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SIX GUAIANOLIDES FROM *STYLOTRICHIUM ROTUNDIFOLIUM**

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Key Word Index—*Stylotrichium rotundifolium*; Compositae; Eupatorieae; sesquiterpene lactones; guaianolides; germacranolides; geranylnerol derivative.

Abstract—The investigation of *Stylotrichium rotundifolium* afforded the epoxide of β-sesquiphellandrene, a new derivative of geranylnerol and six guaianolides not isolated previously. Furthermore, two germacranolides also present in a *Lasiolaena* species and several known compounds were isolated. The structures were elucidated by detailed ^{1}H NMR investigations. The chemotaxonomic situation is discussed briefly.

INTRODUCTION

The small Brazilian genus *Stylotrichium* is placed in the diverse *Gyptis* group (Compositae, tribe Eupatorieae) [1]. In continuation of our chemotaxonomic studies of the Eupatorieae, we have now investigated *S. rotundifolium* Mattf. to see whether the chemistry gives any indication of relationship to other genera placed in the *Gyptis* group. The isolation of several sesquiterpene lactones and of a new diterpene shows there is a close relationship to *Lasiolaena*, which also belongs to the *Gyptis* group [1].

RESULTS AND DISCUSSION

The roots of *S. rotundifolium* afforded β-sesquiphellandrene, dammaradienyl acetate, the *p*-hydroxyacetophenone derivatives **1**, **2** [2], **3** [2] and the dehydronerolidol derivative **10** [3], while the aerial parts gave germacrene D, bicyclogermacrene, α-humulene, caryophyllene, β-sesquiphellandrene, the angelate **4** [4], taraxasterol and its acetate, the germacranolides **11** and **12** [5] as well as several new compounds, namely the epoxide of β-sesquiphellandrene (**5**), the geranylnerol derivative **6** and the guaianolides **13**–**18**. The structure of **5** was deduced from the ^{1}H NMR data, which were very close to those of β-sesquiphellandrene (see Experimental). However, the signals of the isopropylidene group were replaced by two singlets at 1.32 and 1.27 ppm and a triplet at 2.71 ($J = 6$ Hz). The latter was obviously the signal of an epoxide proton. The relative stereochemistry at C-10 could not be assigned. The structure of **6** also followed from the ^{1}H NMR data (Table 1), those of the products obtained by manganese dioxide oxidation (**7** and **8**) and of the corresponding diacetate **9**. As could easily be deduced from these data, a geranylnerol derivative must be present with an additional hydroxyl group at C-18 or C-19 and a keto group at C-13 since the methyl groups at C-15 and the proton at C-14 were shifted downfield. From the data of the aldehydes **7** and **8** the position of the second oxygen function could be deduced. As the H-12 signal was not shifted downfield in the spectrum of **8**, the aldehyde group must be placed at C-7. The stereochemistry of the 2,3-double bond followed from the chemical shifts of H-20 in the spectrum of **7** and **8**. **6** is closely related to a corresponding diterpene isolated from a *Lasiolaena* species [5]. The ^{1}H NMR data of **13**–**18** (Table 2) showed that all six lactones were closely related to each other. **16** obviously was the 5′-*O*-acetate of agriantholide (**19**), isolated from an *Agrianthus* species [6]. Very similar compounds were isolated from *Liatris* and *Eupatorium* species [7, 8]. The ^{1}H NMR data therefore were also similar. In the spectra of **13**–**15** the presence of a 10,14-double bond clearly followed from the typical broadened singlets between 5.4 and 5.25 ppm, while the presence of the corresponding epoxide in **16**–**18** was indicated by the two doublets around 3.0 ppm. Furthermore, an olefinic signal about 5.7 ppm and a broadened singlet at 1.0–2.0 ppm are typical for guaianolides with a 3,4-double bond. Spin decoupling showed that in all cases 6,12-lactones were present. Starting with the H-7 signals the protons for H-1 through H-3, H-5 through H-9 and H-13 could readily be assigned. Surprisingly there were, however, two groups with different couplings $J_{8,9}$. Those lactones with a 9-hydroxy function showed a coupling of about 5 Hz and those with a 9-ester group a 2 Hz coupling. Furthermore, in the spectrum of **14** and **15** a downfield shift of H-1 was observed. The small couplings for $J_{7,8}$ in the spectra of all lactones indicated a β-orientation for the oxygen functions at C-8 in all cases. The stereochemistry at the other centres was obviously the same too in all compounds and corresponded with that of the lactones with known stereochemistry [6–8]. The nature of the oxygen function also clearly followed from the ^{1}H NMR data. Most probably, **16**–**18** are 10,14α-epoxides as the H-1 signals of **15**–**18** were at lower field like the H-1 signal in agrianth©lide.

