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THREE GERMACRANOLIDES AND OTHER CONSTITUENTS FROM *EREMANTHUS* SPECIES*

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Key Word Index—*Eremanthus glomerulatus*; *E. mollis*; Compositae; Vernonieae; sesquiterpene lactones; germacranolides; guaianolide; phenylpropanol derivative.

Abstract—The re-investigation of *Eremanthus glomerulatus* afforded three new germacranolides and a guaianolide, while from *E. mollis* two known furanoheliangolides and a new phenylpropanol derivative were isolated. The germacranolides most probably are precursors of the widespread glaucolides. The structures were elucidated by spectroscopic methods. The chemotaxonomic situation is discussed briefly.

INTRODUCTION

So far, five species have been investigated chemically from the Brazilian genus *Eremanthus* (Vernonieae) [1]. In addition to simple guaianolides, highly oxygenated germacranolides, especially furanoheliangolides, were isolated [2–4]. We have now studied the constituents of *E. mollis* and re-investigated those of *E. glomerulatus* [4] on a somewhat larger scale, since only traces of lactones were observed in the previous investigation [4]. Both species again afforded in addition to several widespread compounds sesquiterpene lactones (four of them being new ones), three germacranolides (probably precursors of glaucolides) and a guaianolide.

RESULTS AND DISCUSSION

The re-investigation of the aerial parts of *E. glomerulatus* Less. [4] afforded in addition to the compounds isolated before a polar fraction, which gave four sesquiterpene lactones. Their structures are most probably **1**–**4**, though the stereochemistry could not be established unambigiously in all cases. The ^{1}H NMR data of **1** (Table 1) showed the presence of a *trans*-fused 6,12-methylene lactone, an angelate residue and an epoxide. The broadened singlet of the epoxide proton was very similar to that of estafiatin, already indicating the presence of a guaianolide. This assumption was established by spin decoupling, which allowed the assignments of the 5-H signal by irradiation of the 6-H signal, which further changed the signal at 4.13 ppm to a three-fold doublet. The latter was coupled with the methylene protons and therefore was the 7-H signal. 5-H was coupled with the three-fold doublet at 2.32 ppm, which therefore was 1-H. By further decouplings all signals were assigned. Inspection of models indicated the α-position of the 10-hydroxy group, as in this configuration only the downfield shift of the 7-H signal could be explained, and the couplings $J_{7,8}$ and $J_{8,9}$ best agreed with an α-orientation of the angelate residue at C-8. This configuration further supported the α-orientation of the epoxide, as a β-epoxide should lead to a downfield shift of the 6-H signal.

The ^{1}H NMR data of **2** (Table 2) were close to those of neuroleanin A [5], its structure being confirmed by X-ray

Table 1. ^{1}H NMR spectral data of compound **1** (270 MHz, $CDCl_3$)

1α-H	2.32 *ddd*
2α-H	2.06 *dd*
2β-H	1.46 *dd*
3-H	3.32 *br s*
5-H	2.61 *dd*
6-H	3.99 *dd*
7-H	4.13 *dddd*
8-H	5.23 *ddd*
9α-H	2.17 *dd*
9β-H	1.88 *br d*
13-H	6.18 *d*
13′-H	5.52 *d*
14-H	1.65 *s*
15-H	1.22 *s*
OAng	6.19 *qq*
	2.04 *dq*
	1.92 *dq*

J (Hz): 1α,2α = 7; 1α,2β = 11; 1α,5 = 7.5; 2α,2β = 13; 5,6 = 11; 6,7 = 9; 7,8 = 9; 7,13 = 3.5; 7,13′ = 3; 8,9α = 5.5; 9α,9β = 17; 3′,4′ = 7; 3′,5′ = 4′,5′ = 1.5.

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*Part 320 in the series "Naturally Occurring Terpene Derivatives". For Part 319 see Bohlmann, F., Jakupovic, J., King, R. M. and Robinson, H. (1981) *Phytochemistry* **20**, 1613.

