121.5	119.2	119.3	119.4	119.9	119.6	119.6	55.7
12	138.2	138.2	138.3	137.6	145.0	144.0	138.4	138.6	138.4	138.6	138.7	139.5	81.2
13	8.7	8.8	9.2	8.4	7.7	8.5	8.4	8.5	8.2	7.1	8.4	9.1	11.6
14	16.6[b]	17.2[b]	15.0[b]	15.7[b]	18.1	14.8	15.7	15.8	17.8[a]	17.3	16.5	13.7	14.5
15	15.1[b]	14.9[b]	15.8[b]	18.1[b]	8.9	13.1	9.2	9.4	14.8	9.1	14.6	23.1	16.4
OMe				55.0		34.8							
OR	177.0	176.6			175.9		176.2	176.0	176.6				178.3
	34.4	41.6			41.3		34.7	41.3	41.2				38.4
	19.4	26.2			25.8		18.7	25.8	26.4				25.3
	18.7	16.8			15.9		18.5	16.6	17.0[a]				16.4
		11.9			12.0			11.7	11.7				14.0

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



Scheme 1

with a *cis*-A/B ring junction can adopt a 'steroid-like' conformation in which H-6α and the π orbitals of the carbonyl group at C-1 are close spatially. Thus, once the base attacks the carbonyl ester group, the leaving alcoholate can rearrange to **3g** as shown in Scheme 1. Transannular hydride shifts have been reported previously, mainly in medium ring systems [16].

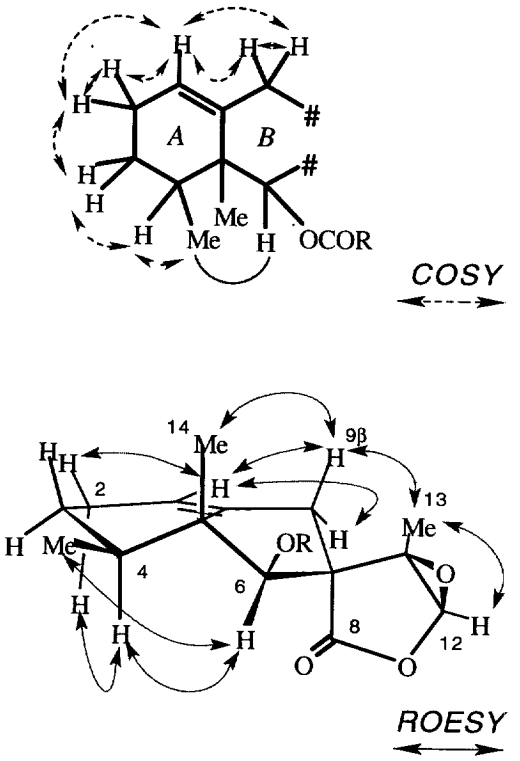
Compound **4** was suspected to be a furanoeremophilane derivative, as deduced from initial examination of the spectral data. However, the IR spectrum suggested that a γ-lactone ring (1790 cm^{-1}) is present instead of the furan ring. The IR also reveals the absence of free hydroxyl groups and also shows absorption bands of an ester group (1735 cm^{-1}), a carbon–carbon double bond (1660 cm^{-1}) and an epoxide (880 cm^{-1}). The molecular ion of **4**, $[M]^+$ at *m/z* 348, and the ^{13}C NMR data gave the molecular formula $C_{20}H_{28}O_5$ whose unsaturation number (*un* = 7) fits in with the presence of a bicyclic system, apart from the lactone and epoxide rings, the ester group and the C=C double bond detected by IR.

The ^1H NMR spectrum of **4** (Table 1) displayed three methyl group signals (δ 0.86, *d*, *J* = 6.5 Hz; 1.05, *s* and 1.64, *s*), one of them deshielded by a geminal oxygenated function, as well as the characteristic signals for a methylbutyrate ester geminal to a singlet proton (δ 5.34, *s*). The ^{13}C NMR spectrum (Table 2) confirmed the presence of the methylbutyric ester, and also showed signals of three methyl groups, three methylene groups, three methynes (two geminal to oxygen), three saturated quaternary carbon atoms (two deshielded by oxygen function) and three C_{sp^2}, corresponding to one trisubstituted carbon–carbon double bond and to the lactone carbonyl group. These data, as well as the isolation of the previous compounds, initially suggested the structure of an eremophilanolide.

