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MODIFIED EUDESMANOLIDES AND OTHER SESQUITERPENE LACTONES FROM *WUNDERLICHIA MIRABILIS* AND *ACTINOSERIS POLYMORPHA*[*]

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Key Word Index—*Wunderlichia mirabilis*; *Actinoseris polymorpha*; Compositae; Mutisieae; sesquiterpene lactones; modified eudesmanolides; germacranolides.

Abstract—Re-investigation of *Wunderlichia mirabilis* afforded three new modified eudesmanolides of the same type isolated previously from an *Onoseris* species, and minute amounts of a germacranolide for which a structure only could be proposed. *Actinoseris polymorpha* also contained a new germacranolide, the angelate of desacetyllaurenobiolide. Structures were elucidated by spectroscopic methods and by some chemical transformations. The significance of these findings is discussed briefly.

INTRODUCTION

Previous chemical investigations of representatives of Mutisieae, subtribe Gochnatiinae [1] have shown that sesquiterpene lactones were present in most of the species, while the other subtribes mainly contain other characteristic compounds. So far six genera belonging to this subtribe are reported to yield sesquiterpene lactones. *Moquinia velutina* contained eudesmanolide [2], *Dicoma anomala* germacranolides [3], *Gochnatia* guaianolides [4], *Wunderlichia* a germacranolide [5], *Cnicothammus lorentzii* germacranolides and a guaianolide [6] and *Onoseris albicans* modified eudesmanolide [7]. Only *Oldenburgia* gave no lactones [8]. We have now investigated *Wunderlichia mirabilis* Riedel ex Baker and *Actinoseris polymorpha* (Less.) Cabrera. The former has been studied previously [5]. The compounds isolated showed some interesting relationships to those isolated from other genera of this subtribe.

RESULTS AND DISCUSSION

The aerial parts of *W. mirabilis* afforded germacrene D, lupeyl acetate, lupeol, the pentaynene **1** and several sesquiterpene lactones. The main lactone was obviously closely related to onoseriolide, a eudesmanolide with a cyclopropane ring [7]. However, the presence in the ^{1}H NMR spectrum of a double doublet at δ 5.11, which was coupled with two further double doublets showed that the 8,9-double bond in onoseriolide was hydrogenated. Therefore, the new lactone was **2**. All ^{1}H NMR data (Table 1) fully agreed with this assumption. Spin decoupling allowed the assignment of all signals. Irradiation of the broadened triplet at δ 1.97 changed the signals at δ 1.38, 0.93 and 0.85 and collapsed the signals of the vinylic protons (H-15) to doublets, clearly indicating that these signals were those of the cyclopropane ring. Irradiation of the four-fold doublet at δ 2.55 allowed the assignment of H-5 and H-6. The stereochemistry at C-1 and C-3 was obviously the same as that in onoseriolide, while that at C-8 followed from the couplings of H-8.

Two further lactones had the same carbon skeleton as **2**. The ^{1}H NMR data were in agreement with structures **3** and **4** only (Table 1). While **4** could not be induced to crystallize, the corresponding acetate **5** was crystalline. Again all signals in the spectrum of **3** could be assigned by spin decoupling, either in $CDCl_3$ or C_6D_6. In the latter solvent only the signals of the cyclopropane protons could be interpreted by first-order analysis. The couplings observed were in agreement with the proposed stereochemistry. The stereochemistry at C-5 and C-6 in **4** followed from the couplings $J_{5,6}$ and $J_{6,7}$, while the presence of a *trans*-8,12-lactone in both **3** and **4** was deduced from the couplings of H-7 through H-9. We have named **3** 13-desoxyisoonoseriolide. A further lactone, isolated in minute amounts, most probably was **6**. The stereochemistry was deduced by comparing the ^{1}H NMR chemical shifts and couplings with those of the known isomeric types of lactones (Table 2). A lactone isolated from a *Dicoma* species [3] shows different chemical shifts. The given configuration of the 1,10-double bond, however, has to be changed to *cis*, which follows from the chemical shift of H-14. The ^{1}H NMR data of **6** were also different from those of the melampolides especially from those of alloschkuhriolide [9] and its isomer prepared with base. Models showed that the couplings observed would agree best with the proposed stereochemistry. In particular, the couplings of H-7 and H-8 agreed well with a model of a *cis,cis*-germacranolide. The downfield shift of the H-7 signal was also explained by the model. Due to the small amount of material, the structure could not be established with certainty. We have named **6** wunderolide.

The aerial parts of *A. polymorpha* afforded lupeyl acetate as well as the isomeric Δ9,11- and 12,13-dihydrolupeyl acetates, cycloartenone, methyl coumarate

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[*] Part 337 in the series "Naturally Occurring Terpene Derivatives". For Part 336 see Bohlmann, F., Ziesche, J., King, R. M. and Robinson, H. (1981) *Phytochemistry* **20**, 1335.

