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LONGIPIN, A NEW MELAMPOLIDE FROM *MELAMPODIUM LONGIPES*

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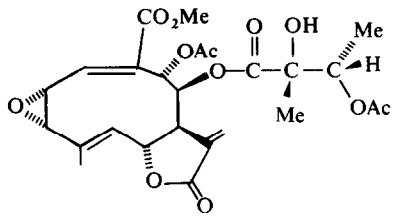
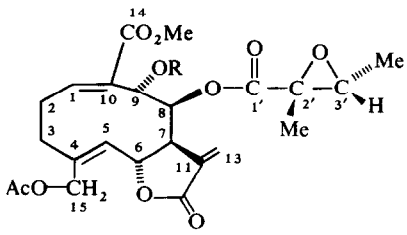
Key Word Index—*Melampodium longipes*; Heliantheae; Compositae; sesquiterpene lactone; melampolide.

INTRODUCTION

The sesquiterpene lactone analysis of *Melampodium longipes* (A. Gray) Robins yielded a known melampolide, melampodinin (**1**) [1], previously isolated from *Melampodium americanum* L., and a new melampolide, longipin (**2a**). We report here the isolation and structural elucidation of the new compound.



1 Melampodinin



2a R = H
2b R = Ac

RESULTS AND DISCUSSION

The structure of longipin (**2a**) was deduced by comparison of the NMR data of **2a** and its acetate (**2b**) with those of other known melampolides (Table 1) [1]. The 100 MHz NMR spectrum of longipin displayed two one-proton doublets at 6.22 ppm (J = 3.5 Hz) and 5.66 ppm (J = 3.0 Hz) and a broad one-proton multiplet at 2.52 ppm that are characteristic of α,β-unsaturated γ-lactones. A one-proton quartet at 3.02 ppm (J = 5.5 Hz), a singlet (3H) at 1.55 and a doublet (3H) at 1.26 ppm (J = 5.5 Hz) indicated the presence of an epoxyangeloyl moiety [1]. A singlet (3H) at 3.69 ppm was assigned the methyl group of a carbomethoxy moiety in which the carboxyl group represents C-14, typical for α,β-unsaturated methyl ester-containing melampolides from *Melampodium* species [1]. The broad doublet of a doublet at 6.86 ppm was assigned H-1. The presence of an oxygenated methylene group (C-15) was indicated by an AB pattern centered at 4.79 ppm; its chemical shift suggested the presence of an ester function at C-15. A singlet (3H) at 2.04 ppm indicated an acetate group and a broadened triplet (1 H) was assigned to H-9. Irradiation at the center of the multiplet at 2.52 ppm (H-7) of **2a** collapsed the doublet of a doublet at 6.29 ppm to a doublet ($J_{8,9}$ = 8.5 Hz), reduced the H-13a and b doublets at 5.66 and 6.22 ppm, respectively, to singlets, and affected the overlapping H-5 and H-6 signals at 5.07–5.33 ppm. Saturation at 5.17 ppm sharpened the AB pattern centered at 4.79 ppm (2H-15) and affected the region containing the H-7 signal. Irradiation of H-8 at 6.29 ppm collapsed the broadened triplet at 4.11 ppm to a broadened doublet ($J_{8,9}$ = 8.5 Hz). When the quartet at 3.02 ppm was irradiated, the doublet at 1.26 ppm (3′-C$\underline{H}_3$) collapsed to a singlet.

Table 1. ^{1}H NMR parameters* of longipin (**2a**) and acetate (**2b**)

	2a	**2b**
H-1	6.86 *brdd* (7.5, 10.0)	7.01 *brdd* (7.5, 10.0)
H-2 α and β	2.00–3.00	2.00–3.00
H-3 α and β	2.00–3.00	2.00–3.00
H-5		
H-6	5.07–5.33 *m*	5.00–5.35
H-7	2.52 *m*	
H-8	6.29 *dd* (1.5, 8.5)	6.66 *dd* (1.5, 8.5)
H-9	4.11 *brt* (9.0, 8.5)	5.31 *d* (8.5)
H-13a	5.66 *d* (3.0)	5.76 *d* (3.0)
H-13b	6.22 (3.5)	6.28 (3.5)
H-15	4.79†	4.99†
H-3′	3.02 *q* (5.5)	3.02 *q*
2′-Me	1.55 *s*	1.44 *s*
3′-Me	1.26 *d* (5.5)	1.12 *d* (5.5)
Ac	2.04 *s*	2.00 *s*
		2.04 *s*

* Spectra were run in $CDCl_3$ at 100 MHz and TMS was used as internal standard. Values are recorded in ppm relative to TMS. Multiplets are designated as follows: *s*, singlet; *d*, doublet; *t*, triplet; *q*, quartet; *m*, multiplet whose center is given; *br*, broad. Figures in parentheses are coupling constants or line separations in hertz.

† Intensity two protons, center of AB system.

Acetylation of **2a** yielded the acetate **2b**. Most notably, the H-9 signal shifted downfield and appeared as a doublet at 5.31 ppm ($J_{8,9}$ = 8.5 Hz). The 100 MHz spectrum showed a doublet of doublets centered at 6.66 ppm (H-8).

Since the NMR coupling parameters and CD spectral data of **2a** are very similar to those of other melampolides [1, 2], the configuration and conformation of **2a** appear to be the same as in melampodin A, a compound with known absolute configuration [2].