The arrangement of the functional groups and the full structure could be deduced from the 2D COSY and ROESY spectra. Apart from the geminal couplings of the methylene groups, the following $\delta_{H/H}$ correlations were observed (Scheme 2): H-1 (5.68) with H-2a (2.18), H-2b (2.05), H-9a (2.38) and H-9b (2.89); H-2a and H-2b with H-3 (1.50); H-3 with H-4 (1.72) and H-4 with Me-15 (0.86). These correlations and the observed NOE effects of H-6 with H-4 and Me-15 determine the partial structure shown for the rings A and B.

The remaining tertiary C-H signals (δ_C 81.2; δ_H 5.31, *s*) could be assigned to C-8 in an eremophilanolide skeleton. However, the multiplicity of this proton (a singlet not coupled with the two contiguous H-9 protons) and the observed NOE correlation of this proton with those of Me-13 led to the conclusion that lactone **4** was a bakkenolide.

The configuration of the lactone moiety was deduced from the ROESY spectrum. A configuration with the lactone carbonyl group β-oriented should bring Me-13 close either to H-9α or to H-6 but no



Scheme 2

additional NOE was observed between these proton atoms and Me-13. The opposite configuration, with the lactone carbonyl group α-oriented, brings Me-13 close either to H-9β or to the methylbutyryl ester. As the only weak correlation peaks observed for Me-13 in the ROESY spectrum were with H-9β and H-12, we assigned the β-configuration for the epoxide ring as shown in structure **4**. The only three 11,12-epoxybakkenolides previously reported are spirosenbergiolide and its 7-epimer from *Senecio bergii* [7] and palmosalide C from *Coelogorgia palmosa* [17, 18]. Because of the plant origin of the new bakkenolide, we propose for lactone **4** the name senauricolide.

α-Tocopherol [19, 20] and sitosterol [21] were isolated from the aerial parts of *S. auricula*. Also, two chromatographic fractions each of which seemed to be homogeneous on TLC, were in fact fatty esters mixtures which gave on saponification the triterpene alcohols β-amyrin (**5**) [22] and 20(29)-lupene-3β,16β-diol (**6**) [23, 24], both of which were identified by comparison with authentic samples.

The fatty acids attached to the C-3 hydroxyl group of **5** were identified by GC of the methyl esters as myristic, palmitic, stearic and linoleic (main component) acids and those esterifying **6** were identified as lauric, myristic, palmitic (main component) and stearic acids.

EXPERIMENTAL

General. Mp: uncorr. UV spectra were recorded in 96% EtOH. ^{1}H and ^{13}C NMR: 300 and 75 MHz, respectively, with TMS as int. standard, δ in ppm. EIMS was carried out at 70 eV.

Material, extraction and isolation. Plant material was collected from La Mata (Alicante, Spain) during March 1991. A voucher specimen is deposited at the Herbarium of Department of Botany of the University of Salamanca (SALA 49010). The air-dried plant material was extracted with Me_2CO, the crude extract was suspended in H_2O–MeOH and then extracted with hexane–Et_2O (2:1). The resulting extract was defatted (MeOH, −30°) and chromatographed on silica gel (Merck, 7734) with a hexane–Et_2O gradient (0–100% Et_2O). Known compounds were identified by comparing the ^{1}H NMR spectra with those of authentic material.

The roots (266 g) afforded **1a**/**b** (3.2 g), **2a**/**b** (25 mg), **2c** (10 mg), **3a**–**3d** (265 mg), **4** (30 mg), while the aerial parts (1725 g) gave α-tocopherol (15 mg), sitosterol (25 mg), fatty esters of **5** (β-amyrin, 450 mg) and fatty esters of **6** (20(29)-lupene-3β,16β-diol, 425 mg).

Saponification of the triterpene ester mixts with 5% KOH–MeOH gave the alcohols **5** (60 mg) and **6** (40 mg), respectively. The fatty acids linked to **5** were esterified with CH_2N_2–Et_2O and the main components were identified by GC-MS as methyl myristate (20%), methyl palmitate (24%), methyl linoleate (40%) and methyl stearate (10%). The fatty acids bonded to **6** were likewise identified (GC-MS of methyl esters), as lauric (7%), myristic (40%), palmitic (45%) and stearic acids (8%).

6α-Methoxyeuryopsin (**1d**). Saponification of **1a**+**b** $[\alpha]_D = +10.2°$ (*c*, 1, $CHCl_3$) with KOH–MeOH gave a colourless oil. IR ν_{max}^{film} cm^{-1}: 1610, 1440, 1350, 1190, 1080, 960, 945, 875, 740; ^{1}H NMR: see Table 1; ^{13}C NMR: see Table 2; EIMS (GC) 70 eV, *m/z* (rel. int.): 246 $[M]^+$ (14), 214 (68), 199 (88), 172 (24), 159 (20), 145 (100), 128 (20), 125 (47), 123 (21), 115 (19), 90 (23), 77 (18).

