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MELAMPOLIDES AND OTHER GERMACRANOLIDES FROM *BLAINVILLEA DICHOTOMA**

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Key Word Index—*Blainvillea dichotoma*; Compositae; sesquiterpene lactones; melampolides; germacranolides.

Abstract—The aerial parts of *Blainvillea dichotoma* afforded, in addition to known compounds, seven new sesquiterpene lactones, four related to elephantin, two melampolides and a further *cis,cis*-germacranolide. The chemotaxonomic situation is discussed briefly.

INTRODUCTION

The genus *Blainvillea* (Compositae, tribe Heliantheae) is placed by Stuessy [1] in the subtribe Ecliptinae together with *Enhydra* and *Eclipta*, where chemical data are already available [2, 3]. *Blainvillea* species have not been investigated before, except that the presence of the widespread tridecaptentaynene is recorded [4]. The investigation of *B. dichotoma* afforded several new germacranolides, which indicate relationships to *Enhydra* but not to *Eclipta*.

RESULTS AND DISCUSSION

The aerial parts of *B. dichotoma* (Murr.) Cass. afforded germacrene D, bicyclogermacrene, caryophyllene, lupeol, its acetate, lupenone and β-amyrin acetate as well as a complex mixture of minute amounts of sesquiterpene lactones. Only by combination of TLC and HPLC was a complete separation possible. Two compounds, however, still were unresolved as a mixture. Careful ^{1}H NMR studies including extensive spin decoupling of all lactones as well as of the corresponding acetates led to the structures **1**–**4**, **7**, **9** and **12**. **1**–**4** are closely related to elephantin [4]. We have named the lactones without a C-8 oxygen function blainvilleolide.

7, **9** and **12** are closely related to acanthospermal B (**11**) [5, 6], where we had introduced the name acanthospermolide [6] for the compound without oxygen functions at C-8, C-9 and C-14.

The ^{1}H NMR data of **1** and **2** (see Table 1) together with the molecular formula clearly indicate the presence of a second lactone ring. The corresponding chemical shifts of 1- and 2-H are very similar to those of elephantin [4]. The β-orientation of the ester residues follows from the observed couplings $J_{7,8}$ and $J_{8,9}$, while the 4,5-*trans* double bond is indicated by the typical couplings for $J_{5,6}$ and $J_{6,7}$. The structures of the two alcohols **3** and **4**, which were not separated, follow from the ^{1}H NMR data of the corresponding acetates **5** and **6**, which also were not separated (see Table 1). The data of **5** are very close to those of **1**, while the chemical shifts in the spectrum of **6** are slightly different due to the missing 11,13-double bond. The observed coupling 7,11 indicates an α-orientated 11-methyl, while the stereochemistry at all other centres in **5** and **6** must be the same as in that of **1** and **2**.

The lactones **7** and **9**, both transformed to the acetates **8** and **10** respectively, obviously must be isomers. If we compare the ^{1}H NMR spectra with that of the 9-epimer acanthospermal B [5] the only possible difference between **9** and the latter is in the stereochemistry at C-9. Consequently $J_{8,9}$ is smaller in the spectra of **9** and **10**. The other observed couplings indicate the same stereochemistry as in acanthospermal B at all other centres. The second lactone (**7**), isolated only as its acetate **8** showed more pronounced differences in the ^{1}H NMR spectrum (see Table 1). Especially the chemical shifts of 5-, 7-, 9- and 15-H are very different from those of **10**. Inspection of models indicates a 4,5-*cis*-double bond and a different conformation of the 10-membered ring. Probably due to the steric hindrance of the 4-methyl and the oxygen function at C-9 in **10**, here the conformation is different from that of acanthospermal B. A model of **8** showed that here the most probable conformation would agree with the observed chemical shifts and couplings. Especially the chemical shift of 15-H indicates a 4,5-*cis*-double bond, though due to the minute amounts the configuration could not be finally established.

