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SESQUITERPENE LACTONES FROM TWO *BEJARANOA* SPECIES

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Key Word Index—*Bejaranoa balansae*; *B. semistriata*; Compositae; sesquiterpene lactones; furanoheliangolides; pyranoheliangolides.

Abstract—The investigation of two *Bejaranoa* species from South America yielded, in addition to known sesquiterpene lactones and some other widespread metabolites, six new furanoheliangolides and a new pyranoheliangolide.

INTRODUCTION

The genus *Bejaranoa* belongs to the tribe Eupatorieae. The only two recognized species are distinctly separated geographically, *B. balansae* in Paraguay and Bolivia and *B. semistriata* in Eastern Brasil [1]. Both species have been investigated chemically. *B. balansae* from Paraguay contained germacranolides, guajanolides and linear sesquiterpenes [2], while in *B. semistriata* heliangolides were present instead of guajanolides [3]. In this paper we present our results with *B. balansae* from Bolivia and a further investigation of *B. semistriata* from Brasil.

RESULTS AND DISCUSSION

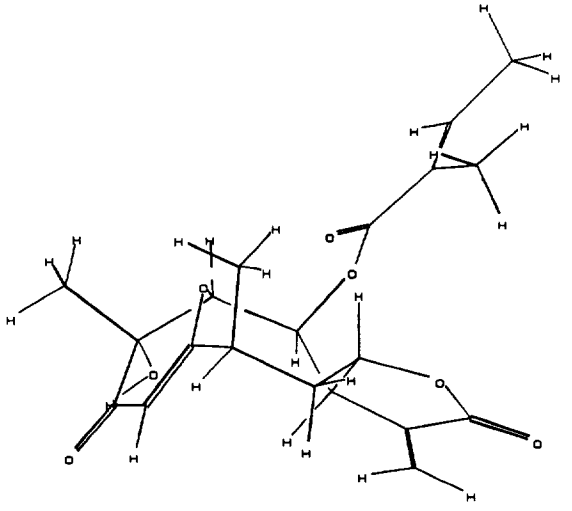
B. balansae (Hieron.) King et Robins. contained in addition to some widespread compounds (Experimental) the sesquiterpene lactones **5** [4], **6**, **7**, **8** [2], **9**–**11** and **13** [5]. The ^{1}H NMR spectra of **6** and **7** were similar to that of **5** (Table 1). The olefinic exomethylene signals were missing. Instead, the H-13 signals appeared as geminally splitted doublets at higher field. In the case of **6** the couplings indicated the presence of an epoxide. The stereochemistry at C-11 was deduced from the results of NOE difference experiments. By saturation of the H-8 resonance frequency important effects were observed at H-7(4%), H-9(6%) and H-13(7%). Similarly H-7 showed interaction with H-8 (3%) and H-9 (5%) but not with H-13 confirming presence of an α-epoxide. The molecular formula of compound **7** was established as $C_{20}H_{23}ClO_8$ by HR-mass spectrometry. Obviously a chlorohydrin was present. The appearance of the H-13 signals as sharp doublets in the ^{1}H NMR spectrum and the mass spectrometry fragment M − CH_2Cl support the structure. The opening of the epoxide ring in cooccurring **6** by nucleophilic attack of Cl^- at C-13 would give **7** with an α-hydroxy group at C-11. That this chlorohydrin was an artifact could not be excluded though no $CHCl_3$ or any other HCl source was used during work up. The spectra of **9** and **10** showed the same fragments as that of **7** (Table 1). The missing Δ^4 double bond and the additional hydroxy group at C-5 were established by spin decoupling. The stereochemistry, already indicated by couplings, was confirmed by NOE experiments. Effects were observed between H-7 and H-5 (5%), between H-15 and H-2 (3%) as well as between H-8, H-7 (1.5%), H-9 (3%) and H-13 (5%). In the literature epoxylactones and chlorohydrins of both α- and β-stereochemistry at C-11 and several epoxylactones with unassigned C-11 stereochemistry were described. Probably all epoxides and chlorohydrins posses the same stereochemistry at C-11 corresponding to that of **6** and **7**. The correct stereochemistry has already been assigned to 11,13-epoxides described in several papers [6–8] in which the authors stated that some epoxylactones most likely have the reverse configuration at C-11. Thus the stereochemistry of 11,13-epoxides or the corresponding chlorohydrins from *Calea* [9–14], and *Trichogonia* [15] should be revised or for the first time assigned.