13–**15** were derived from preeupatundin [8] and **16**–**18** from agrianthOlide ([6]; see Note Added in Proof). The chemistry of *Stylotrichium* is very close to that of

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*Part 345 in the series "Naturally Occurring Terpene Derivatives". For Part 344 see Bohlmann, F. and Fritz, G. (1981) *Tetrahedron Letters* 95.

Table 1. ^1H NMR spectral data of compounds **6–9** (270 MHz, $CDCl_3$, TMS as internal standard)

	6	7	8	9
H-1	4.08 *br d*	9.91 *d*	9.92 *d*	4.55 *br d*
H-2	5.48 *br t*	5.91 *br d*	5.96 *br d*	5.40 *br t*
H-4 H-5	2.20 *m*	2.64 *t* 2.36 *dt*	2.80 *m*	2.20 *m*
H-6	5.33 *br t*	5.33 *br t*	6.42 *br t*	5.37 *br t*
H-8 H-9	2.20 *m*	2.20 *m*	2.15 *m* 2.24 *br dt*	2.20 *m*
H-10	5.26 *br t*	5.24 *br t*	5.19 *br t*	5.23 *br t*
H-12	3.05 *br s*	3.06 *br s*	3.04 *br s*	3.04 *br s*
H-14	6.11 *qq*	6.11 *qq*	6.10 *qq*	6.10 *qq*
H-16	1.89 *d*	1.89 *d*	1.89 *d*	1.88 *d*
H-17	2.15 *d*	2.14 *d*	2.14 *d*	2.14 *d*
H-18	1.63 *br s*	1.62 *br s*	1.60 *br s*	1.63 *br s*
H-19	4.10 *br s*	4.13 *br s*	10.09 *s*	4.59 *s*
H-20	1.77 *br s*	1.99 *d*	2.01 *d*	1.76 *br s*
OAc	—	—	—	2.06 *s* 2.04 *s*

J (Hz): 1,2 = 5, 6 = 9, 10 = 7; 14, 16 = 14, 17 = 1.3.

Lasiolaena [5] and *Agrianthus* [6]. The constituents of the other genera placed in the *Gyptis* group so far investigated, however, are of different types. Only *Trichogonia* [10] and *Conocliniopsis* [11] also contain sesquiterpene lactones, mainly furanoheliangolides.

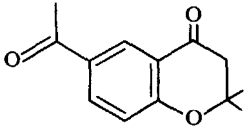
EXPERIMENTAL

The air-dried plant material (voucher RMK 8149) was extracted with Et_2O–petrol (1:3) and the resulting 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 ^1H NMR spectra with those of authentic material. The roots (80 g) afforded 15 mg β-sesquiphellandrene, 10 mg dammaradienyl acetate, 3 mg **1**, 15 mg **2**, 10 mg **3** and 30 mg **10**, while the aerial parts gave 10 mg germacrene D, 40 mg β-sesquiphellandrene, 20 mg bicyclogermacrene, 20 mg α-humulene, 10 mg taraxasterol and 50 mg of its acetate, 20 mg caryophyllene, 50 mg **4**, 5 mg **5** (Et_2O–petrol, 1:20), 11 mg **6** (Et_2O–petrol, 3:1), 10 mg **11**, 3 mg **12**, 4 mg **13** and **14** ($CHCl_3$–Me_2CO, 4:1), 3 mg **15** ($CHCl_3$–Me_2CO, 3:2), 10 mg

