Phytochemistry, Vol. 25, No. 9, pp. 2167–2170, 1986.
Printed in Great Britain.

0031–9422/86 $3.00 + 0.00
Pergamon Journals Ltd.

BALANSOLIDE AND OTHER SESQUITERPENE LACTONES FROM *BEJARANOA BALANSAE*

G. SCHMEDA-HIRSCHMANN, J. JAKUPOVIC*, V.P. PATHAK* and F. BOHLMANN*

Facultad de Ciencias Quimicas, Universidad de Asuncion, Paraguay; *Institute for Organic Chemistry, Technical University of Berlin, D-1000 Berlin 12, West Germany

(*Received* 29 *October* 1985)

Key Word Index—*Bejaranoa balansae*; Compositae; sesquiterpene lactones; germacranolides; guaianolides; diterpenes; geranyl nerol derivatives.

Abstract—The aerial parts of *Bejaranoa balansae* afforded in addition to known sesquiterpene lactones six new ones, two highly oxygenated germacranolides and four guaianolides including balansolide with a 2,9-ether bridge. Furthermore, two geranyl nerol derivatives were present. The configuration of some 10,14-epoxyguaianolides have been revised from 10β to 10α and the stereochemistry at C-4 in 4,5-dihydrofuroheliangolides has also been corrected to 4β-methyl. The structures were elucidated by NMR spectroscopy.

INTRODUCTION

The new genus *Bejaranoa* [1] is related to *Conocliniopsis* and therefore should be placed in the subtribe Gyptidinae [2]. The first results on one species supported this proposal [3]. We have studied a second species from Paraguay, *B. balansae* (Hieron.) King et Robins. and the results are discussed in this paper.

RESULTS AND DISCUSSION

The aerial parts of *B. balansae* afforded 9-hydroxy-lasiolaenolide [4], 9β,10α-dihydroxy-1-oxo-8β-tigloxy-germacra-4,11(13)-dien-6,12-olide [5], 9β-hydroxy-8β-tigloxy-costunolide [4], 3β,9β-dihydroxy-8β-tigloxy-costunolide [6], the guaianoides **1**, **2** [7] and **3**–**5**, the germacranolides **6** and **7** as well as the geranyl nerol derivatives **8** and **9**.

The structure of **1** was deduced from the ^{1}H NMR spectrum (Table 1) which was close to those of pre-eupatundin derivatives from *Lasiolaena santosii* [4, 8]. All signals could be assigned by spin decoupling. Also, the structure of **3** was deduced from the ^{1}H NMR spectrum (Table 1) which was close to that of the tiglate **2** [7]. The presence of a 5-hydroxy group was indicated by the fact that H-6 was a doublet. Accordingly, the spectrum was close to that of euparotin [9] which is the corresponding 9-desoxy-8-angeloyloxy derivative.

The ^{1}H NMR spectrum of **4** (Table 1) was also close to that of **2**. However, the relative position of the oxygen functions at C-8 and C-9 was changed as followed from the chemical shifts. Furthermore, the presence of the corresponding 10,14-diol was indicated by the downfield shift of the H-14 signals as well as by the mass spectrum which showed a clear molecular ion for $C_{20}H_{26}O_8$ and after loss of water the elimination of CH_2OH. The configuration at C-10 followed from the downfield shifts of the H-1 and H-2 signals if compared with those of **2**.

The ^{1}H NMR spectrum of **5** (Table 1), which we have named balansolide, was close to that of **2**. However, several signals were shifted and showed different couplings indicating a changed conformation. The molecular formula agreed with the presence of an ether ring. This was supported by inspection of a model and by NOE difference spectroscopy. Clear effects were obtained between H-1, H-2, H-5 and H-14, between H-5, H-1 and H-7, between H-14′, H-8 and H-9, between H-8, H-7 and H-9 as well as between H-2, H-1 and H-3 (the first mentioned proton was always the irradiated one). The presence of a 10α-epoxide was deduced from the observed downfield shift of H-7.

We have again inspected the ^{1}H NMR spectra and the models of all known 10,14-epoxides from the tribe Eupatorieae. Most likely all compounds have the same configuration at C-10 and the presence of a *W*-coupling (9α,14) is only an indication that the molecule is present in a conformation with C-14 quasi axial and the oxygen function at C-8 slightly distorted from quasi axial to equatorial. This conformation is changed if a hydrogen bridge is present either between the 2β-hydroxy and a 9β-oxygen function or between a 5α-hydroxy and the 10α,14-epoxide group. This can be deduced from the small coupling $J_{8,9\alpha}$ which is large in those lactones where the hydrogen bridge is absent. These differences in conformation were also present in the corresponding 10-oxomethylene derivatives. The reported configurations at C-10 for some epoxides therefore should be revised to 10α,14-epoxides (**28**–**31** in lit. [10]).

