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GERMACRANOLIDES FROM *PIPTOLEPIS ERICOIDES* AND *VANILLOSMOPSIS* SPECIES*

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Key Word Index—*Piptolepis ericoides*; *Vanillosmopsis brasiliensis*; *V. pohlii*; Vernonieae; Compositae; sesquiterpene lactones; germacranolides.

Abstract—The aerial parts of *Piptolepis ericoides* afforded in addition to known compounds two new germacranolides, a zexbrevanolide and piptolepolide, tentatively characterized as a germacranolide with a *trans*-disubstituted double bond. From the aerial parts of two *Vanillosmopis* species in addition to goyazensolide, a new isomer with an exocyclic double bond was isolated.

INTRODUCTION

In continuation of our investigations on representatives of the tribe Vernonieae, which is taxonomically very complicated [1], we have now isolated the main constituents of a *Piptolepis* and of two *Vanillosmopis* species. In addition to known compounds, three new sesquiterpene lactones were present.

RESULTS AND DISCUSSION

Piptolepis is a small Brazilian genus (tribe Vernonieae), its relationship to other genera in the tribe is not clear. So far the presence of flavanols has been reported from one species only [2]. The aerial parts of *P. ericoides* (Less.) Sch. Bip. afforded the widespread pentaynene **1a**, polyisoprene, lupenone and two sesquiterpene lactones, the angelates **5** and **6**. The structure of **5** easily could be deduced from the ^{1}H NMR data, which were very close to those of the corresponding tiglate and methacrylate isolated from *Eremanthus bicolor* [3]. The nature of the ester residue clearly followed from the typical ^{1}H NMR signals (Table 1).

Structure **6** of the second lactone, present only in minute amounts, though not fully established, was in good agreement with the spectroscopic data. While in the MS under EI conditions no molecular ion could be detected, chemical ionisation gave a clear M + 1 peak, which corresponded with the proposed molecular formula ($C_{22}H_{28}O_8$). Further prominent peaks were formed by the elimination of water, acetic acid and angelic acid (*m/e* 403, 361, 321, 261). The interpretation of the ^{1}H NMR spectrum in $CDCl_3$ (Table 1) caused some difficulties because of a two proton singlet at δ 6.69 ppm, whose nature was not clear at first. However, in C_6D_6 this signal was split into two double doublets, their couplings indicating the presence of a *trans*-double bond ($J = 16$ Hz). Double resonance experiments showed that the additional couplings were due to a vicinal and an allylic coupling with a hydrogen, which was further coupled with the methyl protons (15-H) and a double doublet ($\delta = 3.58$, 5-H). The latter was further coupled with the hydrogen under the lactone proton (6-H), which could be assigned by spin decoupling. Irradiation at the multiplet at 2.51 caused a change of the signals at 4.10 *dd*, 5.29 *br. d*, 6.23 *d* and 5.16 *d*, clearly indicating that the multiplet could be assigned only to 7-H. As the signal at 5.29 was obviously that of a hydrogen on a carbon bearing ester group, which was coupled further with two double doublets, the hydrogens 2-H through 9-H could be assigned and the presence of a germacranolide with a *trans*-double bond was obvious. Inspection of models supported the proposed stereochemistry at C-4 through C-8. The coupling $J_{7,8}$ being close to zero suggested 8β-configuration. However, the assignments are not secure because of the flexibility of such systems. The absence of a separated IR band below 1725 cm^{-1} indicated that the keto group was out of plane with the 2,3-double bond, which was probably the reason for the unusual coinciding of the 2- and 3-H signals in the ^{1}H NMR spectrum in $CDCl_3$. The downfield shift of the 14-H signal must be due to strong deshielding effects. Similar observations were made with a germacranolide isolated from an *Eremanthus* species [5], which also has a 2,3-*trans*-double bond. The relative position of the acetate and the angelate groups was assigned on the basis of biogenetical considerations only. The proposed stereochemistry at C-10 was also not established and is based on analogy only. **6** shows some relationship to zexbrevin C [4], which, however, differs in the stereochemistry at C-8. The presence of a desoxytitifruticin-like lactone [6] could be excluded due to the

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*Part 314 in the series 'Naturally Occurring Terpene Derivatives'. For Part 313 see: Bohlmann, F., Dhar, A. K., Jakupovic, J., King, R. M. and Robinson, H. (1981) *Phytochemistry* **20**, 838.