A last minor lactone **12** obviously is the epoxide of **9**. Again only the corresponding acetate **13** could be isolated in a pure state. All ^{1}H NMR signals (see Table 1) are in good agreement with the expected ones. The observed couplings for 1-H indicate an α-orientation, while $J_{8,9}$ again supports the *cis*-configuration at C-8 and C-9. The stereochemistry at C-5 to C-8 is obviously the same as that of **10**, indicating that **12** is formed in the plant by epoxidation of **9**. The changed stereochemistry at C-10 caused a large difference in the chemical shifts of 9-H in

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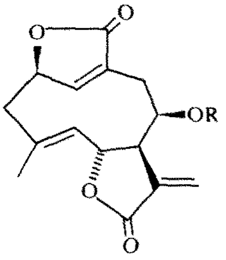
Table 1. ^{1}H NMR data of **1**–**6**, **8**–**10** and **13** (270 MHz, TMS as internal standard, $CDCl_3$)

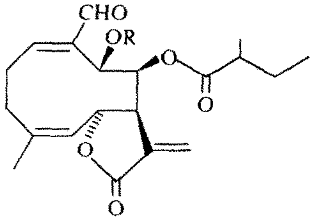
	1	**2**	**3**	**4**	**5**	**6***	**8**	**9**	**10**	**13**
1-H	6.95 *s(br)*	6.90 *s(br)*	7.01 *s(br)*	6.96 *s(br)*	6.93 *s(br)*	6.93 *s(br)*	6.79 *dd*	6.62 *ddd*	6.61 *ddd*	3.25 *dd*
2-H	5.37 *d(br)*	5.38 *d(br)*	5.14 *d(br)*	5.14 *d(br)*	5.35 *m*	5.35 *m*	2.63 *m*	3.20 *dddd*	2.55 *m*	
3-H	3.00 *ddd* 2.38 *dd*	3.02 *d(br)* 2.41 *dd*	2.95 *m* 2.31 *dd*	2.36 *dd*	3.02 *d(br)* 2.35 *dd*	2.94 *d(br)* 2.40 *dd*		2.11 *dd* 2.39 *m*		
5-H	5.20 *dq*	5.22 *d(br)*	5.34 *d(br)*	5.09 *dd*	5.22 *d(br)*	5.11 *d(br)*	5.52 *d(br)*	4.77 *d(br)*	4.87 *d(br)*	5.36 *d(br)*
6-H	4.95 *dd*	4.96 *dd*	5.24 *dd*		4.94 *dd*	4.83 *dd*	4.90 *dd*	5.08 *dd*	5.06 *dd*	5.14 *dd*
7-H	3.09 *dddd*	3.13 *dddd*	2.95 *m*		3.11 *dddd*		3.23 *dddd*	2.64 *dddd*	2.65 *dddd*	3.14 *dddd*
8-H	5.68 *dd(br)*	5.72 *dd(br)*	4.58 *dd*	4.27 *dd*	5.68 *m*	5.35 *m*	6.03 *d(br)*	6.28 *s(br)*	6.36 *dd*	6.11 *d(br)*
9-H	2.91 *dd(br)* 2.66 *dd(br)*	2.96 *dd(br)* 2.60 *dd(br)*	2.77 *dd(br)* 2.55 *m*	2.79 *dd*	2.92 *dd* 2.79 *dd*	2.65 *dd*	5.77 *s(br)*	5.08 *s(br)*	6.46 *d(br)*†	4.76 *d*
13-H	6.30 *d*	6.31 *d*	6.27 *d*	1.26 *d*	6.31 *d*	1.31 *d*	6.27 *d*	6.25 *d*	6.26 *d*	6.38 *dd*
13′-H	5.67 *d*	5.66 *d*	5.51 *d*		5.65 *d*		5.71 *d*	5.54 *d*	5.55 *d*	5.72 *dd*
14-H	—	—	—	—	—	—	9.40 d	9.34 s	9.35 s	9.97 s
15-H	1.74 *d*	1.73 *d*	1.66 *d*	1.65 *d*	1.72 *d*	1.70 *d*	1.68 *d*	1.84 *d*	1.98 *d*	1.75 *d*
OCOR	5.66 *qq*	2.37 *dt*	—	—	—	—	1.02 *d*	2.39 *dt*	2.24 *dt*	2.26 *dt*
	2.21 *d*	1.71 *tq*	—	—	—	—	0.89 *t*	1.67 *tq*	1.65 *tq*	1.65 *m*
	1.94 *d*	1.54 *tq*	—	—	—	—	—	1.50 *tq*	1.40 *tq*	1.45 *m*
		1.16 *d*	—	—	—	—	—	1.13 *d*	1.02 *d*	1.15 *d*
		0.95 *t*		—	—	—		0.92 *t*	0.88 *t*	0.92 *t*
OAc	—	—	—	—	2.12 *s*	2.16 *s*	2.08 *s*	—	2.17 *s*	2.05 *s*

* 11-H 2.40 *dq* (J = 9, 7); † homoallylic coupling with 2-H.