The ^{1}H NMR spectrum of **6** (Table 1) was in part similar to that of the main constituent, the 9β,10α-dihydroxy-1-oxo-8β-tigloxy germacra-4,11(13)-dien-6,12-olide [5]. However, the absence of the 4,5-double bond clearly followed from the results of spin decoupling which allowed the assignment of all signals. The chemical shift of the broadened doublet at δ3.91 for H-5 required a hydroxy group at C-5 as the doublet was sharpened by

Table 1. ^{1}H NMR spectral data of compounds **1** and **3**–**7** ($CDCl_3$, 400 MHz, TMS as internal standard)

H	**1**	**3**	**4**	**5**	**6** (57°)	**7***
1	3.26 *d*	2.57 *d*	3.07 *dd*	2.63 *dd*	—	—
2 2′	5.01 *ddq*	4.68 *br dd*	5.08 *br d*	4.90 *dd*	2.95 *ddd* (α) 2.68 *ddd* (β)	5.60 *d*
3	5.79 *dq*	5.78 *br s*	5.79 *br s*	5.65 *dq*	2.87 *ddd* (α) 1.90 *ddd* (β)	—
5	—	—	2.87 *dd*	2.72 *dd*	3.90 *br d*	2.56 *ddd* 2.06 *br d*
6	5.04 *d*	5.30 *d*	4.86 *dd*	4.74 *dd*	4.76 *dd*	4.20 *dd*
7	3.64 *dddd*	3.81 *dddd*	2.97 *dddd*	3.41 *dddd*	3.56 *dddd*	3.32 *dddd*
8	5.63 *dd*	5.52 *dd*	4.53 *ddd*	5.39 *dd*	5.79 *d*	5.18 *dd*
9	4.68 *d*	4.19 *d*	4.98 *d*	4.38 *dd*	4.09 *s*	4.16 *br d*
13	6.33 *d*	6.32 *d*	6.36 *d*	6.26 *d*	6.31 *d*	6.36 *d*
13′	5.59 *d*	5.51 *d*	5.62 *d*	5.43 *d*	5.59 *d*	5.72 *d*
14	5.50 *br s*	3.15 *d*	3.99 *d*	3.23 *d*	1.64 *s*	1.67 *s*
14′	5.27 *br s*	2.79 *d*	3.67 *d*	3.14 *d*		
15	1.90 *dd*	1.94 *br s*	2.07 *br s*	2.01 *d*	1.36 *s*	1.39 *d*
OH	†	2.49 *br s*	5.08 *d*	—	2.53 *s* 2.40 *br s*	3.86 *br d*
OCOR	6.82 *br q*	6.88 *br q*	7.03 *qq*	6.81 *br q*	6.81 *br q*	6.79 *qq*
	1.80 *br s*	1.79 *br s*	1.94 *br s*	1.78 *br s*	1.80 *br s*	1.83 *dq*
	1.79 *br d*	1.78 *br d*	1.87 *br d*	1.77 *br d*	1.79 *br d*	1.78 *dq*

*H-4 3.06 *br dq*.

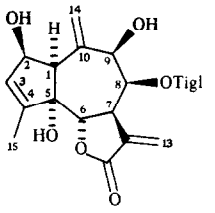
†Obscured.

J (Hz): 7, 13 = 3.5; 7, 13′ = 3; compound **1**: 1, 2 = 7; 2, 3 = 2, 15 = 3, 15 ~ 2; 6, 7 = 9; 7, 8 = 8, 9 = 3; compound **3**: 1, 2 = 6; 2, 3 = 2.5; 6, 7 = 9.5; 7, 8 = 8, 9 = 3; **14**, 14′ = 5; compound **4**: 1, 2 = 6.5; 1, 5 = 9; 5, 6 = 6, 7 = 10; 7, 8 = 8, 9 ~ 3; 8, OH = 9; 14, 14′ = 11; compound **5**: 1, 2 = 3.5; 1, 5 = 5, 6 = 7; 2, 3 = 2.5; 3, 15 = 2; 6, 7 = 10.5; 7, 8 = 4; 8, 9 = 5; 14, 14′ = 4; compound **6**: 2α, 2β = 3α, 3β = 16; 2α, 3α = 2α, 3β = 2β, 3β = 5; 2β, 3α = 11; 3α, 15 ~ 0.5; 5, 6 = 6, 7 = 9.5; 7, 8 = 2.5; compound **7**: 2, 4 = 1; 4, 5 = 4, 15 = 7; 5, 5′ = 14; 5, 6 = 9.5; 6, 7 = 5; 7, 8 = 1.5; 8, 9 = 3; 9, OH = 9.

