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A MELAMPOLIDE FROM *MELAMPODIUM HETEROPHYLLUM*

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Key Word Index—*Melampodium heterophyllum*; Compositae; sesquiterpene lactones; melampolides; melampodin; 11β,13-dihydromelampodin.

Abstract—The sesquiterpene lactones melampodin and 11β,13-dihydromelampodin have been isolated from *Melampodium heterophyllum*.

Typical sesquiterpene lactones of the genus *Melampodium* (Compositae, tribe Heliantheae, subtribe Melampodiinae) and related genera are the melampolides [1]. We have now investigated *M. heterophyllum* Lag. The aerial parts afforded a mixture of two sesquiterpene lactones, which could not be separated even by HPLC. The ^{1}H NMR spectral data (Table 1) clearly indicated that one of the lactones was melampodin (**1**) [2, 3], while the second compound was the dihydro derivative **2**. Addition of excess of diazomethane to the mixture transformed **1** completely to the corresponding pyrazoline derivative, while **2** remained unchanged and could then be separated by TLC. Inspection of the ^{1}H NMR spectral data including spin decoupling results allowed the assignment of all signals (Table 1). Irradiation of the broadened doublet at δ 1.73 collapsed the double doublet at 4.99 to a doublet and the double quartet at 2.10 to a quartet. The latter was further coupled with the doublet at 1.29, thus indicating that we were dealing with the signals of H-6, H-7, H-11 and H-13. As $J_{7,11}$ was 12 Hz the proton at C-11 must be β-orientated. The other signals were very similar to those of **1**, though of course the chemical shifts were slightly different due to the missing deshielding effect of the 11,13-double bond.

The isolation of **1** and **2** again shows that these lactones are typical for the genus *Melampodium*.

Table 1. ^{1}H NMR spectral data of compounds **1** and **2** (TMS as internal standard, $CDCl_3$)

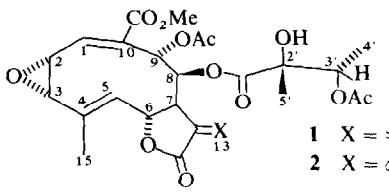
	1*	2†
H-1	7.01 *d*	7.01 *d*
H-2	3.64 *dd*	3.63 *dd*
H-3	3.74 *d*	3.71 *d*
H-5	5.32 *dq*	5.18 *dq*
H-6	5.21 *dd*	4.99 *dd*
H-7	2.65 *br.ddd*	1.83 *br.dd*
H-8	6.67 *br.d*	6.02 *br.d*
H-9	5.36 *d*	5.41 *d*
H-11	—	2.10 *dq*
H-13	6.22 *d*	1.29 *d*
H-13′	5.81 *d*	
H-15	2.19 *d*	2.16 *d*
H-3′	5.18 *q*	5.16 *q*
H-4′	1.27 *d*	1.32 *d*
H-5′	1.25 *s*	1.29 *s*
OAc	2.00 *s*	1.99 *s*
	1.90 *s*	1.98 *s*
OMe	3.83 *s*	3.83 *s*

* 270 MHz.
† 400 MHz.
J(Hz): Compound **2**: 1,2 = 2.3; 2,3 = 3.5; 5,6 = 6,7 = 10; 7,8 ~ 1; 7,11 = 12; 8,9 = 8.7; 11,13 = 7; 3′,4′ = 6.5.

EXPERIMENTAL

The aerial parts of *M. heterophyllum* (2.7 kg) were collected 40 km south of Acapulco. Soxhlet extraction with petrol afforded an extract, which was further extracted with MeOH. The soluble part (28 g) was separated by CC (Si gel). Elution with C_6H_6–Me_2CO (4:1) gave 1.3 g of a mixture of **1** and **2**. Excess CH_2N_2 was added to 20 mg of **1** and **2**. After 10 min the soln was evapd and the residue separated by TLC ($CHCl_3$–C_6H_6–Et_2O, 1:1:2).

11β,13-Dihydromelampodin (**2**). Colourless crystals, mp 217° (CH_2Cl_2–Et_2O); IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3540 (OH), 1780 (γ-lactone), 1740 (CO_2R, OAc); MS *m/z* (rel. int.): 524.189 (M^+, 1)



1 X = =CH_2
2 X = α-Me, H

($C_{25}H_{32}O_{12}$), 492 (M − MeOH, 1), 480 (M − CO_2, 17), 464 (M − HOAc, 2), 438 (480 − MeOH, 9), 348 (M − RCO_2H, 1), 288 (348 − HOAc, 19), 57 (100).

$$[\alpha]_{24^\circ}^{\lambda} = \frac{589 \quad 578 \quad 546 \quad 436 \quad 365\,\text{nm}}{+15.5 \quad +16.5 \quad +18.5 \quad +41.5 \quad +94.0}$$

(c = 0.2, $CHCl_3$).

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SIX CADINENE DERIVATIVES FROM *AGERATINA ADENOPHORA**

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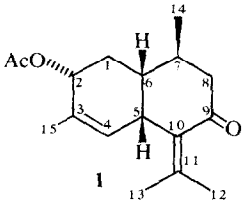
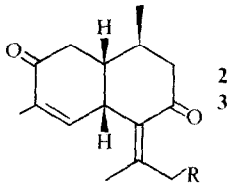
Key Word Index—*Ageratina adenophora*; Compositae; Eupatorieae, sesquiterpenes; cadinene derivatives.

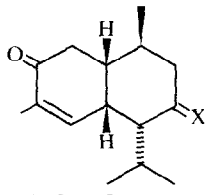
The aerial parts of *A. adenophora* (Spreng.) K. et R. afforded β-farnesene, germacrene D, bisabolene, caryophyllene and six further sesquiterpenes, the cadinene derivatives **1**–**6**, of which only **1** had been isolated previously [1]. The structures of **2**–**6** followed from the ^{1}H NMR data (Table 1) and spin decoupling. The ^{1}H NMR signals of **2** could only be interpreted completely in C_6D_6. Spin decoupling clearly indicated the presence of a cadinene derivative. Irradiation of the signal at δ 1.53 collapsed the double doublets at δ 2.63 and 2.11 to doublets and changed the signals at δ 3.55 and 1.83 as well. The signal at δ 3.55 was further coupled with the signal of the olefinic proton at δ 5.83 and with that of the olefinic methyl (δ 1.74 *dd*) thus indicating the sequence H-1, H-6, H-5 and H-4 and the presence of a six-membered ring. The signal at δ 1.83 was further coupled with that of



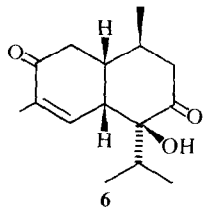
1



2 R = H
3 R = OH



4 X = O
5 X = β-OH, H



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*Part 333 in the series "Naturally Occurring Terpene Derivatives". For Part 332 see Bohlmann, F., Zdero, C., Pickardt, J., Robinson, H. and King, R. M. (1981) *Phytochemistry* **20**, 1323.