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TWO SESQUITERPENE AND THREE DITERPENE LACTONES FROM *ACANTHOSPERMUM AUSTRALE*[*]

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Key Word Index—*Acanthospermum australe*; Compositae; Heliantheae; sesquiterpene lactones; melampolide; *cis,cis*-germacranolide; diterpene lactones derived from geranylgeraniol.

Abstract—The aerial parts of *Acanthospermum australe* afforded two new sesquiterpene lactones, an acid and a *cis,cis*-germacranolide, as well as three diterpene lactones of a new type, most probably formed by intermolecular nucleophilic attack of the carboxyl group of an acid epoxide derived from geranylgeraniol. The structures were proposed on the basis of spectroscopic studies.

So far from the small American genus *Acanthospermum* (Compositae, tribe Heliantheae, subtribe Melampodiinae), melampolides [1–3] similar to those from the genus *Melampodium* [4] have been isolated. A re-investigation of *A. australe* (Loefl.) Ktze. afforded, in addition to germacrene D, a further melampolide, the diangelate **1** with a carboxyl group at C-10, traces of the *cis,cis*-germacranolide **2** and the geranylgeraniol derivatives **3**, **4** and **6**. The ^1H NMR data of **1** (Table 1) were similar to those of related aldehydes [1,2]. The stereochemistry at C-8 and C-9 followed from the observed couplings and that of the 1,10-double bond from the chemical shift of H-1. The presence of a 10-carboxyl group was deduced from the IR spectrum, the molecular formula and the chemical shift of H-1, while the nature of the ester residues followed from the typical ^1H NMR signals. The ^1H NMR data of **2** (Table 1) again showed the presence of a diangelate, which, however, had a hydroxyl group at C-15 (4.10, *br. s*). The 4,5-*cis* configuration followed from the characteristic differences in the chemical shifts of H-5 and H-6 and the coupling $J_{6,7}$ [2], while the stereochemistry at C-8 and C-9 was deduced from the coupling $J_{8,9}$ and $J_{9,14}$. The latter was a typical *W*-coupling between H-9 and H-14 [2]. The presence of a 1(10)-*cis*-double bond followed from the chemical shift of H-1. Though some signals overlapped (H-2 and H-3), the proposed structure was very likely. The ^1H NMR data were characteristically different from those of orientalide [5].

Table 1. ^1H NMR spectral data of sesquiterpene lactones **1** and **2** (270 MHz, TMS as internal standard, $CDCl_3$)

	1	**2**
H-1	7.20 *br. dd*	6.80 *br. dd*
H-2	2.83 *m*	2.80 *m*
H-5	5.02 *br. d*	5.60 *br. d*
H-6	5.16 *dd*	5.47 *dd*
H-7	2.54 *m*	2.64 *m*
H-8	6.77 *dd*	6.70 *dd*
H-9	5.50 *d*	5.89 *br. d*
H-13	6.29 *d*	6.43 *d*
H-13′	5.86 *d*	5.89 *d*
H-14	—	9.43 *d*
H-15	2.04 *br. s*	4.10 *br. s*
OAng	6.10, 6. 05 *qq*	6.15, 6.00 *qq*
	1.95, 1.90 *dq*	1.96, 1.86 *dq*
	1.81, 1.79 *dq*	1.81, 1.79 *dq*

J (Hz): Compound **1**: 1, 2 = 10; 1, 2′ = 7.5; 5, 6 = 6, 7 = 10; 7,8 = 1.5; 7, 13 = 3.5; 7, 13′ = 3; 8, 9 = 9; compound **2**: 1, 2 = 9; 1, 2′ = 6; 5, 6 = 10; 6, 7 = 5; 7, 8 = 2; 7, 13 = 3; 7, 13′ = 2.6; 8, 9 = 10; 9, 14 = 1.5; OAng: 3′, 4′ = 7; 3′, 5′ = 4′, 5′ = 1.5.

The structures of **3**, which was isolated as its diacetate **5**, and of the isomeric acetates **4** and **6** were deduced by the ^1H NMR data (Table 2). The spectra of **4** and **6** showed characteristic differences. While in the spectrum of **4** the presence of a secondary hydroxyl was indicated by the broadened double doublet at δ 3.50 ppm, this signal was replaced in the spectrum of **6** by a double doublet at 4.52 ppm. Furthermore, the singlet at 1.35 was shifted to 1.27. The presence of unsaturated lactones in both compounds followed from the IR band at 1700 cm^{-1} and from their molecular formulae. The position of the hydroxyl in **4** was deduced by spin decoupling. The broadened triplet at 5.38 had to be assigned to H-2, as on irradiation the double doublets of the CH_2OAc group collapsed to doublets. H-2, however, showed allylic

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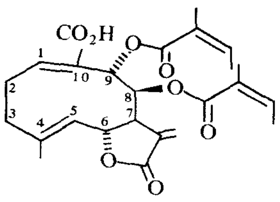
[*] Part 331 in the series "Naturally Occurring Terpene Derivatives". For Part 330 see Rustaiyan, A., Niknejad, A., Bohlmann, F. and Schuster, A. (1981) *Phytochemistry* **20**, 1154.

