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SESQUITERPENE LACTONES FROM *LEUCANTHEMOPSIS PULVERULENTA*

J. De Pascual Teresa, M. A. Moreno Valle, M. S. González and I. S. Bellido

Department of Organic Chemistry, Salamanca University, Spain

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Key Word Index—*Leucanthemopsis pulverulenta*; Compositae; 4,5-*cis*-germacranolide.

Abstract—From *Leucanthemopsis pulverulenta*, two guaianolides, 8α-hydroxyestafiatin and epiligustrin, and one 4,5-*cis*-germacranolide, named pulverulide, have been isolated. Epiligustrin and pulverulide are new natural compounds.

INTRODUCTION

In a previous paper [1] we reported the isolation of several heliangolides and germacranolides from the aerial parts of *Leucanthemopsis pulverulenta* (Lag.) Heywood, and we report now the isolation of two guaianolides (**1**, **2**) and one 4,5-*cis*-germacranolide (**3**) from the most polar fraction of the chloroform extract.

RESULTS AND DISCUSSION

Lactone **1** was a solid of mp 142° and $[\alpha]_D$ +49.6° (*c* 2.5; $CHCl_3$) and had spectral properties identical in all respects with those reported by Bohlmann and Zdero [2] for 8α-hydroxyestafiatin isolated as a colourless gum from *Tanacetum partheniuum*.

Lactone **2**, $C_{15}H_{18}O_3$, was also a solid, mp 132° and $[\alpha]_D$ +77.4° (*c* 0.90; $CHCl_3$). Its IR and ^1H NMR spectra identified it as epiligustrin (**2**), identical to a lactone synthesized from cumambrina-A by Ito *et al.* [3].

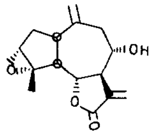
Lactone **3**, $C_{15}H_{20}O_4$, named pulverulide, was a colourless oil with $[\alpha]_D$ +8.4° (*c* 0.83; $CHCl_3$). The IR spectrum in chloroform suggested the presence of an α-methylene-γ-lactone (1760, 1660, 880 cm^{-1}), unsaturations of the type $C{=}CH_2$ and $C{=}CH$ (1630, 890, 820 cm^{-1}) and hydroxyl groups (3600, 3400 cm^{-1}). These functionalities were confirmed by the ^1H NMR spectrum (Table 1), which was typical of a 3β-hydroxy-4,5-*cis*-germacranolide [1].

By double-resonance experiments, we established the sequence –CH(OH)–CH$_2$–CH(OH)–; by irradiation at δ2.30, the signals at 4.15 and 4.45 became two singlets, which provided proof of the location of the hydroxyl groups at C-1 and C-3. The multiplicity of the signals due to the geminal hydroxyl protons, the paramagnetic shift of the signal due to H-6 (δ5.97), the intramolecular association between the hydroxyl groups (IR broad band at 3400 cm^{-1}) and the biogenetic correlation with lactone **4**, also present in the plant, suggested β-dispositions for both hydroxyl groups.

The CD curve of **3**, recorded in methanol, exhibited a negative minimum at 213 nm (Δε = −6.93) like other heliangolides, but the absence of an absorption at 250 nm, attributable to the lactone ring [4, 5], could be explained by assuming that the lactone ring was planar. For a planar lactone ring, the dihedral angle H-6–H-7 should be *ca* 120°, and could explain the observation that *trans* $J_{6,7}$ = 4 Hz is greater than in typical heliangolides [1, 6].

From all these data and from careful analysis of Dreiding models, we propose that for **3** the most probable conformation is that depicted by structure **3a** in Fig. 1.

In an effort to prepare **3**, lactone **4**, previously reported from *L. pulverulenta* [1], was treated with *p*-toluenesulphonic acid. This gave only **5**, a colourless oil of $[\alpha]_D$ −4.6° (*c* 1.3; $CHCl_3$), whose ^1H NMR spectrum (Table 1) was in agreement with the proposed structure and conformation **5a** (Fig. 1).



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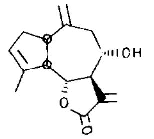

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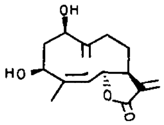

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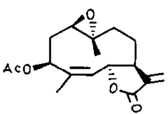

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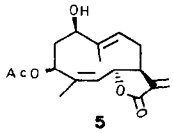

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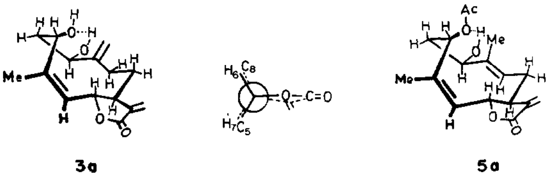

3a **5a**

Fig. 1. The probable conformations of pulverulide (**3a**) and lactone **5**.