6β-(2-Methylbutyryloxy)-furanoeremophilan-1-one (**3b**). Colourless oil. IR ν_{max}^{film} cm^{-1}: 1710, 1630, 1450, 1370, 1180, 1140, 1090, 1010, 950, 740; ^{1}H NMR: see Table 1; ^{13}C NMR: see Table 2; EIMS (GC) 70 eV, *m/z* (rel. int.): 332 $[M]^+$ (9), 248 (15), 230 (22), 215 (54), 208 (25), 188 (20), 173 (10), 145 (10), 125 (100), 124 (55), 123 (13), 91 (12), 85 (74), 57 (63), 55 (13), 41 (22).

6β-Isobutyryloxysenberginone (**3c**). Colourless oil. IR ν_{max}^{film} cm^{-1}: 1710, 1630, 1450, 1370, 1180, 1140, 1090, 1010, 950, 740; ^{1}H NMR: see Table 1; EIMS (GC) 70 eV, *m/z* (rel. int.): 318 $[M]^+$ (3), 248 (3), 233 (2), 230 (30), 215 (10), 188 (11), 146 (100), 125 (49), 91 (11), 85 (6), 71 (28), 43 (29), 41 (12).

6β-(2-Methylbutyryloxy)-senberginone (**3d**). Colourless oil. IR ν_{max}^{film} cm^{-1}: 1710, 1630, 1450, 1370, 1180, 1140, 1090, 1010, 950, 740; ^{1}H NMR: see Table 1; ^{13}C NMR: see Table 2; EIMS (GC) 70 eV, *m/z* (rel. int.): 332 $[M]^+$ (3), 248 (6), 233 (2), 230 (40), 215 (13), 188 (14), 146 (100), 125 (46), 91 (10), 85 (31), 57 (40), 55 (10), 41 (15).

Alkaline hydrolysis of **3a–3d**. A methanolic soln of compounds **3a–3d** (200 mg) were hydrolysed with 5% methanolic KOH for 6 hr at 80°, to give, after chromatography on silicagel (hexane–Et_2O 4:1–7: 3), the pure alcohols **3e** (25 mg), **3f** (15 mg) and **3g** (20 mg).

6β-Hydroxy-10αH-furanoeremophilan-1-one (**3e**). Colourless crystals. UV_{max}^{EtOH} nm: 281.5 sh, 227.9; ^1H NMR: see Table 1; ^{13}C NMR: see Table 2; EIMS (GC) 70 eV, *m/z* (rel. int.): 248 $[M]^+$ (18), 215 (2), 175 (2), 161 (2), 159 (2), 128 (13), 125 (100), 124 (79), 123 (36), 91 (7), 79 (9), 41 (9).

6β-Hydroxy-10βH-furanoeremophilan-1-one (**3f**). Oil. UV_{max}^{EtOH} nm: 278 sh, 227.9; IR ν_{max}^{film} cm^{-1}: 3440, 1370, 1040, 920, 750; ^1H NMR: see Table 1; ^{13}C NMR: see Table 2; EIMS (GC) 70 eV, *m/z* (rel. int.): 248 $[M]^+$ (10), 215 (2), 162 (3), 159 (2), 146 (3), 125 (100), 124 (73), 123 (29), 91 (6), 41 (7).

1β-Hydroxy-10βH-furanoeremophilan-6-one (**3g**). Colourless crystals; mp 136–137° (hexane); UV_{max}^{EtOH} nm: 270, 224.5; IR ν_{max}^{kBr} cm^{-1}: 3300, 1655, 1610, 1555, 1460, 1445, 1425, 1060, 1035, 1005, 950, 775, 740; ^1H NMR: see Table 1; ^{13}C NMR: see Table 2; EIMS (GC) 70 eV, *m/z* (rel. int.): 248 $[M]^+$ (25), 233 (8), 230 (26), 215 (10), 197 (5), 175 (5), 163 (43), 162 (24), 161 (14), 148 (12), 135 (5), 122 (100), 109 (13), 94 (24), 91 (10), 65 (11).