Table 2. ^1H NMR spectral data of compounds **13–18** (270 MHz, $CDCl_3$, TMS as internal standard)

	13	14	15	16	17	18
H-1	3.23 *br dd*	3.63 *br dd*	3.69 *br dd*	2.67 *dd*	2.85 *dd*	2.65 *dd*
H-2	4.98 *br d*	4.79 *br d*	4.77 *br d*	4.78 *br d*	4.57 *br dd*	4.83 *br d*
H-3	5.72 *dq*	5.65 *dq*	5.60 *dq*	5.65 *dq*	5.84 *dq*	5.63 *br s*
H-5	2.88 *br dd*	2.85 *br dd*	2.84 *br dd*	2.81 *br dd*	2.76 *br dd*	2.83 *br dd*
H-6	4.61 *dd*	4.98 *dd*	5.08 *dd*	5.15 *dd*	4.94 *dd*	5.16 *dd*
H-7	2.98 *dddd*	3.29 *dddd*	3.29 *dddd*	3.24 *dddd*	3.17 *dddd*	3.28 *dddd*
H-8	4.49 *dd*	5.88 *dd*	5.58 *dd*	5.50 *dd*	6.00 *dd*	5.54 *dd*
H-9	5.19 *br d*	4.72 *br d*	4.69 *br d*	3.96 *d*	5.32 *d*	3.84 *d*
H-13	6.41 *d*	6.29 *d*	6.28 *d*	6.32 *d*	6.24 *d*	6.32 *d*
H-13′	5.46 *d*	5.51 *d*	5.57 *d*	5.56 *d*	5.54 *d*	5.55 *d*
H-14	5.41 *br s*	5.38 *br s*	5.33 *br s*	3.01 *d*	3.00 *d*	2.95 *d*
H-14′	5.36 *br s*	5.30 *br s*	5.26 *br s*	2.86 *d*	2.88 *d*	2.90 *d*
H-15	1.90 *br s*	1.94 *br s*	1.95 *br s*	1.99 *br s*	2.03 *br s*	1.99 *br s*
OCOR	7.29 *q*	7.15 *q*	6.96 *q*	7.14 *q*	7.20 *q*	6.96 *q*
	2.03 *d*	1.97 *d*	1.89 *d*	1.94 *d*	1.95 *d*	1.90 *d*
	4.99 *br s*	4.85 *d* 4.78 *d*	4.38 *d* 4.27 *d*	4.87 *d* 4.78 *d*	4.90 *d* 4.80 *d*	4.34 *d* 4.27 *d*
OAc	2.09 *s*	2.03 *s*	—	2.01 *s*	2.10 *s* 1.99 *s*	—

J (Hz): 1,2 = 7; 1,5 = 9.5; 2,3 ~ 2; 3,15 = 1; 5,6 = 10.5; 6,7 = 9; 7,8 ~ 3.5; 7,13 = 3.5; 7,13′ = 3; 8,9 = 5 (**14–16**, **18**; **13** and **17**: 1.8); **16–18**: 14,14′ = 4.5; 3′,4′ = 7; $5'_1,5'_2$ = 12.5.



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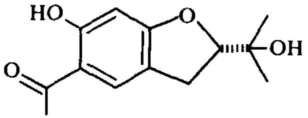

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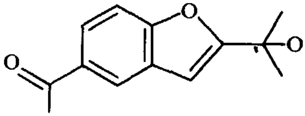

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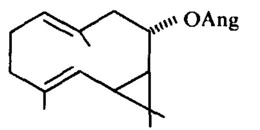

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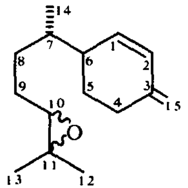

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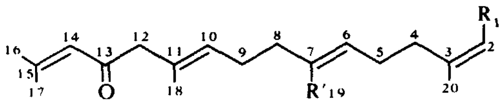
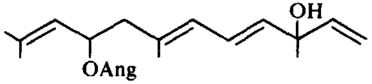