In the ^{1}H NMR spectrum of **11** the H-9 signal appeared as a sharp singlet, while the other signals resembled those of **8** (Table 1). As an additional D_2O exchangeable singlet at δ 3.77 could only be assigned to a tertiary hydroxy group the presence of an isomer with a pyranone moiety was very likely. The final proof was achieved through an HMBC experiment and the ^3J correlation between H-9 and C-3. This type of intramolecular C-3/C-9 ether formation has not been described previously. The stereochemistry followed from the results of NOE difference spectroscopy. Effects were observed between H-15, H-6 (4%) and H-5 (2%), between H-14 and H-9 (12%), between H-4, H-2 (7%) and H-5′ (5%), between H-7, H-8 (5%) and H-5′ (5%), as well as between OH and H-8 (3%). The energy minimized conformation calculated using PCMODEL molecular modeling program (Scheme 1) is in accordance with spectroscopic results. The conformational similarity of the *oxa* bridged ten membered ring with conformations observed in

Table 1. ^{1}H NMR data ($CDCl_3$, 400 MHz, int. standard solvent peak = 7.26 ppm)

H	3	4	6	7	9	10	11
2	5.62 *s*	5.60 *s*	5.63 *s*	5.61 *s*	5.66 *brs*	5.66 *brs*	5.60 *s*
4	—	—	—	—	3.36 *brdq*	3.36 *brdq*	2.92 *ddq*
5	6.01 *dq*	6.02 *dq*	6.03 *dq*	6.04 *dq*	4.58 *brdd*	4.59 *brdd*	2.31 *ddd*
5′	—	—	—	—	—	—	2.01 *ddd*
6	5.34 *ddq*	5.26 *ddq*	4.99 *ddq*	4.98 *m*	4.12 *dd*	4.16 *dd*	5.27 *ddd*
7	3.24 *dd*	3.37 *dd*	3.16 *dd*	3.21 *dd*	3.00 *dd*	3.00 *dd*	3.29 *dddd*
8	5.12 *ddd*	5.12 *ddd*	4.95 *dd*	4.98 *m*	4.95 *dd*	5.02 *dd*	5.89 *d*
9	2.43 *dd*	2.51 *dd*	3.94 *brdd*	4.14 *brs*	4.14 *m*	4.14 *m*	4.77 *s*
9′	2.19 *dd*	2.34 *dd*	—	—	—	—	—
13	3.34 *d*	4.28 *d*	3.44 *d*	4.46 *d*	4.40 *d*	4.43 *d*	6.32 *d*
13′	3.30 *d*	3.89 *d*	3.42 *d*	3.96 *d*	3.93 *d*	3.95 *d*	5.63 *d*
14	1.46 *s*	1.47 *s*	1.65 *s*	1.67 *s*	1.65 *s*	1.64 *s*	1.55 *s*
15	2.09 *dd*	2.08 *dd*	2.08 *dd*	2.05 *dd*	1.30 *d*	1.31 *d*	1.34 *d*
OH			3.41 *brd*		3.83 *d*	3.86 *d*	3.77 *s*
OR	7.08 *q*	7.08 *q*	6.85 *qq*	6.82 *qq*	6.83 *qq*	6.18 *qq*	6.81 *qq*
	1.96 *d*	1.96 *d*	1.83 *dq*	1.86 *dq*	1.83 *dq*	1.93 *dq*	1.80 *dq*
	4.87 *d*	4.86 *d*	1.77 *dq*	1.74 *dq*	1.76 *dq*	1.84 *dq*	1.78 *brs*
	4.67 *d*	4.65 *d*					
	2.03 *s*	2.03 *s*					