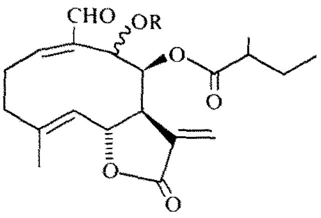
J = (Hz): **1**–**6**: 2, 3 = 1.5; 2, 3′ = 5; 3, 3′ = 14.5; 5, 6 = 10.5; 5, 15 = 1.5; 6, 7 = 9.5; **7**: 8 ~ 1; 7, 13 = 3.5; 7, 13′ = 3; 8, 9 = 4; 8, 9′ = 2.5; 9, 9′ = 14.5; **8**: 1, 2 = 11; 1, 2′ = 7; 5, 6 = 10; 5, 15 = 1.5; 6, 7 = 9; 7, 13′ = 3; 8, 9 = 1.5; 9, 14 = 1; **9**/**10**: 1, 2 = 10; 1, 2′ = 8; 1, 9 = 1.5; 5, 6 = 10; 5, 15 = 1.3; 6, 7 = 9; 7, 13 = 3.5; 7, 13′ = 3; 7, 8 = 2.5; 8, 9 = 6.5; **13**: 1, 2 = 11; 1, 2′ = 2.5; 5, 6 = 10; 5, 15 = 1.5; 6, 7 = 9; 7, 13 = 3.5; 7, 13′ = 3; 8, 9 = 3; 13, 13′ = 0.5; OCOR: 2′, 3′ = 2′, 5′ = 3′, 4′ = 7; $3'_1$, $3'_2$ = 14.



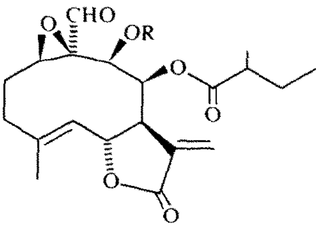
1 R = Sen
2 R = MeBu
3 R = H
4 R = H, 11β, 13-H
5 R = Ac
6 R = Ac, 11β, 13-H



7 R = H
8 R = Ac



9 R = β-OH
10 R = β-OAc
11 R = α-OH



12 R = H
13 R = Ac

the spectra of **10** and **13**, probably due to a shielding effect of the aldehyde group.

The compounds isolated from this species support the already discussed problems concerning the taxonomy of the subtribe Ecliptinae. Further investigations are necessary to clarify the relationships of the genera placed together in this subtribe [1].

EXPERIMENTAL

^{1}H NMR: 270 MHz, TMS as int. standard; optical rotation: $CHCl_3$; MS: 70 eV, direct inlet; Cl, isobutane. The air-dried plant material collected in North Eastern Brazil was extracted with Et_2O–petrol (1:2) and the extract was first separated by column chromatography (SiO_2, act. grade II) and further by TLC (SiO_2, GF 254). The most polar fractions were finally separated by HPLC (reversed phase). The aerial parts (100 g) afforded 20 mg germacrene D, 5 mg bicyclogermacrene, 10 mg caryophyllene, 5 mg lupeol, 10 mg lupeol acetate, 10 mg lupenone, 10 mg β-amyrin acetate, 8 mg **1** and 7 mg **2** (HPLC, MeCN–H_2O, 1:1), 2 mg **3** and 4 mg **4** (TLC, Et_2O–MeOH, 30:1, not separated), 0.5 mg **7** and 4 mg **9** (separated by HPLC, MeOH–H_2O, 3:2) and 0.5 mg **12** (isolated as its acetate **13**, TLC Et_2O–petrol, 7:3).

8β-*Senecioyloxyblainvilleolide* (**1**). Colourless gum, IR $\nu_{\max}^{CCl_4}$ cm^{-1}: 1770 (γ-lactone); 1735, 1650 (C=CCO_2R); MS: M^+ *m/e* (rel. int.) 358.142 (0.5) ($C_{20}H_{22}O_6$); 258 (2) (M − RCO_2H); 243 (0.5) (258 − $^{\cdot}$Me); 230 (1) (258 − CO); 83 (100) ($C_4H_7CO^+$).

$$[\alpha]_{24}^{\lambda} = \frac{589 \quad 578 \quad 546 \quad 436\,\text{nm}}{+30.4 \quad +32.0 \quad +36.6 \quad +61.8}\ (c = 0.77).$$

8β-[*2-Methylbutyryloxy*]-*blainvilleolide* (**2**). Colourless gum, IR $\nu_{\max}^{CCl_4}$ cm^{-1}: 1770 (γ-lactone), 1750 (CO_2R); MS: M^+ *m/e* (rel. int.) 360.157 (0.5) ($C_{20}H_{24}O$); 276 (9) [M − O=C=C(Me)Et]; 258 (4) (M − RCO_2H); 243 (0.5) (258 − $^{\cdot}$Me); 85 (48) ($C_4H_9CO^+$); 57 (100) (85 − CO).