11β,12β-Epoxy-6β-(2-methylbutyryloxy)-$\Delta^{1(10)}$*-7-epidihydrobakkenolide A* (*senauricolide*) (**4**). Oil. UV λ_{max}^{EtOH} nm: 295.7; IR ν_{max}^{film} cm^{-1}: 2960, 2920, 2860, 1785, 1725, 1660, 1615, 1445, 1375, 1290, 1140, 1065, 1040, 990, 880; ^1H NMR: see Table 1; ^{13}C NMR: see Table 2; EIMS (GC) 70 eV, *m/z* (rel. int.): 348 $[M]^+$ (3), 291 (1), 246 (28), 218 (6), 190 (15), 189 (29), 187 (9), 175 (12), 174 (26), 173 (13), 121 (9), 120 (6), 119 (9), 107 (11), 105 (17), 93 (10), 92 (24), 85 (38), 79 (13), 77 (14), 57 (100), 55 (17), 43 (31), 41 (35).

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REFERENCES

1. Torres, P., Mancheño, B., Chinchilla, R., Asensi, M. C. and Grande, M., *Planta Medica*, 1988, **54**, 257.
2. Torres, P., Chinchilla, R., Asensi, M. C. and Grande, M., *Phytochemistry*, 1989, **28**, 3093.
3. Torres, P., Chinchilla, R. and Grande, M., *Studia Chemica*, 1992, **XVII**, 53.
4. Rigual Magallón, A., *Flora y Vegetación de la Provincia de Alicante*, ed. I. E. A. Excma. Diputación Provincial de Alicante, Alicante, 1972.
5. Heywood, W. H. and Humphries, C. J., *The Biology and Chemistry of the Compositae*. Academic Press, London, 1977; Robins, D. J., *Fortschritte der Chemie Organischer Naturstoffe*, 1982, **41**, 115.
6. Martín Panizo, F. and Rodríguez, B., *Anales de Quimica*, 1974, **70**, 1043.
7. Bohlmann, F., Jakupovic, J., Warning, U., Grenz, M., Chau-Thi, T. V., King, R. M. and Robinson, H., *Bulletin des Societies Chimiques Belges*, 1986, **95**, 707.
8. Bohlmann, F. and Zdero, C., *Phytochemistry*, 1977, **16**, 135.
9. Harmatha, J., Samek, Z., Novotny, L., Herout, V. and Sorm, F., *Collection of Czechoslovak Chemical Communications*, 1969, **34**, 1739.
10. Samek, Z., Harmatha, J., Novotny, L. and Sorm, F., *Collection of Czechoslovak Chemical Communications*, 1969, **34**, 2792.
11. Mericli, A. H., Mericli, F., Jakupovic, J., Bohlmann, F., Domínguez, X. A. and Vega, H. S., *Phytochemistry*, 1989, **28**, 1149.
12. Bohlmann, F. and Zdero, C., *Chemische Berichte*, 1976, **109**, 819.
13. Bohlmann, F., Zdero, C., Jakupovic, J., Misra, L. N., Benarjee, S., Singh, P., Baruah, R. N., Metwally, M. A., Schmeda-Hirschmann, G., Vincent, L. P. D., King, R. M. and Robinson, H., *Phytochemistry*, 1985, **24**, 1249.
14. Kitagawa, I., Shibuya, H. and Kawai, M., *Chemical and Pharmaceutical Bulletin*, 1977, **25**, 2638.
15. Rivett, D. E. A. and Woolard, G. R., *Tetrahedron*, 1967, **23**, 2431.
16. Brown, H. C., Brewster, J. H. and Shechter, H., *Journal of the American Chemical Society*, 1954, **76**, 467.
17. Wiemer, D. F., Wolfe, L. K., Fenical, W., Strobel, S. A. and Clardy, J., *Tetrahedron Letters*, 1990, **31**, 1973.
18. Hartmann, B., Deprés, J.-P., Greene, A. E. and Freire de Lima, M. E., *Tetrahedron Letters*, 1993, **34**, 1478.
19. Schudel, P., Mayer, H., Metzger, J., Ruegg, R. and Isler, O., *Helvetica Chimica Acta*, 1963, **46**, 333.
20. Mayer, H., Schudel, P., Ruegg, R. and Isler, O., *Helvetica Chimica Acta*, 1963, **46**, 650.
21. Steele, J. A. and Mosettig, E., *Journal of Organic Chemistry*, 1963, **28**, 571.
22. Narayanan, C. R., Kulkarni, A. K., Quasim, C. and Wadia, M. S., *Indian Journal of Chemistry, Section B*, 1976, **14B**, 906.
23. Wenkert, E., Baddeley, G. V., Burfitt, I. R. and Moreno, L. N., *Organic Magnetic Resonance*, 1978, **11**, 337.
24. Baddeley, G. V., Bealing, A. J., Jefferies, P. R. and Retallack, R. W., *Australian Journal of Chemistry*, 1964, **17**, 908.