Table 1. ^{1}H NMR data of compounds **2**–**5** (400 MHz, $CDCl_3$, TMS as internal standard)

	2	**3**	**3** (C_6D_6)	**4**	**5**
H-1	0.85 *m*	0.85 *m*	0.71 *ddd*	0.85 *m*	0.88 *m*
H-2	0.93 *m*		0.60 *ddd*		0.93 *m*
H-2′	1.38 *ddd*	1.31 *ddd*	0.90 *ddd*	1.35 *m*	1.37 *ddd*
H-3	1.97 *dd* (*br*)	1.89 *dd* (*br*)	1.73 *dd* (*br*)	1.95 *dd* (*br*)	1.95 *dd* (*br*)
H-5	2.55 *dddd*	2.41 *dddd*	2.19 *dddd*	2.78 *ddd*	2.94 *ddd*
H-6α	2.11 *dd*	1.96 *dd* (*br*)	1.48 *ddd*	—	—
H-6β	2.88 *dd*	1.65 *ddd*	1.14 *m*	4.22 *dd*	5.19 *dd*
H-7	—	3.24 *ddddd*	2.51 *ddddd*	3.54 *dddd*	3.77 *dddd*
H-8	5.11 *dd* (*br*)	4.94 *ddd*	4.35 *ddd*	4.88 *ddd*	4.93 *ddd*
H-9α	1.58 *dd*	1.42 *dd*	1.14 *m*	1.40 *m*	1.47 *dd*
H-9β	2.67 *dd*	2.48 *dd*	2.09 *dd*	2.39 *dd*	2.43 *dd*
H-13	4.39 *d* (*br*)	6.35 *d*	6.23 *d*	6.40 *d*	6.38 *d*
H-13′		5.56 *d*	4.94 *d*	6.38 *d*	6.06 *d*
H-14	0.79 *s*	0.60 *s*	0.24 *s*	0.60 *s*	0.67 *s*
H-15	5.02 *s* (*br*)	4.96 *ddd*	5.03 *ddd*	5.11 *ddd*	5.06 *ddd*
H-15′	4.75 *s* (*br*)	4.69 *s* (*br*)	4.67 *s* (*br*)	5.17 *s* (*br*)	4.79 *s* (*br*)
OAc	—	—	—	—	2.14 *s*
OH	2.72 *t*				

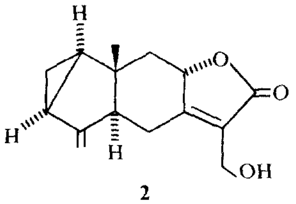
J (Hz): 1, 2 = 5; 1, 2′ = 1, 3 = 3.5; 2, 2′ = 2, 3 = 2′, 3 = 8; 3, 5 = 5, 15 ~ 2; 6, 7 = 11.5; **2**: 5, 6α = 3; 5, 6β = 13.5; 6α, 6β = 13.5; 8, 9α = 12; 8, 9β = 6.5; 9α, 9β = 12; 13, OH = 6; **3**: 5, 6α = 2.5; 5, 6β = 13; 6α, 6β = 14; 6α, 7 = 1; 6β, 7 = 12; 7, 8 = 8; 7, 13 = 3.5; 7, 13′ = 3; 8, 9α = 10; 8, 9β = 7; 9α, 9β = 12.5; **4**/**5**: 5, 6 = 12; 6, 7 = 6; 7, 8 = 7; 7, 13 = 3.5; 7, 13′ = 3; 8, 9α = 10; 8, 9β = 6.5.

and a sesquiterpene lactone, the angelate of desacetyllaurenobiolide (**7**). As usual the ^{1}H NMR spectrum (Table 2) was very uncharacteristic, all signals being broadened, even at 80°. However, addition of diazomethane afforded **8**, which gave a very clear spectrum. Spin decoupling allowed the assignment of most signals, which were very similar to those of the laurenobiolide adduct, only some being shifted slightly due to the effect of the unsaturated ester residue (H-5, H-6 and H-16).