Table 2. ^{1}H NMR spectral data of compounds **2–4**

	2 (400 MHz, $CDCl_3$)	**3** (270 MHz, $CDCl_3$)	**4** (270 MHz, $CDCl_3$)	**4** (270 MHz, C_6D_6, 81°)
2α-H 2β-H	6.60 *d*	6.54 *dd*	2.91 *dd*	2.56 *dd*
			3.17 *dd*	2.78 *dd*
3-H	5.94 *dd*	6.72 *dd*	4.23 *br dd*	3.91 *br dd*
4-H	3.48 *ddd*	2.90 *m*	2.08 *m*	2.01 *m*
5α-H	1.80 *ddd*	2.0 *m*		1.90 *m*
5β-H	1.48 *ddd*	2.25 *br d*	1.53 *ddd*	1.28 *ddd*
6-H	4.36 *ddd*	4.45 *br d*	4.46 *ddd*	4.21 *ddd*
7-H	3.08 *br d*	3.10 *br d*	2.95 *m*	2.93 *dddd*
8-H	4.87 *ddd*	5.30 *br d*	5.01 *br dd*	5.00 *ddd*
9α-H	2.70 *dd*	2.50 *dd*	2.60 *dd*	2.56 *dd*
9β-H	2.11 *dd*	2.03 *dd*	2.15 *br d*	1.90 *br d*
13-H	6.33 *d*	6.48 *d*	6.33 *d*	6.21 *d*
13′-H	5.75 *d*	5.73 *d*	5.70 *d*	5.32 *d*
14-H	1.88 *s*	1.85 *s*	1.89 *s*	1.66 *s*
15-H	1.12 *d*	1.35 *d*	1.13 *d*	0.88 *d*
OAc	2.06 *s*	2.12 *s*	2.02 *s*	1.74 *s*
OAng	6.13 *qq*	6.12 *qq*	6.17 *qq*	5.80 *qq*
	2.11 *dq*	1.95 *dq*	2.00 *dq*	1.94 *dq*
	1.85 *dq*	1.78 *dq*	1.85 *dq*	1.75 *dq*

J (Hz): Compound **2**: 2,3 = 12; 3,4 = 11; 4,5α = 11; 4,5β = 5; 4,15 = 7; 5α,5β = 13; 5α,6 = 5; 5β,6 = 11.5; 6,7 = 1; 7,8 = 6.5; 7,13 = 1.5; 8,9α = 7.5; 8,9β = 1.5; compound **3**: 2,3 = 16; 2,4 = 1.5; 3,4 = 5; 4,15 = 7; 5α,5β = 14; 6 5β,6 = 9; 7,8 ~ 3; 7,13 = 3; 7,13′ = 2.5; 8,9α = 8.5; 8,9β ~ 3; compound **4**: 2α,3 = 10; 2β,3 = 5; 4,5β = 3.5; 4,15 = 7; 5α,5β = 15; 5α,6 = 5.5; 5β,6 = 7.5; 6,7 = 4.5; 7,8 = 5; 7,13 = 2.5; 7,13′ = 2; 8,9β = 1.5; 8,9α = 8.5; 9α,9β = 15.

analysis. The downfield shift of the 10-methyl signal, however, indicated that the hydroxyl is replaced by an acetoxy group. Furthermore the ester group at C-8 most probably is α-orientated, as the coupling $J_{7,8}$ was different from that in neurolaenin A. Inspection of a model explained the observed shift differences of 2- and 3-H, as the 10α-acetoxy group should deshield these protons. We have named **2** ereglomerulide.

In the ^{1}H NMR spectrum of **3** (Table 2) the signals of 2- and 3-H indicated the presence of the 2,3-*trans*-isomer of **2**. Though the signals for 6-H through 8-H were broadened, the stereochemistry most probably was the same as in **2**. **4** obviously was the precursor of **2** and **3**. Careful inspection of the ^{1}H NMR data in different solvents and spin decoupling led to the assignment of all signals. Most probably the hydroxyl group at C-3 was β-orientated and hydrogen-bonded with the keto group, which followed also from the corresponding IR band. This probably led to a stable conformation of **4**, resulting in a very clear ^{1}H NMR spectrum, unusual for compounds of this type. **2–4** are probably the 4,5-dihydro derivatives of the precursor of the glaucolides, which are widespread in the Vernonieae [6].

The aerial parts of *E. mollis* Sch. Bip. afforded germacrene D, bicyclogermacrene, α-humulene, α-cedrene, lupeol, its acetate, *p*-methoxycinnamic acid, the flavonols kaempferol 3-methyl ether **9** and kaempferol 3,7-dimethyl ether **10**, the heliangolides **5** [7] and **6** [3] as well as a mixture of a *cis*- and a *trans*-coumarate, which could not be separated completely. The ^{1}H NMR data indicated the presence of **7** and **8** (Table 3). The substitution pattern clearly followed from the signal of the aromatic protons. The roots only gave lupeyl acetate.