EXPERIMENTAL

Melampodium longipes (Hartman-Funk No. 4283; voucher deposited at OS; Mexico: Jalisco: Hwy 15, 2 mi NW of Tequila).

Stems and leaves (780 g) were extracted in 3 l. of $CHCl_3$ and worked up according to a standard procedure [3] to yield 14.5 g of crude syrup. The syrup was chromatographed over 250 g of Si gel taking 20 ml fractions. $CHCl_3$ was used an an eluant followed by $CHCl_3$–Me_2CO mixtures (95:5, 90:10, 80:20, etc). Fractions 25–33 contained melampodinin, and fractions 35–46 yielded 130 mg crystalline longipin, mp 203–206° (EtOAc); CD (c 4.31 × 10^{-5}, MeOH) $[\theta]_{216} = -7.89 \times 10^4$, $[\theta]_{251} = 5.57 \times 10^3$; IR ν_{max}: 3500 (OH), 1760 (γ-lactone), 1730 (ester), 1225 (acetate); the low resolution MS (70 eV) showed significant peaks at m/e (rel. int.): 464 (0.01, M^+), 422 (0.02, $M-C_2H_2O$), 404 (0.04, $M-C_2H_4O_2$), 350 (0.03, $M-C_5H_6O_3$), 349 (0.17, $M-C_5H_7O_3$), 290 (0.06, $M-C_2H_4O_2-C_5H_6O_3$), 289 (0.35, $M-C_5H_7O_3-C_2H_4O_2$), 288 (0.28, $M-C_5H_8O_3-C_2H_4O_2$), 270 (0.31, $M-C_5H_8O_3-C_2H_4O_2-H_2O$), 256 (0.70, $M-C_5H_8O_3-C_2H_4O_2-CH_4O$), 71 (0.26, C_4H_7O), 43 (100, C_2H_3O); (Calc. for $C_{16}H_{18}O_5$: 290.1154. Found: (MS) 290.1161).

Acetylation of 100 mg of **2a** in 1 ml of Py and 1 ml Ac_2O for 24 hr followed by the usual work-up gave **1b** (gum); IR ν_{max} (CCl_4): 1765 (γ-lactone), 1750, 1730, 1720 (esters), 1670, 1650 (double bonds); the low resolution MS (70 eV) showed significant peaks at m/e (rel. int.): 506 (0.01, M^+), 464 (0.01, $M-C_2H_2O$), 446 (0.02, $M-C_2H_4O_2$), 404 (0.02), $M-C_2H_4O_2-C_2H_2O$), 392 (0.02, $M-C_5H_6O_3$), 391 (0.01, $M-C_5H_7O_3$), 350 (0.03, $M-C_5H_6O_3-C_2H_2O$), 332 (0.02, $M-C_5H_6O_3-C_2H_4O_2$), 300 (0.03, $M-C_5H_6O_3-C_2H_2O-C_2H_4O_2$), 272 (1.00, $M-C_5H_6O_3-C_2H_4O_2-C_2H_4O_2$), 240 (0.27, $M-C_5H_6O_3-C_2H_4O_2-C_2H_4O_2-CH_4O$), 71 (0.17, C_4H_7O), 43 (0.96, C_2H_3O).

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GERMACRENE-D FROM *FALCARIA VULGARIS**

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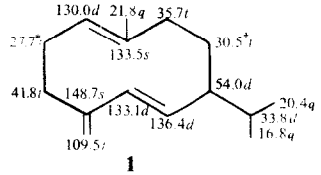
Key Word Index—*Falcaria vulgaris*; Apiaceae/Umbelliferae; essential oil; sesquiterpene; germacrene-D; spectroscopy.

From the essential oil of the fresh herb of *Falcaria vulgaris* Bernh., germacrene-D (**1**) was isolated by column chromatography on Si gel. The structure was determined by comparing GLC behaviour and IR, MS, ^1H NMR spectra with published data [1, 2] and ^{13}C NMR spectroscopy. Assignments of chemical shifts are indicated on structure **1**. The splittings refer to the off-resonance spectrum.



1

As far as we know, germacrene-D, a key intermediate in sesquiterpene biogenesis, has been found for the first time in a volatile oil of the Apiaceae. A similar high amount (71%) of this sesquiterpene hydrocarbon has been isolated from aerial parts of *Acanthopanax sciaphylloides* (Araliaceae) [3], showing once more the close chemical relationship of these two families.

EXPERIMENTAL

Above ground parts of flowering plants were collected near Wuerzburg in August 1977. The volatile oil (0.3–0.4% yield) was obtained from the fresh herb by steam distillation with a receiver, as used by the European Pharmacopoeia for determination of volatile oil in drugs. The pale yellow oil (d_{20}^{20} = 0.8925; n_D^{20} = 1.5040) was subjected to CC using Si gel for dry CC (Woelm) and *n*-pentane as eluent [4]. Repeated chromatography of the hydrocarbon fraction (nearly 90% of the total oil) at −20° with Si gel–pentane [5] yielded 62% germacrene-D, which was identified by GLC and spectrometric methods. $C_{15}H_{24}$ (M^+ at m/e 204). GLC: $I^{150°}_{carbowax\ 20M}$ = 1715. MS m/e (rel. int.): 161 (100), 105 (40), 204 (34), 41 (33), 91 (32).

* Part 5 in the series "On the Essential Oils from the Apiaceae." For Part 4 see Kubeczka, K.-H. (1976) *Z. Naturforsch.* **31**, 283.

† Indicates a possible signal reversal.