Table 2. ^1H NMR spectral data of diterpene lactones **3**–**6** (270 MHz, TMS as internal standard, $CDCl_3$)

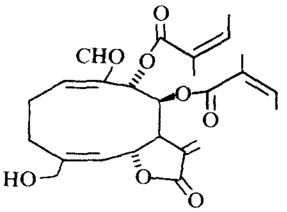
	3	**4**	**5**	**6**
H-1	4.20 *dd*	4.66 *dd*	4.53 *br. d*	4.63 *dd*
H-1′	4.02 *dd*	4.60 *dd*		4.50 *dd*
H-2	5.58 *br. t*	5.38 *br. t*	5.37 *br. t*	5.36 *br. t*
H-4	2.15 *m*	2.31 *m*	2.15 *m*	2.14 *m*
H-5	1.77 *m*	1.77 *m*	1.75 *m*	1.53 *m*
H-5′	1.55 *m*	1.50 *m*	1.50 *m*	
H-6	3.47 *dd*	3.50 *dd*	4.98 *dd*	4.52 *dd*
H-9	2.50 *m*	2.50 *m*	2.47 *m*	2.53 *m*
H-10	6.29 *br. t*	6.28 *br. t*	6.27 *br. t*	5.98 *br. t*
H-12	2.15 *m*	2.15 *m*	2.10 *m*	2.14 *m*
H-14	5.08 *br. t*	5.09 *br. t*	5.09 *br. t*	5.09 *br. t*
H-16	1.59 *br. s*	1.60 *br. s*	1.58 *br. s*	1.59 *br. s*
H-17	1.68 *br. s*	1.69 *br. s*	1.67 *br. s*	1.67 *br. s*
H-19	1.36 *s*	1.35 *s*	1.34 *s*	1.27 *s*
H-20	1.74 *br. s*	1.78 *br. s*	1.76 *br. s*	1.77 *br. s*
OAc	—	2.06 *s*	2.04 *s*	2.04 *s*
		—	2.12 *s*	—

J (Hz): 1, 1′ = 12; 1, 2 = 7; 5, 6 = 2.5; 5′, 6 = 10; 9, 10 = 4.5; 13, 14 = 6.

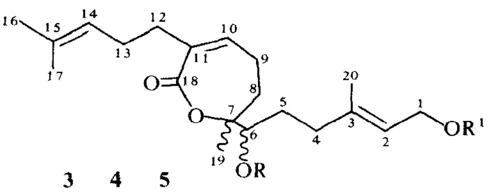
couplings with the protons at C-4, which were coupled with two further protons. The latter were coupled with the proton at the carbon bearing the hydroxyl, clearly indicating the sequence H-1 through H-6. In the spectrum of **6**, the H-6 signal overlapped the H-1 signal. Irradiation of the H-2 signal, however, clearly showed that the H-6 signal was a double doublet. The chemical shifts of the other protons were similar in all compounds, except that of H-10, which was at higher fields in the spectrum of **6**. The signals of H-12 through H-17 were typical for such end groups, while the stereochemistry of the 2,3-double bond followed from the chemical shifts of H-2 and H-20,



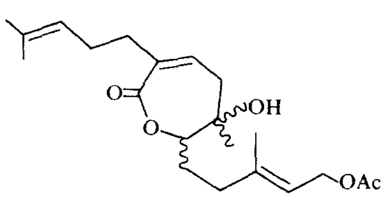
1



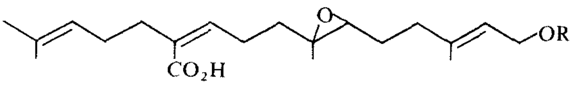
2



	3	**4**	**5**
R	H	H	Ac
R^1	H	Ac	Ac



6



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when compared with those of geranyl and neryl acetate. The configuration at C-6 and C-7, however, could not be assigned. Compounds **4** and **6** obviously were formed via the epoxide **7** by nucleophilic attack of the carboxyl group at C-7 and C-8 respectively. We have named **3** acanthoaustralide and **6** isoacanthoaustralide-1-*O*-acetate.

The isolation of **1** and **2** confirm that the genus *Acanthospermum* can be characterized by the occurrence of melampolides and *cis,cis*-germacranolides. These lactones, however, are also typical for the genus *Melampodium* [4] and for *Smallanthus* [2]. Further investigations are necessary to determine whether the diterpenes are characteristic.