Table 1. ^1H NMR spectral data for lactones **3** and **5** ($CDCl_3$, 60 MHz, TMS as internal standard)

H	3	J (Hz)	5	J (Hz)
H-1	4.15 *dd*	5, 11	4.80 *dd*	6, 11
H-2	2.30 *m**		2.35 *m**	
H-3	4.45 *t*	3	5.50 *t*	3
H-5	5.05 *br d*	10	5.35 *br d*	10
H-6	5.97 *dd*	4, 10	5.65 *dd*	3, 5
H-7	2.85 *m**		2.85 *m**	
H-8	2.10 *m**		2.65 *dd*	3, 9
			2.95 *br d*	5
H-9	2.60 *m**		5.40 *m**	
H-13	5.62 *d*	2.5	5.57 *d*	2
H-13′	6.25 *d*	2.5	6.24 *d*	2
H-14	5.20 *s*		1.79 *br s*	
H-14′	5.38 *s*			
H-14′	5.38 *s*			
H-15	1.72 *br s*		1.90 *s*	
OAc	—		2.00 *s*	

*Unresolved signals.

EXPERIMENTAL

Mps are uncorr. ^1H NMR spectra were recorded at 60 MHz using TMS as internal standard. Analytical TLC was performed on silica gel G (Merck No. 7731) and CC on silica gel 60 (Merck No. 7734).

Isolation of compounds. The plant material was identified by Professor B. Casaseca Mena from the Department of Botany, Salamanca University, where a specimen is held (Herbarium No. 8669). The most polar fraction of the dry, chromatographed chloroform extract of *L. pulverulenta* (2.485 g, 40% of the whole extract) was chromatographed on 100 g silica gel to give, after purification by TLC or crystallization, 125 mg **1**, 263 mg **2** ($CHCl_3$–Et_2O, 4:1) and 237 mg **3** ($CHCl_3$–Et_2O, 7:3).

8α-Hydroxyestafiatin (**1**). Mp 142° (Et_2O), $[\alpha]_D$ +49.6° (*c* 2.5; $CHCl_3$); IR ν_{max} cm^{-1}: 3600, 3080, 1770, 1665, 1380, 1150, 1090, 950, 880, 825; MS *m/z* (rel. int.): 262 $[M]^+$ (5), 247 $[M - Me]^+$ (9), 244 $[M - H_2O]^+$ (4), 149 (40), 97 (76), 95 (54), 71 (40), 43 (100).

Epiligustrin (**2**). Mp 132° (Et_2O), $[\alpha]_D$ +77.4° (*c* 0.9; $CHCl_3$); IR ν_{max} cm^{-1}: 3400, 3080, 1760, 1640, 1280, 1173, 1060, 900, 840; MS *m/z* (rel. int.): 246 $[M]^+$ (8), 228 $[M - H_2O]^+$ (7), 203 (10), 160 (47), 121 (43), 107 (51), 91 (100), 79 (66), 43 (82).

Pulverulide (**3**). Viscous oil, $[\alpha]_D$ +8.4° (*c*, 0.83, $CHCl_3$); IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3600, 3400, 3020, 1760, 1660, 1630, 1385, 1280, 1140, 980, 880, 820; ^1H NMR (see Table 1); MS *m/z* (rel. int.): 264 $[M]^+$ (4), 249 $[M - Me]^+$ (2), 246 $[M - H_2O]^+$ (4), 228 $[M - 2 \times H_2O]^+$ (2), 185 (10), 149 (27), 133 (22), 95 (38), 71 (30), 43 (100); CD (MeOH): $\Delta\varepsilon_{213} = -6.93$.

Lactone **5**. Treatment of **4** (80 mg) with dry C_6H_6 (5 ml) and *p*-toluenesulphonic acid (5 mg) with heating for 1 hr gave **5** (60 mg), viscous oil, $[\alpha]_D$ −4.6° (*c* 1.3; $CHCl_3$); IR ν_{max} cm^{-1}: 3600, 1770, 1740, 1675, 1380, 1250, 1220, 1150, 1100, 1025, 875, 830; ^1H NMR (see Table 1); $[M]^+$ 306 ($C_{17}H_{22}O_5$); CD (MeOH); $\Delta\varepsilon_{219} = -3.93$, $\Delta\varepsilon_{260} = -0.3$.

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