The compounds now isolated again show that highly oxygenated germacranolides are typical for the genus *Eremanthus*. These, however, can be found as well in related genera. So far, no clear classification of this tribe is possible on chemical grounds. Further work is necessary to get a clearer picture.

EXPERIMENTAL

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

Eremanthus glomerulatus (*voucher RMK* 8354). The aerial parts (650 g) afforded 200 mg germacrene D, 100 mg bicyclogermacrene, 50 mg α-humulene, 100 mg lupeol, 100 mg lupenone, 100 mg **1** (Et_2O–petrol, 3:1), 6 mg **2** (Et_2O–petrol, 3:1), 5 mg **3** (Et_2O–petrol, 3:1) and 10 mg **4** (Et_2O–petrol, 3:1).

Eremanthus mollis (*voucher RMK* 8231). The roots (50 g) afforded 200 mg lupeyl acetate and the aerial parts (500 g) 100 mg germacrene D, 50 mg bicyclogermacrene, 200 mg α-humulene, 10 mg α-cedrene, 200 mg lupeol, 300 mg lupeyl acetate, 5 mg 4-methoxycinnamic acid, 50 mg **5**, 50 mg **6**, 20 mg **7** (Et_2O–petrol, 1:1), 10 mg **8** (Et_2O–petrol, 1:1) and 10 mg **9** and 20 mg **10**.

8α-Angeloyloxy-10α-hydroxy-10,14-dihydroestafiatin (**1**). Colourless crystals, mp 182° (Et_2O–petrol), IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3610 (OH), 1770 (γ-lactone), 1720 (C=CCO$_2$R); MS *m/z* (rel. int.): 362.173 $[M]^+$ (1) ($C_{20}H_{26}O_6$), 347 $[362 - Me]^+$ (2), 262 $[M - AngOH]^+$ (10), 247 $[262 - Me]^+$ (6), 244 $[262 - H_2O]^+$ (5), 83 $[C_4H_7CO]^+$ (100), 55 $[83 - CO]^+$ (40).

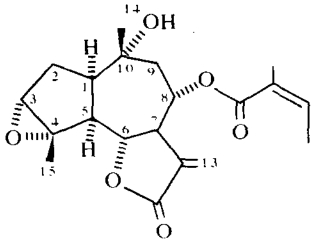
$$[\alpha]_{24^\circ}^{\lambda} = \frac{589 \quad 578 \quad 546 \quad 436\,\text{nm}}{+42.7 \quad +44.6 \quad +51.0 \quad +85.0} \ (c = 1.7, CHCl_3).$$

Ereglomerulide (**2**). Colourless crystals, mp 189° (Et_2O–petrol); IR $\nu_{max}^{CCl_4}$ cm^{-1}: 1780 (γ-lactone), 1750, 1250 (OAc), 1725 (C=CCO$_2$R); MS *m/z* (rel. int.): 404 $[M]^+$ (0.2), 362 $[M - \text{ketene}]^+$ (4), 344.162 $[M - HOAc]^+$ (2) ($C_{20}H_{24}O_5$), 262 $[362 - AngOH]^+$ (4), 83 $[C_4H_7CO]^+$ (100), 55 $[83 - CO]^+$ (31).

Table 3. ^{1}H NMR spectral data of compounds **7** and **8** (270 MHz, $CDCl_3$)

	7	**8**
2,6-H	6.43 *s*	6.39 *s*
7-H	2.68 *t*	2.60 *t*
8-H	2.02 *tt*	1.96 *tt*
9-H	4.23 *t*	4.15 *t*
2′,6′-H	7.43 *d*	7.61 *d*
3′,5′-H	6.85 *d*	6.82 *d*
7′-H	7.63 *d*	7.60 *d*
8′-H	6.31 *d*	5.86 *d*
OMe	3.88*s*	3.87 *s*

J (Hz): 7,8 = 8,9 = 7.5; 2′,3′ = 8; 7′,8′ = 16 (*trans*) and 11.5 (*cis*).