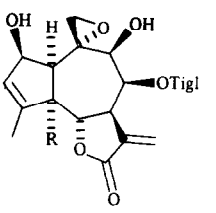
irradiation of the broadened hydroxy singlet at δ2.40. The absence of coupling $J_{8,9}$ would agree with a 4,9-ether bridge which was supported by the molecular formula. This was established by NOE difference spectroscopy. Clear effects were observed between H-7, H-5 and H-3α, between H-14, H-8 and H-9, between H-15, H-6, H-2β and H-3β, between H-8, H-7 and H-14, between H-9, H-8 and H-14 as well as between H-5, H-7 and H-3α. The presence of a 10α-hydroxy group caused a downfield shift of H-3α and H-7. The resulting conformation was also supported by a *W*-coupling between H-3α and H-15. This also excluded the possibility of an ether bridge between H-4 and H-10. Also the ^{13}C NMR data (see Experimental) supported the structure. Most likely the lactone **6** is formed in the plant by attack of the 9-hydroxy group at the 4,5-epoxide of 9β,10α-dihydroxy-1-oxo-8β-tigloxygermacra-4,11(13)-dien-6,12-olide which, however, was not isolated.

The ^{1}H NMR spectrum of **7** (Table 1) was close to that of 4,5-dihydroatripliciolide-8-*O*-angelate [11]. The 9β-hydroxy group in **7** led to an additional lowfield signal at δ4.16. The β-orientation followed from the coupling $J_{8,9}$. The stereochemistry was further established by NOE difference spectroscopy. Clear effects between H-4 and H-5α as well as between H-15, H-2 and H-6 indicated a 4β-methyl group. We therefore have studied again the configuration of the angelate from the *Trichogoniopsis* species [11] and the same NOEs were observed. The configuration at C-4 (compound **16** in lit. [11]) therefore has to be revised to 4β-methyl. The same results were reported for several lactones from *Viguiera* species where the configuration at C-4 of the closely related lactones was revised [12]. It may be that in 4,5-dihydrofuroheliangolides the configuration at C-4 is always the same.

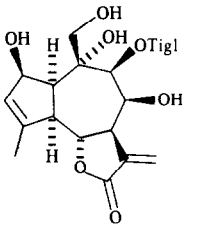
The structures of **8** and **9** also could be established by ^{1}H NMR spectroscopy (see Experimental). Spin decoupling allowed the assignment of all signals. The resulting sequences showed that in addition to the hydroxy group at C-1 both compounds had hydroxy groups at C-9 and C-17. In the spectrum of **9** the location of the additional hydroxy group could be assigned by spin decoupling. Starting with the irradiation of the H-9 signal those of H-10 and H-8 were assigned. As the latter showed an allylic coupling with H-6 which in turn showed an allylic coupling with H-19 and since H-10 only was coupled with one olefinic methyl, the position of the last hydroxy group was settled. NOE difference spectroscopy allowed the assignment of the configuration of the double bonds. Thus clear effects were observed between H-20 and H-2, between H-19 and H-5, between H-18 and H-9 as well as between H-16 and H-14. Accordingly, both compounds were derivatives of geranyl nerol. These diterpenes may be chemotaxonomically important as they have been isolated from *Stylotrichium* [8], *Lasiolaena* [4, 13] and *Trichogoniopsis* [11], species which are placed in the same subtribe. Furthermore, since similar sesquiterpene lactones have



1



2 R = H
3 R = OH



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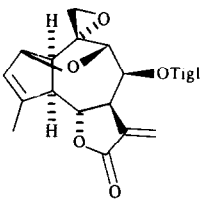
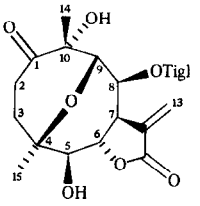
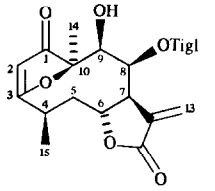