Table 1. ^{1}H NMR spectral data of compounds **5** and **6** (270 MHz, TMS as internal standard)

		6	
	5 (CDCl$_3$)	CDCl$_3$	C$_6$D$_6$
2-H	5.69 *br. s*	6.69 *br. s*	6.39 *dd*
3-H			6.25 *dd*
4-H	3.05 *br. dq*	3.17 *m*	2.88 *ddq*
5α-H	2.50 *ddd*	—	—
5β-H	2.11 *br. d*	3.85 *br. dd*	3.58 *br. dd*
6-H	4.36 *ddd*	4.30 *dd*	4.10 *dd*
7-H	3.35 *m*	2.96 *m*	2.51 *m*
8-H	4.53 *ddd*	5.38 *br. dd*	5.29 *br. d*
9α-H	2.34 *dd*	2.03 *br. d*	1.7 *br. d*
9β-H	2.46 *dd*	2.42 *dd*	2.32 *dd*
13-H	6.19 *d*	6.42 *d*	6.23 *d*
13′-H	5.42 *d*	5.80 *d*	5.16 *d*
14-H	1.48 *s*	1.92 *s*	1.81 *s*
15-H	1.43 *d*	1.35 *d*	0.97 *d*
OAng	6.07 *qq*	6.17 *qq*	5.64 *qq*
	1.88 *dq*	1.96 *dq*	1.83 *dq*
	1.78 *dq*	1.79 *dq*	1.66 *dq*
OAc	—	2.12 *s*	1.80 *s*

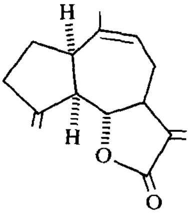
J (Hz): Compound **5**: 4, 5α = 7; 4, 15 = 7; 5, 5′ = 14; 5α, 6 = 11; 6, 7 = 5; 7, 8 = 4; 7, 13 = 3.3; 7, 13′ = 3; 8, 9α = 10; 8, 9β = 2; 9, 9′ = 13; compound **6**: 2, 3 = 16; 2, 4 = 1.3; 3, 4 = 3.5; 4, 5 = 4.5; 5, 6 = 10; 6, 7 = 5; 7, 13 = 2.5; 8, 9α = 8; 9α, 9β = 14.

Table 2. ^{1}H NMR spectral data of compound **4a** (270 MHz, TMS as internal standard)

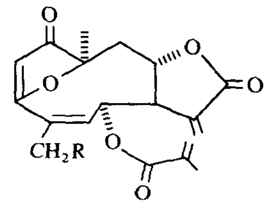
	CDCl$_3$	C$_6$D$_6$	(D$_3$C)$_2$CO/CDCl$_3$
2-H	5.97 *s*	5.38 *s*	5.99 *s*
5-H	4.69 *ddd*	5.12 *br. d*	4.75 *br. d*
6-H	4.60 *dd*	4.60 *dd*	4.53 *dd*
7-H	3.66 *dddd*	3.14 *m*	3.74 *m*
8-H	4.39 *ddd*	4.40 *br. d*	4.40 *ddd*
9-H	2.50 *dd*	1.89 *dd*	2.63 *dd*
9′-H	2.37 *d*	2.19 *dd*	2.35 *dd*
13-H	6.28 *d*	6.22 *d*	6.20 *d*
13′-H	5.57 *d*	5.12 *d*	5.59 *d*
14-H	1.53 *s*	1.18 *s*	1.54 *s*
15-H	6.26 *br. s*	6.01 *br. s*	6.27 *dd*
15′-H	6.01 *br. s*	5.36 *br. s*	6.03 *dd*
OH	3.23 *s*	2.90 *s*	
OCOR	6.01 *br. s*	5.86 *br. s*	6.01 *br. s*
	5.56 *br. s*	5.10 *br. s*	5.56 *br. s*
	1.83 *br. s*	1.60 *br. s*	1.83 *dd*

J (Hz): 5, 6 = 9.5; 5, 15 = 5, 15′ = 2; 6, 7 = 5; 7, 8 = 2; 7, 13 = 3.5; 7, 13′ = 3; 8, 9 = 11.5; 8, 9′ = 2; 9, 9′ = 13; 15, 15′ = 1; 3′, 4′ ~ 1.5.