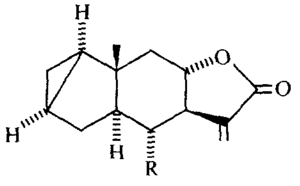
The results obtained showed that *Wunderlichia* may be closely related to *Onoseris*, as these are the only two genera from which the modified eudesmanolides have been isolated. The isolation of a sesquiterpene lactone

$Me[C{\equiv}C]_5CH{=}CH_2$

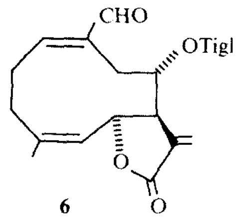
1



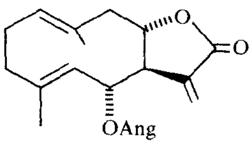
2



3 R = H
4 R = OH
5 R = OAc



6



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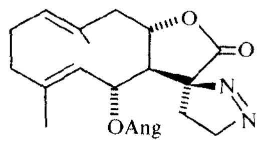

8

Table 2. ^{1}H NMR data of compounds **6**–**8** (400 MHz, TMS as internal standard)

	6		**7**	**8**
	($CDCl_3$, 60°)	(C_6D_6, 80°)	(C_6D_6, 77°)	($CDCl_3$)
H-1	6.56 *dd (br)*	5.79 *br dd*		4.91 *ddq*
H-2	2.58 *m*	1.85 *m*	all *br*	2.25 *m*
H-2′	2.42 *dddd*	1.63 *dddd*		
H-3	2.1 *m*	2.07 *m*		
H-3′	1.9 *m*			
H-5	5.31 *d (br)*	4.96 *d (br)*		4.55 *d (br)*
H-6	5.45 *dd*	5.01 *dd*		5.70 *dd*
H-7	3.49 *d (br)*	3.11 *d (br)*		2.84 *dd*
H-8	4.87 *m*	4.83 *m*		5.09 *dd (br)*
H-9	2.73 *dd*	2.60 *dd*		3.05 *d (br)*
H-9′	2.49 *d (br)*	2.12 *d (br)*		2.55 *dd*
H-13	6.42 *d*	6.32 *d*	6.42 *s (br)*	2.32 *m*
H-13′	5.95 *d*	5.65 *d*	5.76 *s (br)*	1.95 *m*
H-14	9.36 *s*	9.09 *s*	1.34 *s (br)*	1.63 *s (br)*
H-15	1.72 *s (br)*	1.26 *s (br)*	1.52 *s (br)*	1.78 *s (br)*
H-16	—	—	—	4.65 *t (br)*
OCOR	6.90 *q (br)*	6.99 *qq*	5.79 *q (br)*	5.99 *qq*
	1.82 *d (br)*	1.50 *dq*	1.76 *d (br)*	1.90 *dq*
	1.88 *s (br)*	1.89 *dq*	1.67 *s (br)*	1.78 *s (br)*

J (Hz): **6**: 1, 2 = 10; 1, 2′ = 7; 2, 2′ ~ 14; 2′, 3 = 2′, 3′ ~ 3; 5, 6 = 9; 6, 7 = 9; 7, 13 = 3.3; 7, 13′ = 3; 8, 9 = 5.5; 9, 9′ = 15, OTigl: 3′, 4′ = 7; 3′, 5′ = 1; 4′, 5′ = 1; **8**: 1, 2 = 11; 1, 2′ ~ 3; 1, 14 ~ 1.5; 5, 6 = 6, 7 = 10; 7, 8 = 9; 8, 9 ~ 1.5; 8, 9′ = 10; 9, 9′ = 12.5; OAng: 3′, 4′ = 7; 3′, 5′ = 4′, 5′ = 1.

from the *Actinoseris* species supports the assumption that in the subtribe Gochnatiinae the sesquiterpene lactones may be typical, while they are absent in the others, except a *Dinoseris* species, where a eudesmanolide was isolated [10]. The usual sesquiterpene lactones of a completely different type are, however, present in *Trixis* species (subtribe Nassauviineae) [10].

EXPERIMENTAL

The air-dried plant material, collected in north-eastern Brazil, was extracted with Et_2O–petrol (1:2) and the extracts obtained were separated first by column chromatography (Si gel) and further by repeated TLC (Si gel). Known compounds were identified by comparison with authentic materials (IR, ^{1}H NMR).

Wunderlichia mirabilis (voucher RMK 8239). The aerial parts (1200 g) afforded 20 mg germacrene D, 40 mg lupeyl acetate, 50 mg lupeol, 0.3 mg **1**, 30 mg **2** (Et_2O–petrol, 1:1), 15 mg **3** (Et_2O–petrol, 1:3, after sublimation at 0.1 torr and 120° to remove lupeol), 10 mg **4** (Et_2O–petrol, 1:1) and 2 mg **6** (Et_2O–petrol, 3:1).

Actinoseris polymorpha (voucher RMK 8387). The roots (30 g) afforded 3 mg lupeyl acetate, and the aerial parts (200 g) 20 mg lupeyl acetate, 10 mg of the Δ9,11 and 12,13 isomers, 10 mg cycloartenone, 5 mg methyl-*p*-coumarate and 15 mg **7** (Et_2O–petrol, 1:1).