EXPERIMENTAL

The air-dried aerial parts (70 g, voucher RMK 8187) were extracted with Et_2O–petrol (1:2). The extract obtained was separated first by column chromatography (Si gel). While germacrene D was in the petrol fraction, all the other compounds were eluted with Et_2O–MeOH (9:1). This fraction was separated further by repeated TLC (Si gel) using $CHCl_3$–MeOH (20:1) as solvent. Finally 70 mg germacrene D, 6 mg **1**, 2 mg **2**, 4 mg **3**, 18 mg **4** and 10 mg **6** were obtained.

8β,9α-Diangeloyloxy-14-oic-acanthospermolide (**1**). Colourless gum, IR $\nu^{CCl_4}_{max}$ cm^{-1}: 3500–2600, 1700 (C=CCO_2H), 1785 (γ-lactone), 1730, 1650 (C=CCO_2R); MS *m/z* (rel. int.): 458.194 (M^+, 6) ($C_{25}H_{30}O_8$), 440 (M − H_2O, 0.5), 412 (440 − CO, 0.5), 359 (M − ˙OAng, 18), 358 (M − AngOH, 14), 258 (358 − AngOH, 63), 213 (258 − ˙CO_2H, 12), 83 ($C_4H_7CO^+$, 100).

$$[\alpha]^{\lambda}_{24^\circ} = \frac{589 \quad 578 \quad 546 \quad 436\,\text{nm}}{+64 \quad +66 \quad +68 \quad +83}\ (c = 0.3, \text{CHCl}_3).$$

8β,9α-Diangeloyloxy-15-hydroxy-14-oxo-4,5-cis-*acanthospermolide* (**2**). Colourless gum, IR $\nu^{CCl_4}_{max}$ cm^{-1}: 3600 (OH), 1780 (γ-lactone), 1730 (C=CCO_2R), 1700 (C=CCHO); MS (CI, isobutane) *m/z* (rel. int.): 459 (M + 1, 1) ($C_{25}H_{30}O_8$), 359 (459 − AngOH, 31), 259 (359 − AngOH, 11), 241 (259 − H_2O, 3), 101 (AngOH + 1, 100), 83 ($C_4H_7CO^+$, 25).

$$[\alpha]^{\lambda}_{24^\circ} = \frac{589 \quad 578 \quad 546 \quad 436\,\text{nm}}{-22.5 \quad -25 \quad -27 \quad -57.5}\ (c = 0.2, \text{CHCl}_3).$$

Acanthoaustralide (**3**). Colourless gum, which was purified as its diacetate. 4 mg **3** were heated for 1 hr in 0.5 ml Ac_2O at 70°. TLC (Et_2O–petrol, 1:1) afforded 4 mg **5**, colourless gum, IR $\nu^{CCl_4}_{max}$ cm^{-1}: 1740 (OAc), 1695 (C=CCO); MS *m/z* (rel. int.): 420.251 (M^+, 1) ($C_{24}H_{36}O_6$), 360 (M − HOAc, 6), 300 (360 − HOAc, 3), 231 (300 − C_5H_9, 10), 69 ($C_5H_9^+$, 100).

Acanthoaustralide-1-O-*acetate* (**4**). Colourless gum, IR $\nu^{CCl_4}_{max}$ cm^{-1}: 3520 (OH), 1740, 1240 (OAc), 1700 (C=CCO); MS *m/z* (rel. int.): 378 (M^+, 0.1), 318.220 (M − HOAc, 7) ($C_{20}H_{30}O_3$), 300 (318 − H_2O, 4), 285 (300 − Me, 2), 249 (318 − C_5H_9, 6), 231 (300 − C_5H_9, 5), 69 ($C_5H_9^+$, 100); CI (isobutane): 379 (M + 1, 7), 335 (379 − CO_2, 19), 319 (379 − HOAc, 100), 301 (319 − H_2O, 17).

$$[\alpha]^{\lambda}_{24^\circ} = \frac{589 \quad 578 \quad 546 \quad 436 \quad 365\,\text{nm}}{+7 \quad +6 \quad +5 \quad -5 \quad -55}\ (c = 0.2, \text{CHCl}_3).$$

Isoacanthoaustralide-1-O-*acetate* (**6**). Colourless gum, IR $\nu^{CCl_4}_{max}$ cm^{-1}: 3520 (OH), 1740 (OAc), 1700 (C=CCO); MS *m/z* (rel. int.): 318.220 (M − HOAc, 6), 300 (318 − H_2O, 4), 249 (318 − C_5H_9, 7), 69 ($C_5H_9^+$, 100); CI (isobutane): 379 (M + 1, 4), 319 (379 − HOAc, 100), 301 (319 − H_2O, 12).

$$[\alpha]^{\lambda}_{24^\circ} = \frac{589 \quad 578 \quad 546 \quad 436 \quad 365\,\text{nm}}{+9.5 \quad +9 \quad +8 \quad +6.5 \quad -8}\ (c = 0.2, \text{CHCl}_3).$$

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