	6	**7**	**8**	**9**
R	CH_2OH	CHO	CHO	CH_2OAc
R′	CH_2OH	CH_2OH	CHO	CH_2OAc



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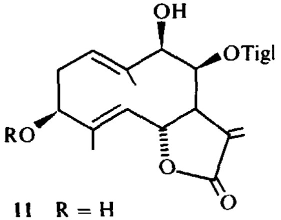
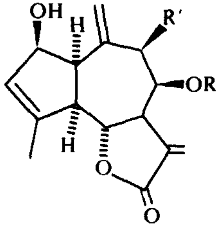
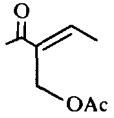
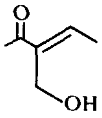
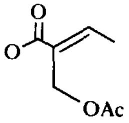
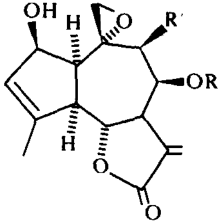
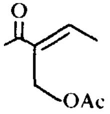
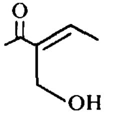


11 R = H
12 R = Ac

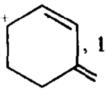


	13	**14**	**15**
R	H		
R′		OH	OH



	16	**17**	**18**	**19**
R				Tigl
R′	OH	OAc	OH	OH

16 and 3 mg **17** ($CHCl_3$–Me_2CO, 6:1) and 5 mg **18** ($CHCl_3$–Me_2CO, 3:2).

Epoxy-β-sesquiphellandrene (**5**). Colourless oil; IR $\nu_{\max}^{CCl_4}$ cm^{-1}: 2940, 2860, 1645, 1470, 1385, 1365, 1225, 890; MS *m/z* (rel. int.): 220.183 (M^+, 13) ($C_{15}H_{24}O$), 202 ($M - H_2O$, 10), 187 (202 − Me, 8), 93 ( , 100), 71 ($Me_2C - CH$, 64); ^{1}H NMR ($CDCl_3$): 0.88 (*d*, H-14, J = 7 Hz), 1.27 and 1.32 (*s*, H-12, 13), 2.71 (*t*, H-10, J = 6 Hz), 4.76 (*br s*, H-15), 6.17 (*dd*, H-1, J = 10, 2.5 Hz), 5.68 (*br d*, H-2, J = 10 Hz).

19-*Hydroxy*-13-*oxo-geranylnerol* (**6**). Colourless gum: IR $\nu_{\max}^{CCl_4}$ cm^{-1}: 3620 (OH), 1690, 1625 (C=CCO); MS *m/z* (rel. int.) (CI, *i*-butane): 321 (M + 1, 4), 303 (321 − H_2O, 44), 285 (303 − H_2O, 44), 83 ($MeC{=}CHCO^+$, 100). 10 mg **6** in 2 ml Et_2O was stirred for 1 hr with 50 mg MnO_2. TLC (Et_2O) afforded 6 mg **7** and 3 mg **8**. **7**: Colourless gum, IR $\nu_{\max}^{CCl_4}$ cm^{-1}: 3630 (OH), 2760, 1685 (CHO), 1685, 1625 (C=CCO); MS *m/z* (rel. int): 318.220 (M^+, 0.3), 83 ($Me_2C{=}CHCO^+$, 100); **8**: Colourless gum, IR $\nu_{\max}^{CCl_4}$ cm^{-1}: 1680, 1620 (C=CCO); MS *m/z* (rel. int.): 316.204 (M^+, 0.2), 83 ($MeC{=}CHCO^+$, 100). 1 mg **6** was heated for 30 min in 0.1 ml Ac_2O at 70°. TLC (Et_2O–petrol, 1:1) afforded 1 mg **9**, colourless gum (^{1}H NMR data, see Table 1).