8β,9-Dihydro-onoseriolide (**2**). Colourless crystals, mp 174° (Et_2O–petrol). IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3480 (OH), 1748 (lactone), 895 ($C{=}CH_2$); MS *m/z* (rel. int.): 246.125 (M^+, 36) ($C_{15}H_{18}O_3$), 228 ($M - H_2O$, 66), 213 (228 − ·Me, 20), 185 (213 − CO, 22), 91 ($C_7H_7^+$, 100);

$$[\alpha]^{\lambda}_{24^\circ} = \frac{589 \quad 578 \quad 546 \quad 436 \quad 365\ \text{nm}}{-203 \quad -216 \quad -249 \quad -466 \quad -835}$$

(c = 0.31, $CHCl_3$).

13-Desoxyisoonoseriolide (**3**). Colourless crystals, mp 84° (petrol), IR $\nu_{max}^{CCl_4}$ cm^{-1}: 1775 (γ-lactone), 895 ($C{=}CH_2$); MS *m/z* (rel. int.): 230.131 (M^+, 17), 215 (M − ·Me, 18), 119 (100), 91 (98);

$$[\alpha]^{\lambda}_{24^\circ} = \frac{589 \quad 578 \quad 546 \quad 436 \quad 365\ \text{nm}}{-140 \quad -140 \quad -161 \quad -286 \quad -490}$$

(c = 0.11, $CHCl_3$).

6α-Hydroxy-13-desoxyonoseriolide (**4**). Colourless gum, IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3620 (OH), 1775 (γ-lactone), 910 ($C{=}CH_2$); MS *m/z* (rel. int.): 246.125 (M^+, 2) ($C_{15}H_{18}O_3$), 228 ($M - H_2O$, 7), 213 (228 − ·Me, 11), 199 (228 − ·CHO, 7), 107 (100), 91 (87). To 10 mg **4** in 1 ml $CHCl_3$ were added 10 mg 4-pyrolidinopyridine and 0.1 ml Ac_2O. After 12 hr, TLC (Et_2O–petrol, 1:1) afforded 10 mg **5**, colourless crystals, mp 192° (Et_2O–petrol). IR $\nu_{max}^{CCl_4}$ cm^{-1}: 1775 (γ-lactone), 1750 (OAc), 910 ($C{=}CH_2$); MS *m/z* (rel. int.): 246.125 (M − ketene, 12) ($C_{15}H_{18}O_3$), 228 (M − HOAc, 28), 213 (228 − ·Me, 18), 57 (100);

$$[\alpha]^{\lambda}_{24^\circ} = \frac{589 \quad 578 \quad 546 \quad 436 \quad 365\ \text{nm}}{-286 \quad -297 \quad -339 \quad -592 \quad -957}$$

(c = 0.19, $CHCl_3$).

Wunderolide (**6**). Colourless gum, IR $\nu_{max}^{CCl_4}$ cm^{-1}: 1780 (γ-lactone), 2720, 1705 (CHO), 1710, 1655 ($C{=}CO_2R$); MS *m/z* (rel. int.): 344.162 (M^+, 0.5) ($C_{20}H_{24}O_5$), 316 (M − CO, 0.5), 244 (M − TiglOH, 15), 83 ($C_4H_7CO^+$, 100), 55 (83 − CO, 61).

Desacetyllaurenobiolide-6-O-acetate (**7**). Colourless gum, IR $\nu_{\max}^{\mathrm{CCl_4}}$ cm^{-1}: 1772 (γ-lactone), 1720, 1640 ($C{=}CCO_2R$); MS *m/z* (rel. int.): 330.183 (M^+, 0.5) ($C_{20}H_{26}O_4$), 230 (M − AngOH, 17) 83 ($C_4H_7CO^+$, 100), 55 (83 − CO, 80). To 8 mg **7** was added excess CH_2N_2 in Et_2O. The resulting adduct **8** crystallized directly, colourless crystals, mp 178°; IR $\nu_{\max}^{\mathrm{CHCl_3}}$ cm^{-1}: 1780 (γ-lactone), 1725 ($C{=}CCO_2R$); MS *m/z* (rel. int.): 344.199 (M − N_2, 2) ($C_{21}H_{28}O_4$), 244 (344 − Ang OH, 7), 229 (244 − $^{\cdot}$Me, 5), 83 ($C_4H_7CO^+$, 100);

$$[\alpha]^{\lambda}_{22^\circ} = \frac{589 \qquad 578 \qquad 546 \qquad 436 \qquad 365\,\mathrm{nm}}{-146.9 \quad -155.2 \quad -187.9 \quad -505.2 \quad -1967}$$

($c = 0.58$, $CHCl_3$).

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