6 Vokac, K , Samek, Z , Herout, V and Šorm, F (1969) *Coll. Czech Chem Comm* **34,** 2288
7 Cekan, Z., Herout, V and Šorm , F (1956) *Chem Ind London* 1234
8 Appendino, G and Gariboldi, P (1982) *Phytochemistry* **21,** 2555.
9. Bax, A (1982) *Two Dimensional Nuclear Magnetic Resonance in Liquids* Delft University Press

---

Phytochemistry, Vol. 27, No 11, pp 3672–3673, 1988
Printed in Great Britain

0031 9422/88 $3 00+0 00
Pergamon Press plc

SESQUITERPENE LACTONES FROM *LEUZEA LONGIFOLIA*

SUSANA M. B. P. SANTOS, FERNANDO M S BRITO PALMA, JULIO G URONES* and MANUEL GRANDE*

CECUL, Departamento de Química, Faculdade de Ciências, Universidade de Lisboa, 1200 Lisboa, Portugal, *Departamento de Química Orgánica, Facultad de Ciências Químicas, Universidade de Salamanca, 37008 Salamanca, Spain

(*Received* 20 *January* 1988)

Key Word Index—*Leuzea longifolia*, Compositae; sesquiterpene lactones, guaianolides

Abstract—From aerial parts of *Leuzea longifolia*, three new natural products, 11α,13-dihydro-8α-methacryloyloxyzaluzanine C, 11α-13-dihydro-3β-(2-hydroxymethyl)acryloyloxyzaluzanine C, 11α-13-dihydro-3β-methacryloyloxyzaluzanine C and a previously reported one, 11α-13-dihydro-8α-(2-hydroxymethyl) acryloyloxyzaluzanine C were isolated

INTRODUCTION

In continuation of our research interests about Portuguese endemic plants, we have studied the aerial parts of *Leuzea longifolia.* From the acetone extract, dewaxed with hexane, three major compounds were isolated and identified as 11α,13-dihydro-8α-methacryloyloxyzaluzanine C (**1**), 11α,13-dihydro-8α-(2-hydroxymethyl) acryloyloxyzaluzanine C (**2**), and 11α,13-dihydro-3β-(2-hydroxymethyl)acryloyloxyzaluzanine C (**3**) Although compound **2** has been described in the literature [1] as a gum, we have obtained it as a crystalline solid. A minor lactone, which we were not able to purify, was identified as 11α,13-dihydro-3β-methacryloyloxyzaluzanine C (**4**)

RESULTS AND DISCUSSION

The structure of compound 1 was deduced from spectral data, mainly ^{1}H (Table 1) and ^{13}C (Table 2) NMR, as well as δH/δH (COSY) and δH/δC (HCCORR) bi-dimensional correlations, which allowed unambiguous assignments of the signals. The ^{1}H NMR spectrum of compound **1** showed four signals at δ5 12 (1H, *s*), 5 14 (1H, *s*) and 5 35 (1H, *t*), 5 44 (1H, *t*), characteristic of two exomethylene protons. The *trans* fusion of the lactone ring is concluded from the coupling constant $J_{6,7}$ = 11 Hz, obtained from the peaks at δ4 20 (1H, *t*) and 2.70 (1H, *ddd*) assigned to H-6 and H-7, respectively. A doublet at δ1.16 (3H) and a double quartet at δ2.80 (1H), $J_{11,13}$ = 7 5 Hz, showed the presence of the methyl group in a position α to the lactonic carbonyl The configuration of this methyl group was inferred from the coupling constant $J_{7,11}$ = 7.5 Hz.

Table 1 ^{1}H NMR spectra* of compounds **1–4**

H	**1**	**2**	**3**	**4**
1	2 90 *m*	2 90 *m*	3 00 *m*	2 93 *m*
2	1 78 *ddd*	1 72 *dt*	1 88 *dt*	1 85 *dt*
2	2 31 *ddd*	2 30 *dt*	2 46 *m*	2 45 *m*
3	4 53 *tt*	4 51 *tt*	5 60 *tt*	5 57 *m*
5	2 90 *m*	2 90 *m*	3 00 *m*	2 93 *m*
6	4 20 *br t*	4 19 *br t*	4 18 *dd*	4 16 *br t*
7	2 70 *ddd*	2 70 *dt*	2 80 *m*	2 80 *m*
8	4 90 *ddd*	4 93 *ddd*	3 71 *ddd*	3 70 *ddd*
9	2 87 *dd*	2 83 *dd*	2 74 *dd*	2 73 *dd*
9	2 17 *dd*	2 18 *dd*	2 19 *dd*	2 20 *dd*
11	2 80 *dq*	2 76 *qnt*	2 80 *m*	2 80 *m*
13	1 16 *d*	1 14 *d*	1 27 *d*	1 27 *d*
14a	5 14 *br s*	5 13 *br s*	5 03 *s*	5 02 *s*
14b	5 12 *br s*	5 09 *br s*		
15a	5 44 *t*	5 42 *t*	5 38 *t*	5 36 *t*
15b	5 35 *t*	5 33 *t*	5 28 *t*	5 26 *t*
3′a	6 11 *qnt*	6 23 *q*	6 25 *dt*	6 13 *s*
3′b	5 62 *qnt*	5 88 *q*	5 90 *dt*	5 60 *s*
4′	1 95 *t*	4 33 *br s*	1 28 *s*	1 94 *s*