J (Hz): compound **3**: 5, 6 = 6, 7 = 4; 5, 15 = 6, 15 = 7, 8 = 2; 8, 9 = 4.5; 8, 9′ = 3; 9, 9′ = 15.5; 13, 13′ = 12.5; compound **4**: 5, 6 = 4; 5, 15 = 6, 15 = 2; 6, 7 = 4.5; 7, 8 = 1.5; 8, 9 = 5.5; 8, 9′ = 3.5; 9, 9′ = 15; 13, 13′ = 5; compound **6**: 5, 6 = 4; 5, 15 = 6, 15 = 2; 6, 7 = 4.5; 7, 8 = 1.5; 8, 9 = 3.5; 9, OH = 11.5; 13, 13′ = 5; compound **7**: 5, 6 = 5; 5, 15 = 6, 15 = 2; 6, 7 = 7, 8 = 3; 13, 13′ = 13; compounds **9** and **10**: 4, 5 = 4, 15 = 7.5; 5, 6 = 8.5; 6, 7 = 7, 8 = 8, 9 = 3; 9, OH = 12; 13, 13′ = 13; compound **11**: 4, 5 = 1; 4, 5′ = 4, 15 = 7; 5, 5′ = 13; 5, 6 = 7, 8 = 7, 13 = 7, 13′ = 2; 5′, 6 = 12.



Scheme 1.

taxoid compounds is worthy of note. ^{13}C NMR data are listed in Table 2. All signals were assigned by 2D experiments. The compound with a 4,5 double bond and a free hydroxy group at C-8 we have named balansolide. In Table 2 are included the ^{13}C NMR spectral data of several known compounds, not reported previously.

B. semistriata yielded the sesquiterpene lactones **1** [6], **2** [16], **3**, **4**, **12** [3, 5], **14** [3, 5, 17], **15** [3] and the aromatic compound **16** [18]. The structures of **3** and **4** followed by comparison of the spectral data with those of **2**, **6** and **7**. The ^{1}H NMR spectrum of **3** and **4** showed that in both compounds the ester residue of **2** was also present and that the substitution and stereochemistry at C-11 and C-13 was the same as in **6** and **7** respectively.

Both *Bejaranoa* species contained compounds typical of the tribe Eupatorieae. Moreover, similar lactones were found within the subtribe Gyptidinae [2]. The oxidation pattern of sesquiterpene lactones seems to be characteristic of the species. Those from *B. balansae* have an additional functional group at C-9. The specimen of *B. balansae* from Paraguay contained mainly guaianolides, while the present investigation of the collection from Bolivia afforded mainly heliangolides. However, both collections contained the precursor, 9β,10α-dihydroxy-1-oxo-8β-tigloyloxy-germacra-4,11(13)-dien-6α,12-olide (**13**) in large quantity. Obviously the enzymatic system of the Paraguayan plant is able to perform the cyclisation of germacranolides to guaianolides, while in the Bolivian plant the isomeration to heliangolides take place. Because of an unfavourable conformation, the heliangolides are not able to cyclise to guaianolides. The reinvestigation of *B. semistriata* from Brasil shows a sesquiterpene lactone profile without functional groups at C-9 similar to that of the previous investigation [3]. In the present study, no diterpenes were detected, which may be an important chemotaxonomic aspect.

Table 2. ^{13}C NMR data ($CDCl_3$, 100 MHz, int. standard $CDCl_3$ 77.0 ppm)

Carbon	2	5	7	11	14	mult.
1	205.1	205.6	206.0	193.9	211.5	*s*
2	103.0	104.0	104.1	104.0	42.3 *t*	*d*
3	184.9	186.2	186.8	178.4	73.7 *d*	*s*
4	131.5	130.9	130.3	36.9 *d*	142.1	*s*
5	133.5	134.6	133.7	44.0 *t*	123.8	*d*
6	74.8	73.9	73.7	75.4	74.6	*d*
7	47.8	46.9	53.4	45.6	48.7	*d*
8	74.8	80.3	74.4	72.9	66.5	*d*
9	42.2 *t*	79.0	78.8	91.5	35.9 *t*	*d*
10	87.3	86.8	87.4	71.3	77.3	*s*
11	138.7	139.3	77.7	134.5	134.5	*s*
12	168.4	168.5	173.5	168.3	169.8	*s*
13	123.4	122.4	45.4	124.8	121.8	*t*
14	21.2	20.4	20.6	27.4	28.2	*q*
15	19.1	19.6	19.4	14.9	11.1	*q*
OR	164.4	166.9	167.9	166.3	166.6	*s*
	126.6	127.0	126.9	127.7	127.8	*s*
	146.4	140.5	141.0	139.3	138.5	*d*
	14.5	14.8	14.7	14.6	14.4	*q*
	57.0	11.9	11.8	12.0	11.9	*q*
OAc	170.5					*s*
	20.4					*q*