8β-Hydroxy-9β-[5-acetoxytiglinoyloxy]-preeupatundin (**13**). Colourless gum; IR $\nu_{\max}^{CHCl_3}$ cm^{-1}: 3540 (OH), 1780 (γ-lactone), 1740 (CO_2R); MS *m/z* (rel. int.) (CI, *i*-butane): 419 (M + 1, 8), 391 (419 − CO, 11), 279 (419 − O=C=CR, 8), 117 ($HO_2CC(CH_2OH){=}CHMe$ + 1, 100), 99 (117 − H_2O, 71).

$$[\alpha]^{\lambda}_{24^\circ} = \frac{589 \quad 578 \quad 546 \quad 436\,\mathrm{nm}}{+14 \quad +16 \quad +18 \quad +34} (c = 0.3,\ \mathrm{CHCl_3}).$$

9β-Hydroxy-8β-[5-acetoxytiglinoyloxy]-preeupatundin (**14**). Colourless gum; IR $\nu_{\max}^{CHCl_3}$ cm^{-1}: 3620 (OH), 1765 (γ-lactone), 1730 (CO_2R); MS *m/z* (rel. int.): 418 (M^+, 0.2), 400, 152 (M − H_2O, 2) ($C_{22}H_{24}O_7$), 242 (400 − RCO_2H, 48), 141 (RCO^+, 94), 81 (141 − HOAc, 100); $[\alpha]_{436\,\mathrm{nm}}$ + 9° (c = 0.4, $CHCl_3$).

9β-Hydroxy-8β-[5-hydroxytiglinolyoxy]-preeupatundin (**15**). Colourless gum; IR $\nu_{\max}^{CHCl_3}$ cm^{-1}: 3600 (OH), 1770 (γ-lactone), 1730 (CO_2R); MS *m/z* (rel. int.): 376 (M^+, 0.3), 358.142 (M − H_2O, 1.5) ($C_{20}H_{22}O_6$), 260 (M − RCO_2H, 7), 242 (260 − H_2O, 20), 99 (RCO^+, 100). $[\alpha]_D$ +4° (c = 0.1, $CHCl_3$).

5′-Acetoxy-agriantholide (**16**). Colourless gum; IR $\nu_{\max}^{CHCl_3}$ cm^{-1}: 3600 (OH), 1770 (γ-lactone), 1720 (CO_2R); MS (CI, *i*-butane): 435 (M + 1, 4), 417 (435 − H_2O, 100), 399 (417 − H_2O, 66), 259 (417 − RCO_2H, 64), 241 (259 − H_2O, 63).

5′-Acetoxy-agriantholide-9-O-acetate (**17**). Colourless gum; IR $\nu_{\max}^{CHCl_3}$ cm^{-1}: 3600 (OH), 1760 (γ-lactone), 1730 (CO_2R); MS (CO, *i*-butane): 477 (M + 1, 0.2), 459 (477 − H_2O, 100), 417 (477 − HOAc, 24), 399 (459 − HOAc, 20), 159 (RCO_2H + 1, 14), 141 (159 − H_2O, 12).

$$[\alpha]^{\lambda}_{24^\circ} = \frac{589 \quad 578 \quad 546 \quad 436\,\mathrm{nm}}{+44 \quad +48 \quad +51 \quad +91} (c = 0.3,\ \mathrm{CHCl_3}).$$

5′-Hydroxy-agriantholide (**18**). Colourless gum; IR $\nu_{\max}^{CHCl_3}$ cm^{-1}: 3600 (OH), 1760 (γ-lactone), 1725 (CO_2R); MS *m/z* (rel. int.): 392.147 (M^+, 1) ($C_{20}H_{24}O_8$), 276 (M − RCO_2H, 5), 258 (276 − H_2O, 10), 99 (RCO^+, 100), 81 (99 − H_2O, 70).

$$[\alpha]^{\lambda}_{24^\circ} = \frac{589 \quad 578 \quad 546 \quad 436\,\mathrm{nm}}{+8 \quad +9 \quad +10 \quad +12} (c = 0.4,\ \mathrm{CHCl_3}).$$

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NOTE ADDED IN PROOF

The stereochemistry of agriantholide has to be changed at C-9 following detailed ^{1}H NMR studies on the lactones from *Lasiolaena morii* [9].