*Measured in $CDCl_3$ (**1, 2, 4**) at 200 MHz, int ref. $CHCl_3$ and CD_3CD (**3**), int ref. TMS

J(Hz) Compound **1** 2α,3 = 2β,3 = 7,4, 3,15 = 2, 6,7 = 7,8 = 11, 7,11 = 11,13 = 7 5, 8,9α = 4.5; 8,9β = 8 5; 9α,9β = 12 5 Compound **2** 2α,3 = 2β,3 = 7 4, 3,15 = 2, 6,7 = 7,8 = 10; 7,11 = 11,13 = 7 5, 8,9α = 4 5, 8,9β = 8.4, 9α,9β = 12 8 Compound **3** 2α,3 = 2β,3 = 7 3, 3,15 = 2, 11,13 = 8, 8,9α = 4 5, 8,9β = 9 2, 9α,9β = 12 2 Compound **4**· 3,15 = 2, 11,13 = 7 5, 8,9α = 4 5, 8,9β = 8 5, 9α,9β = 13 4

Table 2 ^{13}C NMR spectra* of compounds **1**–**4**

C	**1**	**2**	**3**	**4**
1	43.7 *d*	43.8 *d*	44.4 *d*	44.3 *d*
2	38.6 *t*	38.6 *t*	46.6 *t*	46.7 *t*
3	73.7 *d*	73.8 *d*	75.6 *d*	75.9 *d*
4	152.6 *s*	152.5 *s*	150.1 *s*	150.3 *s*
5	49.8 *d*	49.9 *d*	50.2 *d*	50.6 *d*
6	79.0 *d*	78.8 *d*	79.1 *d*	79.5 *d*
7	50.7 *d*	50.7 *d*	53.6 *d*	53.5 *d*
8	72.0 *d*	72.2 *d*	70.8 *d*	70.4 *d*
9	40.4 *t*	40.3 *t*	36.5 *t*	36.5 *t*
10	142.2 *s*	142.3 *s*	142.2 *s*	145.4 *s*
11	38.1 *d*	38.1 *d*	39.1 *d*	39.1 *d*
12	178.3 *s*	177.3 *s*	179.2 *s*	179.2 *s*
13	11.3 *q*	11.3 *q*	11.2 *q*	11.2 *q*
14	117.0 *t*	117.3 *t*	115.0 *t*	115.0 *t*
15	112.7 *t*	113.1 *t*	113.6 *t*	113.5 *t*
1′	166.4 *s*	166.8 *s*	165.8 *s*	167.2 *s*
2′	136.2 *s*	144.3 *s*	145.4 *s*	137.6 *s*
3′	126.1 *t*	126.3 *t*	123.2 *t*	126.2 *t*
4′	18.2 *q*	62.3 *t*	61.3 *t*	18.4 *q*

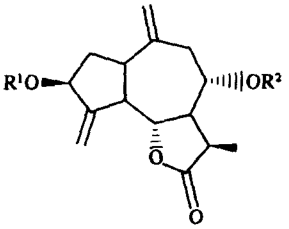
*Run at 50.3 MHz in $CDCl_3$ (**1**, **2**, **4**), int. ref. $CHCl_3$ and CD_3CD (**3**), int. ref. TMS.

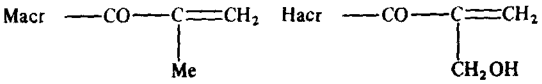
The signal at δ4.90 (1H, *ddd*) was assigned to the H-8 proton. From the coupling constant $J_{7,8} = 11$ Hz the ester group must be α oriented. The signal at δ4.53 (1H, *tt*) was assigned to H-3, geminal with an hydroxyl group, which must be β oriented, since $J_{2\alpha,3} = J_{2\beta,3} = 7.4$ Hz. The ^{1}H NMR spectra also showed that the side chain ester group was a methacrylate group: the signal at δ1.95 (3H, *t*) was assigned to the vinylic methyl group, and those at δ5.62 (1H, *qnt*) and 6.11 (1H, *qnt*) to the terminal methylene. Data from ^{13}C NMR, DEPT (Table 2) and bidimensional correlations, were in agreement with the above conclusions.

The NMR spectra of compound **2** were very similar to those of **1** (Tables 1 and 2). The main difference between the two concerned the signals of the acid that esterifies the C-8 hydroxyl group: the triplet at δ1.95 (3H) in the spectrum of **1**, assigned to H-4′, was replaced by a singlet at 4.33 (2H), characteristic of a $-CH_2-OH$ moiety. Consistently on going from **1** to **2** the C-2′ and C-4′ signals exhibited a shift to lower field.