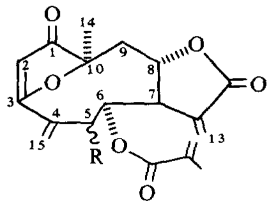
1a $Me[C{\equiv}C]_5CH{=}CH_2$
1b $MeCH{=}CH[C{\equiv}C]_4CH{=}CH_2$



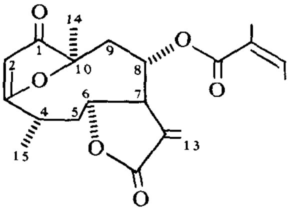
2



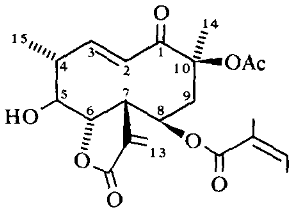
3a R = H
3b R = OH



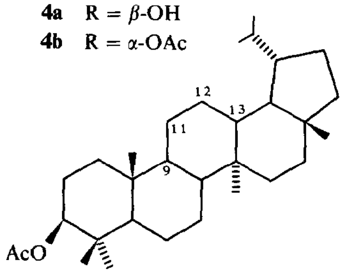
4a R = β-OH
4b R = α-OAc



5



6



7 Δ9(11)
8 Δ12(13)

observed couplings of 4-H. We have named **6** piptolepolide.

The roots afforded again **1a**, polyisoprene and lupenone as well as lupeol and its acetate.

The Brazilian genus *Vanillosmopsis* (tribe Vernonieae) consists of seven species [1]. Only one, *V. erythropappa*, has been investigated so far. In addition to costunolide [7] and eremanthin (**2**) [8], 15-desoxygoyazensolide (**3a**) [9] was isolated. A further report deals with the occurrence of the widespread sesquiterpenes bisabolol and bisabolene [10].

We have now investigated two further species, *V. brasiliensis* (Gardn.) Sch. Bip. and *V. pohlii*. The aerial parts of the first afforded squalene, lupeyl acetate, lupeol, germacrene D, bicyclogermacrene, the pentaynene **1a**, the eneteraynene **1b**, 5,7,4′-trihydroxy-3-methoxyflavone, eremanthin (**2**) [8], goyazensolide (**3b**) [11] and a further lactone, the isomer **4a**. The ^{1}H NMR data (Table 2) had to be measured in different solvents as some signals always overlapped. Careful spin decoupling established the sequence 5-H through 9-H. The stereochemistry at C-6, C-7 and C-8 is obviously the same as that of goyazensolide. 5-H showed a 9.5 Hz coupling. A very similar compound, the acetate **4b**, was obtained on reaction of **3b** with acetic anhydride [11]. The observed coupling $J_{5,6}$ in the spectrum of **4b**, however, was 0.8 Hz, establishing a *cis*-orientation of the oxygen function at C-5 and C-6. In agreement with inspection of models therefore the hydroxyl at C-5 in **4a** was β-orientated. The proposed structure was established accidentally. Traces of HCl, often present in chloroform, transformed **4a** partially to **3b**, thus confirming the presence of a 8,12-lactone, which could not be directly deduced from the ^{1}H NMR data. Following the proposed name for the 6-desacyloxy compound as **3a**, **4a** is 5β-hydroxy-6α-methacryloyloxy-$\Delta^{4,15}$-isogoyazensanolide [3].

The aerial parts of *V. pohlii* Baker also afforded germacrene D, bicyclogermacrene, lupenone, lupeol, its acetate, the isomers **7** and **8**, **1a**, **1b**, **3b** and **4a**.

The constituents isolated from the two *Vanillosmopsis* species indicate that goyazensanolides may be characteristic for this genus. However, they are present also in *Centratherum* [12], *Eremanthus* [3,11], *Lychnophora* [13, 14] and *Proteopsis* [15]. The sesquiterpene lactones isolated from the *Piptolepis* species showed relationships to these genera, but also to Vernonieae. Not enough chemical data are available at this time for a detailed discussion of the chemotaxonomy of the tribe Vernonieae.