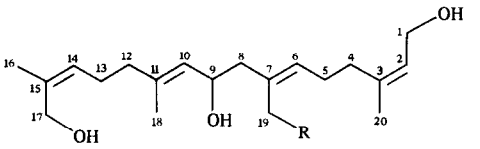
5



6



7



8 R = H
9 R = OH

been isolated from the genera *Agrianthus*, *Bejaranoa*, *Conocliniopsis*, *Lasiolaena*, *Trichogonia* and *Trichogoniopsis* the chemistry of at least this part of the subtribe Gyptidinae is relatively uniform. However, so far these compounds have not been reported from the genera *Conoclinium*, *Campuloclinium* and *Bahianthus*. Perhaps further investigations may show whether these genera of the same subtribe really differ in the chemistry.

EXPERIMENTAL

The aerial parts of *Bejaranoa balansae* (300 g, collected in Paraguay, voucher Schmeda 3653, deposited in the U.S. National Herbarium) were extracted with MeOH–Et_2O–petrol (1:1:1). The extract obtained was defatted by treatment with MeOH affording 2.1 g extract which was separated by CC (silica gel) into four fractions. The first two fractions (Et_2O–petrol, 1:9 and 1:1) gave nothing of interest. Fraction 3 (Et_2O–petrol, 3:1) was separated by flash chromatography (silica gel ϕ 30–60 μ) with Et_2O–petrol mixtures affording four crude fractions (3/1–3/4). TLC of 3/1 (C_6H_6–CH_2Cl_2–Et_2O, 4:4:1, two developments) gave 21 mg 9β-hydroxy-8β-tigloyloxycostunolide (R_f 0.28), 7 mg **4** (R_f 0.25), colourless oil; IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3600 (OH), 1780 (γ-lactone), 1720, 1650 (C=CCO_2R); MS *m/z* (rel. int.): 394.163 (2) (calc. for $C_{20}H_{26}O_8$: 394.163), 376 $[M-H_2O]^+$ (0.3), 345 $[376-CH_2OH]^+$ (2), 276 $[376-RCO_2H]^+$ (1), 258 $[276-H_2O]^+$ (2), 83 $[C_4H_7CO]^+$ (100) and 23 mg **2** (R_f 0.18). TLC of 3/2 (same solvent, three developments) gave 15 mg 9-hydroxylasiolaenolide (R_f 0.35) and 11 mg balsanolide (**5**) (R_f 0.31), colourless oil; IR $\nu_{max}^{CCl_4}$ cm^{-1}: 1770 (γ-lactone), 1720 (C=CC=O); CIMS *m/z* (rel. int.): 359 $[M+1]^+$ (100), 341 $[359-H_2O]^+$ (29), 259 $[359-RCO_2H]^+$ (58), 241 $[259-H_2O]^+$ (44); EIMS: 258 $[M-RCO_2H]^+$ (1.5), 83 $[C_4H_7CO]^+$ (100). Fraction 3/3 gave by crystallization from $CHCl_3$–MeOH 55 mg 9β,10α-dihydroxy-1-oxo-8β-tigloyloxy-germacra-4,11(13)-dien-6,12-olide, mp 228° (lit. [5] 224–226°) and 3/4 gave by TLC (Et_2O–MeOH, 30:1) 11 mg **9** (R_f 0.43), 31 mg **6** (R_f 0.41) and 5 mg **3** (R_f 0.35).

Compound **3**. Colourless oil; IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3600 (OH), 1780 (γ-lactone), 1710 (C=CCO_2R); MS *m/z* (rel. int.): 392.147 $[M]^+$ (0.2) (calc. for $C_{20}H_{24}O_8$: 392.147), 362 $[M-CH_2O]^+$ (1), 344 $[362-H_2O]^+$ (2), 262 $[362-RCO_2H]^+$ (6), 244 $[262-H_2O]^+$ (6), 83 $[C_4H_7CO]^+$ (100).