The most significant difference between the NMR spectra of lactones **2** and **3** is related to the chemical shifts of H-3 and H-8. In compound **2** the signals assigned to H-3 and H-8 resonate at δ4.51 (1H, *tt*) and δ4.93 (1H, *ddd*), respectively. In contrast lactone **3** showed the corresponding signals, at δ5.60 (1H, *tt*) and δ3.71 (1H, *ddd*), respectively. These results supported the conclusions that in this compound the C-3 hydroxyl group was esterified, whilst that at C-8 is free.

From the NMR spectra of **4**, we could deduce the proposed structure. The differences between the ^{1}H NMR spectra of **4** and **1** were the same as those between **2** and **3**, so that we could assign the methacrylate ester to the C-3 proton. This position is supported by ^{13}C NMR data (Table 2).





$\mathrm{Macr}\ -\mathrm{CO}-\underset{\mathrm{Me}}{\underset{|}{\mathrm{C}}}{=}\mathrm{CH_2}$ $\quad$ $\mathrm{Hacr}\ -\mathrm{CO}-\underset{\mathrm{CH_2OH}}{\underset{|}{\mathrm{C}}}{=}\mathrm{CH_2}$

	R¹	R²
1	H	Macr
2	H	Hacr
3	Hacr	H
4	Macr	H

EXPERIMENTAL

General Mps: uncorr. NMR 200 MHz, MS 70 eV.

Isolation and separation Aerial parts of *L. longifolia* Hoff & Link (4.5 kg) were collected in Loures (Portugal) in June 1986, air-dried, finely triturated and extd with *n*-hexane and Me_2CO. The Me_2CO extract (5 g) was chromatographed on a silica gel column and eluted with a *n*-hexane–EtOAc gradient. From fractions 52–55 (284 mg: *n*-hexane–EtOAc, 3:2) white needle crystals were isolated and recrystallized from EtOH–Et_2O to obtain pure compound **1**. From fractions 58–60 (109 mg: *n*-hexane–EtOAc, 3:2), we obtained compound **4**, which after successive TLC (*n*-hexane–EtOAc, 1:1) could not be purified. Compound **2** was obtained from fractions 89–92 (594.5 mg: *n*-hexane–EtOAc, 2:3) as white crystals after recrystallization from EtOAc. Successive CC and TLC of fractions 100–196 (686 mg: *n*-hexane–EtOAc, 3:7) produced compound **3** as a solid.

11α,13-*Dihydro-8α-methacryloyloxyzaluzanine C* (**1**) Needles, mp 141°, IR ν_{max}^{KBr} cm^{-1}: 3500, 1780, 1705 and 1640. MS *m/z* (rel. int.), 70 eV. 332 $[M]^+$ (10), 246 $[M-RCO_2H]^+$ (99), 228 $[246-H_2O]^+$ (50), 69 $[RCO]^+$ (100). $[\alpha]_D^{24} = +103.5$ (EtOH; *c* 0.4).

11α,13-*Dihydro-8α-(2-hydroxymethyl)acryloyloxyzaluzanine C* (**2**) Needles, mp 131°, IR ν_{max}^{KBr} cm^{-1}: 3400, 1760, 1709, 1620. MS *m/z* (rel. int.), 70 eV: 348 $[M]^+$ (14), 246 $[M-RCO_2H]^+$ (72), 228 $[246-H_2O]^+$ (70), 85 $[RCO]^+$ (100), 57 $[85-CO]^+$ (82). $[\alpha]_D^{24} = +112.3$ (EtOH, *c* 0.26).

11α,13-*Dihydro-3β-(2-hydroxymethyl) acryloyloxyzaluzanine C* (**3**). Solid IR ν_{max}^{KBr} cm^{-1}: 3400, 1765, 1710, 1625, MS *m/z* (rel. int.), 70 eV: 348 $[M]^+$ (16), 246 $[M-RCO_2H]^+$ (47), 228 $[246-H_2O]^+$ (19), 85 $[RCO]^+$ (100). $[\alpha]_D^{24} = +96.4$ (EtOH, *c* 0.56).

11α,13-*Dihydro-3β-methacryloyloxyzaluzanine C* (**4**) Gum, IR ν_{max}^{KBr} cm^{-1}: 3400, 1765, 1708, 1640. MS *m/z* (rel. int.), 70 eV: 332 $[M]^+$ (4), 314 $[M-H_2O]^+$ (3), 263 $[M-RCO]^+$ (100), 246 $[M-RCO_2H]^+$ (22), 69 $[RCO]^+$ (99). $[\alpha]_D^{24} = +84.4$ ($CHCl_3$; *c* 0.69).

Acknowledgements—This work was supported by Instituto Nacional de Investigação Científica (INIC), Portugal

REFERENCE

1 Bohlmann, F., Singh, P., Jakupovic, J. and Huneck, S. (1985) *Planta Med* **1**, 74.