EXPERIMENTAL

^{1}H NMR: 270 MHz, TMS as int. stand.; MS: 70 eV, direct inlet. The air dried plant material, collected in north-eastern Brazil, was extracted with Et_2O–petrol (1:2) and the resulting extracts were separated first by column chromatography (SiO_2, act. grade II) and further by repeated TLC (SiO_2). Known compounds were identified by comparing the IR and ^{1}H NMR spectra with those of authentic material.

Piptolepis ericoides (*voucher RMK* 8395). The aerial parts (380 g) afforded 1 g polyisoprene, 500 mg lupenone, 0.2 mg **1a**, 1.5 mg **5** (Et_2O–petrol, 1:3) and 1 mg **6** (HPLC, reversed phase, $MeOH/H_2O$, 7:3), while the roots (180 g) yielded 1 g polyisoprene, 200 mg lupenone, 500 mg lupeol, 2 g of its acetate and 0.3 mg **1a**.

Vanillosmopsis brasiliensis (*voucher RMK* 8046). The aerial parts (600 g) afforded 100 mg squalene, 800 mg lupeol, 300 mg of its acetate, 50 mg germacrene D, 40 mg bicyclogermacrene, 30 mg 5,7,4′-trihydroxy-3-methoxyflavone, 0.3 mg **1a**, 0.2 mg **1b**, 60 mg **2**, 50 mg **3b** and 3 mg **4a** (Et_2O–petrol, 1:3).

Vanillosmopsis pohlii (*voucher RMK* 8291). The aerial parts (500 g) afforded 30 mg germacrene D, 10 mg bicyclogermacrene, 30 mg lupenone, 150 mg lupeol, 100 mg lupeyl acetate, 0.5 mg **1a**, 0.3 mg **1b**, 30 mg **7** and **8** (*ca* 1:1), 80 mg **3b** and 20 mg **4a**.

5β-Hydroxy-6α-methacryloyloxy-$\Delta^{4,15}$-iso-*goyazensanolide* (**4a**). Colourless crystals, mp 226° (Et_2O–petrol), IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3600 (OH), 1770 (γ-lactone), 1710 ($C{=}CCO_2R$, $C{=}CCO$), 1590 ($C{=}COR$); MS *m/e* (rel. int.): 360.120 (M^+, 3) ($C_{19}H_{20}O_7$), 274 ($M - RCO_2H$, 11), 246 (274 − CO, 6), 152 (42), 69 ($C_3H_5CO^+$, 100).

$$[\alpha]_{24^\circ}^{\lambda} = \frac{589 \quad 578 \quad 546 \quad 436\,\text{nm}}{-5.8 \quad -4.6 \quad 0 \quad +103.0}\ (c = 0.26,\ CHCl_3).$$

3 mg **4a** in 2.5 ml $CHCl_3$ after standing at room temp. for 3 hr yielded 2 mg **3b**, identical with authentic material.

8β-Angeloyloxy-zexbrevanolide (**5**). Colourless gum, IR $\nu_{max}^{CCl_4}$ cm^{-1}: 1780 (γ-lactone), 1720 ($C{=}CCO_2R$, $C{=}CCO$), 1600 ($C{=}COR$); MS *m/e* (rel. int.): 360.157 (M^+, 4) ($C_{20}H_{24}O_6$), 260 ($M - RCO_2H$, 1), 83 ($C_4H_7CO^+$, 100), 55 (83 − CO, 44).

Piptolepolide (**6**). Colourless gum, IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3600 (OH), 1785 (γ-lactone), 1755 (OAc), 1725 *br.* ($C{=}CCO$, $C{=}CCO_2R$); MS *m/e* (rel. int.): 360 (M − AcOH, 1), 320 ($M - C_4H_7CO_2H$, 1), 260 (320 − AcOH, 1), 83 ($C_4H_7CO^+$, 100); CI (isobutane): 421 (M + 1, 100), 361 (421 − AcOH, 57), 321 ($421 - C_4H_7CO_2H$, 41), 101 ($C_4H_7CO_2H + 1$, 58).

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