EXPERIMENTAL

The air dried plant material was extracted for 24 hr with PE–methyl-t-butyl ether(MTB)–MeOH(1:1:1) at room temp. After defatting the extract was separated by CC and further by TLC and/or HPLC. The condition for final purification for new compounds are given below (HP1: MeOH–H_2O, 7:3; HP2: MeOH–H_2O, 3:2). Known compounds were identified by comparison of their spectral data with those of authentic samples or with literature data.

B. balansae, 430 g, collected in Bolivia, voucher RMK 9654 deposited in the U.S. National Herbarium contained 15 mg germacrene D, 20 mg lupeyl acetate, 30 mg taraxasteryl acetate, 50 mg 4′,5,7-trihydroxy-6-methoxyflavone, 70 mg **5**, 10 mg **6**, 120 mg **7** (R_t 5 min; HP1), 10 mg **8**, 40 mg **9** (R_t 6.8 min; HP1), 4 mg **10** (R_t; 5.9 min; HP1) and 5 mg **11** (R_t 14.7 min; HP2) 100 mg **13**.

B. semistriata, 406 g, collected in Brasil voucher RMK 8032 deposited in the U.S. National Herbarium contained 20 mg caryophyllene, 25 mg caryophyllene epoxide, 2 mg spathulenol, 100 mg taraxasterylacetate, 10 mg lupeol, 20 mg taraxasterol, 5 mg dammaradienol, 10 mg α-amyrin, 2 mg dehydroleucodin, 370 mg **1**, 830 mg **2**, 1 mg **3**(R_t 9.0 min; HP2), 6 mg **4**(R_t 10.8 min; HP2), 15 mg **12**, 150 mg **14**, 8 mg **15** and 11 mg **16**.

11, 13-*Dihydro*-11α,13-*epoxy*-*atripliciolide*-8-O-(5-*acetoxytiglate*) (**3**). $\nu_{max}^{CHCl_3}$: 1800 (γ-lactone), 1745, 1225 (OAc), 1715 (ester, furanone); MS *m/z* (rel. int.): 432.142 $[M]^+$ (39) (calc for $C_{22}H_{24}O_9$ 432.142), 372 $[M - AcOH]^+$ (13), 264 (56), 141 $[RCO]^+$ (78), 81 $[141 - HOAc]^+$ (100).

11, 13-*Dihydro*-11α-*hydroxy*-13-*chloro*-*atripliciolide*-8-O-(5-*acetoxytiglate*) (**4**). $\nu_{max}^{CHCl_3}$: 3550 (OH), 1787 (γ-lactone), 1730, 1716, 1243 (ester, furanone); MS m/z (rel. int.): 468.119 $[M]^+$ (26) (calc. for $C_{22}H_{25}O_9Cl$ 468.119), 432 $[M - HCl]^+$ (10), 408 $[M - AcOH]^+$ (13), 372 [432 − AcOH]$^+$ (4), 141 $[RCO]^+$ (100), 81 $[141 - AcOH]^+$ (86).

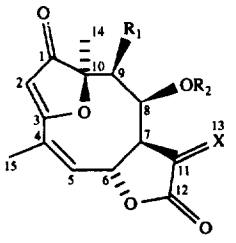
11, 13-*Dihydro*-11α,13-*epoxy*-9β-*hydroxy*-*atripliciolide*-8-O-*tiglate* (**6**). MS *m/z* (rel. int.): 390.132 $[M]^+$ (6) (calc for $C_{20}H_{22}O_8$ 390.132), 290 $[M - TiglOH]^+$ (2), 246 $[290 - CO_2]^+$ (10), 83 $[C_4H_7CO]^+$ (100).