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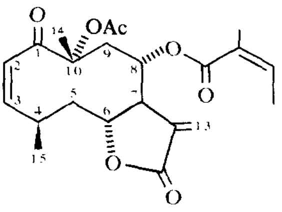

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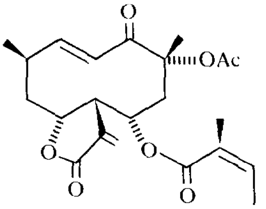

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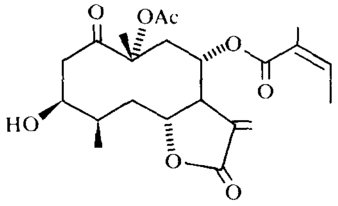

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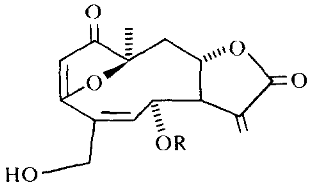
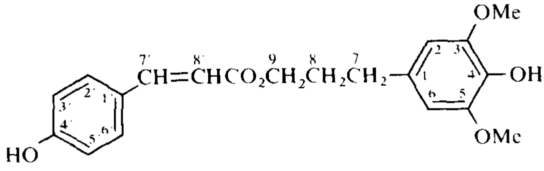
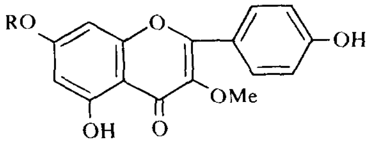


5 R = Ang
6 R = Meacr



7 *trans*
8 *cis*



9 R = H
10 R = Me

$$[\alpha]^{\lambda}_{24^\circ} = \frac{589 \quad 578 \quad 546 \quad 436\,\text{nm}}{-29 \quad -32 \quad -36 \quad -74} \; (c = 0.3).$$

2,3-*trans*-*Ereglomerulide* (**3**). Colourless gum; IR $\nu^{\mathrm{CCl_4}}_{\mathrm{max}}$ cm^{-1}: 1775 (γ-lactone), 1755 (OAc), 1720 (C=CCO$_2$R, C=O); MS m/z (rel. int.): 404 $[M]^+$ (0.1), 344.162 $[M - \mathrm{HOAc}]^+$ (1) ($C_{20}H_{24}O_5$), 244 $[344 - \mathrm{AngOH}]^+$ (1), 83 $[C_4H_7CO]^+$ (100), 55 $[83 - CO]^+$ (38); CI (i-butane): 405 $[M + 1]^+$ (80), 345 $[405 - \mathrm{HOAc}]^+$ (15), 307 $[345 - C_3H_6]^+$ (100), 101 $[RCO_2H + 1]^+$ (73), 83 $[C_4H_7CO]^+$ (58).

$$[\alpha]^{\lambda}_{24^\circ} = \frac{589 \quad 578 \quad 546 \quad 436\,\text{nm}}{-7 \quad -11 \quad -15 \quad -28} \; (c = 0.1).$$

3β-*Hydroxy-2,3-dihydroereglomerulide* (**4**). Colourless crystals, mp 105° (Et_2O–petrol); IR $\nu^{\mathrm{CCl_4}}_{\mathrm{max}}$ cm^{-1}: 3520 (OH-bonded), 1770 (γ-lactone), 1740 (OAc), 1715 (C=CCO$_2$R); MS m/z (rel. int.): 422 $[M]^+$ (0.1), 362.173 $[M - \mathrm{HOAc}]^+$ (7), 262 $[362 - \mathrm{AngOH}]^+$ (4), 83 $[C_4H_7CO]^+$, (100), 55 $[83 - CO]^+$ (65).

$$[\alpha]^{\lambda}_{24^\circ} = \frac{589 \quad 578 \quad 546 \quad 436\,\text{nm}}{-4.6 \quad -5.3 \quad -7.5 \quad -25.1} \; (c = 0.7).$$

3-[3,5-*Dimethoxy-4-hydroxyphenyl*]*propanol*-cis- *and* trans-*coumarate* (**7** *and* **8**). Colourless gum; IR $\nu^{\mathrm{CHCl_3}}_{\mathrm{max}}$ cm^{-1}: 3550 (OH), 1710 (C=CCO$_2$R), 1610 (aromatic); MS m/z (rel. int.): 358.142 $[M]^+$ (19) ($C_{20}H_{22}O_6$), 194 $[M - RCO_2H]^+$ (100), 179 $[194 - Me]^+$ (18), 163 $[194 - OMe]^+$ (42), 147 $[RCO]^+$ (28), 199 $[147 - CO]^+$ (20).

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