Compound **6**. Colourless oil; IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3620 (OH), 1770 (γ-lactone), 1720, 1645 (C=CCO_2R, ROC=CC=O); MS *m/z* (rel. int.): 394.163 $[M]^+$ (3) (calc. for $C_{20}H_{26}O_8$: 394.163), 376 $[M-H_2O]^+$ (1), 294 $[M-RCO_2H]^+$ (0.6), 251 $[294-C_2H_3O]^+$ (4), 83 $[C_4H_7CO]^+$ (100); ^{13}C NMR ($CDCl_3$, C-1–C-15): 209.8 *s*, 36.4 *t*, 34.6 *t*, 81.5 *s*, 85.0 *d*, 80.1 *d*, 43.9 *d*, 79.2 *d*, 67.7 *d*, 81.4 *s*, 134.8 *s*, 168.8 *s*, 122.5 *t*, 24.2 *q*, 24.4 *q*; OCOR: 167.0 *s*, 127.7 *s*, 139.3 *d*, 14.5 *q*, 12.0 *q* (a few signals may be interchangeable).

Compound **9**. Colourless oil: IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3595, 3380 (OH); CIMS: 339 $[M+1]^+$ (6), 321 (78), 303 (40), 285 (100), 267 (32); ^1H NMR ($CDCl_3$, 400 MHz): 4.07 (*br d*, H-1), 5.42 (*br t*, H-2), 2.18 (*m*, H-4), 2.24 (*m*, H-5), 5.39 (*br t*, H-6), 2.33 and 2.20 (*dd*, H-8), 4.46 (*ddd*, H-9), 5.15 (*br d*, H-10), 2.02 (*m*, H-12), 2.15 (*m*, H-13), 5.21 (*br t*, H-14), 1.79 (*br s*, H-16), 4.08 and 4.05 (*br d*, H-17), 1.70 (*d*, H-18), 4.15 and 4.01 (*br d*, H-19), 1.76 (*br s*, H-20); [*J* (Hz): 1,2 = 5,6 = 13,14 = 7; 8,8′ = 14; 8,9 = 3.5; 8′,9 = 9; 9,10 = 8; 10,18 = 1; 17,17′ = 19,19′ = 12].

TLC of fraction (Et_2O–MeOH, 9:1) gave a polar band which by repeated TLC ($CHCl_3$–MeOH, 19:1, three developments) gave 12 mg **8** (R_f 0.63), 5 mg **7** (R_f 0.51), 7 mg 9β-hydroxy-8β-tigloyloxycostunolide (R_f 0.48) and 4.5 mg **1** (R_f 0.42).

Compound **1**. Colourless oil; IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3630 (OH), 1770 (γ-lactone), 1710 (C=CCO_2R); MS *m/z* (rel. int.): 376.152 $[M]^+$ (1) (calc. for $C_{20}H_{24}O_7$: 376.152), 358 $[M-H_2O]^+$ (1.5), 258 $[358-RCO_2H]^+$ (9), 83 $[C_4H_7CO]^+$ (100).

Compound **7**. Amorphous powder; IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3600 (OH), 1760 (γ-lactone), 1720 (C=O, C=CCO_2R); MS *m/z* (rel. int.): 376.152 $[M]^+$ (12) (calc. for $C_{20}H_{24}O_7$: 376.152), 358 $[M-H_2O]^+$ (2), 277 $[M-OCOR]^+$ (3), 83 $[C_4H_7CO]^+$ (100).

Compound **8**. Colourless oil; IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3620, 3400 (OH); CIMS *m/z* (rel. int.): 323 $[M+1]^+$ (0.5), 305 $[323-H_2O]^+$ (6), 287 $[305-H_2O]^+$ (100), 269 $[287-H_2O]^+$ (65); ^1H NMR ($CDCl_3$, 400 MHz): 4.09 (*br d*, H-1), 5.44 (*br t*, H-2), 2.15 (*m*, H-4, H-5), 5.21 (*br t*, H-6), 2.15 (*m*, H-8; in C_6H_6: 2.25 and 2.16 *dd*), 4.41 (*ddd*, H-9), 5.10 (*br d*, H-10), 2.01 (*m*, H-12), 2.15 (*m*, H-13), 5.21 (*br t*, H-14), 1.79 (*br s*, H-16), 4.09 and 4.01 (*br d*, H-17), 1.70 (*d*, H-18), 1.66 (*br s*, H-19), 1.72 (*br s*, H-20); [*J* (Hz): 1,2 = 5,6 = 13,14 = 7; 8,9 = 5; 8′,9 = 9,10 = 8.5; 10,18 = 1.2; 17,17′ = 12].

Acknowledgements—We thank Dr. R. M. King, Smithsonian Institution, Washington, DC 20560, U.S.A., for identification of the plant material. V. P. Pathak is thankful to Alexander von Humboldt-Stiftung for the award of a fellowship.

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