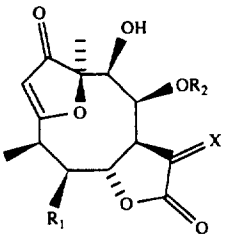
11,13-*Dihydro*-9β,11α-*dihydroxy*-13-*chloro*-*atripliciolide*-8-O-*tiglate* (**7**). $\nu_{max}^{CHCl_3}$: 3460 (OH), 1790 (γ-lactone), 1730, 1710, 1270 (ester, furanone); MS *m/z* (rel. int.): 426.108 $[M]^+$ (52) (calc. for $C_{20}H_{23}O_8Cl$ 426.108), 390 $[M - HCl]^+$ (30), 377 $[M - CH_2Cl]^+$ (5), 326 $[M - TiglOH]^+$ (8), 277 $[326 - CH_2Cl]^+$ (10), 83 $[C_4H_7CO]^+$ (57) 55 $[83 - CO]^+$ (100).

4,5,-11,13-*Tetrahydro*-5β,9β,11α-*trihydroxy*-13-*chloro*-*atripliciolide*-8-O-*tiglate* (**9**). $\nu_{max}^{CHCl_3}$: 3460 (OH), 1785 (γ-lactone), 1725, 1720, 1260 (ester, furanone); MS *m/z* (rel. int.): 444.119 $[M]^+$ (6) (calc. for $C_{20}H_{25}O_9Cl$ 444.119), 408 $[M - HCl]^+$ (3), 308 $[408 - TiglOH]^+$ (1), 83 $[C_4H_7CO]^+$ (100).

4,5-11,13-*Tetrahydro*-5β,9β,11α-*trihydroxy*-13-*chloro*-*atripliciolide*-8-O-*angelate* (**10**). $\nu_{max}^{CHCl_3}$: 3460 (OH), 1785 (γ-lactone), 1725, 1720, 1260 (ester, furanone); MS *m/z* (rel. int.): 444.119 $[M]^+$ (5) (calc. for $C_{20}H_{25}O_9Cl$ 444.119), 408 $[M - HCl]^+$ (3), 308 $[408 - AngOH]^+$ (1), 83 $[C_4H_7CO]^+$ (100).

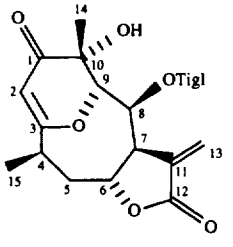
4α,5-*Dihydro*-*balansolide*-8-O-*tiglate* (**11**). $\nu_{max}^{CHCl_3}$: 3500 (OH), 1785 (γ-lactone), 1735, 1275 (ester), 1690 (pyranone);





	1	2	3	4	5	6	7
R_1	H	H	H	H	OH	OH	OH
R_2	Tigl	5-AcOTigl	5-AcOTigl	5-AcOTigl	Tigl	Tigl	Tigl
X	CH_2	CH_2		α-OH,β-CH_2Cl	CH_2		α-OH,β-CH_2Cl

	8	9	10
R_1	H	OH	OH
R_2	Tigl	Tigl	Ang
X	CH_2	α-OH,β-CH_2Cl	α-OH,β-CH_2Cl



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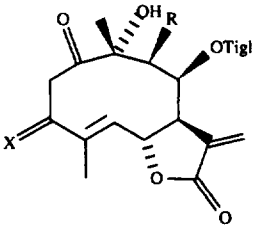
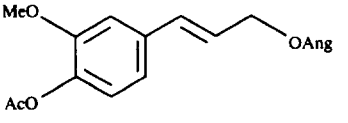


	12	13	14	15
R	H	OH	H	H
X	H_2	H_2	β-OH,H	α-OH,H $\Delta^4(Z)$



16

MS *m/z* (rel. int.): 376.152 $[M]^+$ (3) (calc. for $C_{20}H_{24}O_7$ 376.152), 333 $[M - Me, - CO]^+$ (1), 277 $[M - OTigl]^+$ (2), 233 $[333 - TiglOH]^+$ (6), 178 (6), 83 $[C_4H_7CO]^+$ (100).

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