$$[\alpha]_{24}^{\lambda} = \frac{589 \quad 578 \quad 546 \quad 436\,\text{nm}}{+65.2 \quad +68.4 \quad +79.0 \quad +146.5}\ (c = 0.62).$$

8β-*Hydroxy blainvilleolide* (**3**) *and* 11β,13-*dihydro*-8β-*hydroxy blainvilleolide* (**4**). Colourless gum, not separated. Acetylation (4 hr, Ac_2O, 70°) afforded **5** and **6**, which also were not separated, colourless gum, IR $\nu_{\max}^{CCl_4}$, cm^{-1}: 1760 (γ-lactone, OAc); MS (CI, isobutane): 321 (20, M + 1) 319 (8, M + 1); 261 (62, −HOAc + 1); 259 (28, −HOAc + 1); 217 (100, 261 − CO_2); 215 (20, 259 − CO_2).

$$[\alpha]_{24}^{\lambda} = \frac{589 \quad 578 \quad 546 \quad 436\,\text{nm}}{+38.6 \quad +40.3 \quad +46.6 \quad +87.1}\ (c = 0.35).$$

8β-[*2-Methylbutyryloxy*]-9β-*hydroxy-14-oxo-4,5-cis-acanthospermolide* (**7**). Colourless gum, purified as its acetate **8** (4 hr, Ac_2O, 70), colourless gum, IR $\nu_{\max}^{CCl_4}$, cm^{-1}: 1780 (γ-lactone); 1750 (CO_2R); 1710 (C=CCHO); MS (CI, *iso*-butane) (rel. int.) 405 (10) (M + 1); 345 (31) (M − AcOH + 1); 243 (100) (345 − RCO_2H).

8β-[*2-Methylbutyryloxy*]-9β-*hydroxy-14-oxo-acanthospermolide* (**9**). Colourless gum, IR $\nu_{max}^{CCl_4}$, cm^{-1}: 3600 (OH); 1760 (γ-lactone); 1740 (CO_2R); 1690 (C=CCHO).

$$[\alpha]_{24}^{\lambda} = \frac{589 \quad 578 \quad 546 \quad 436\,\text{nm}}{-4.0 \quad -4.3 \quad -6.0 \quad -16.0}\ (c = 0.3).$$

Acetylation (4 hr, Ac_2O, 70) afforded **10**, colourless gum, MS (CI, isobutane): 405 (10) (M + 1); 345 (34) (M − HOAc + 1); 243 (100) (345 − RCO_2H).

8β-[2-Methylbutyryloxy]-9β-hydroxy-14-oxo-1α,2β-epoxy-1,10-dihydroacanthospermolide (**12**). Purified as its acetate **13** (Ac_2O, 4 hr, 70), colourless gum, IR $\nu_{\max}^{CCl_4}$, cm^{-1}: 1785 (γ-lactone), 1750 (OAc), 1735 (CO_2R, CHO); MS: M^+ *m/e* (rel. int.) 420.178 (0.5) ($C_{22}H_{28}O_8$); 318 (4) (M − RCO_2H); 258 (2) (318 − HOAc); 230 (3) (258 − CO); 85 (48) ($C_4H_9CO^+$); 57 (100) (85 − CO). CI (isobutane): 421 (73) (M + 1); 319 (100) (M − RCO_2H + 1); 259 (52) (319 − HOAc).

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REFERENCES

1. Stuessy, T. F. (1977) *The Biology and Chemistry of the Compositae* (Heywood, V. H., Harborne, J. B. and Turner, B. L., eds.), p. 628. Academic Press, London.
2. Joshi, B. S. and Kamat, V. N. (1976) *Indian J. Chem.* **10**, 771.
3. Bohlmann, F., Burkhardt, T. and Zdero, C. (1973) *Naturally Occurring Acetylenes*. Academic Press, London.
4. Kupchan, S. M., Aynehchi, Y., Cassady, J. M., Schnoes, H. K. and Burlingame, A. L. (1969) *J. Org. Chem.* **34**, 3867.
5. Herz, W. and Kalyanaraman, P. S. (1975) *J. Org. Chem.* **40**, 3486.
6. Bohlmann, F., Jakupovic, J., Zdero, C., King, R. M. and Robinson, H. (1979) *Phytochemistry* **18**, 625.