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HIGHLY OXYGENATED GUAIANOLIDES FROM *BISHOPANTHUS SOLICEPS*

PAHUP SINGH, JASMIN JAKUPOVIC, FERDINAND BOHLMANN, ROBERT M. KING* and HAROLD ROBINSON*

Institute for Organic Chemistry, Technical University of Berlin, D-1000 Berlin 12; *Smithsonian Institution, Department of Botany, Washington, DC 20560, U.S.A.

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Key Word Index—*Bishopanthus soliceps*; Compositae; sesquiterpene lactones; guaianolides; eudesmanolides.

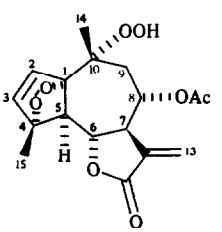
Abstract—In addition to known compounds several highly oxygenated guaianolides and eudesmanolides, derived from 1β-hydroxyarbusculin A, were isolated from the aerial parts of *Bishopanthus soliceps*, a member of a new genus of the tribe Liabeae.

INTRODUCTION

In view of the absence of any information about the chemistry of the new monotypic genus *Bishopanthus* (tribe Liabeae) [1], we have undertaken an investigation of *Bishopanthus soliceps* H. Robins.

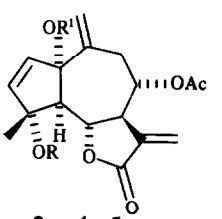
RESULTS AND DISCUSSION

The aerial parts of *B. soliceps* afforded ferulic acid, the flavones pectolinarigenin [2], 3-desmethoxycentaureidin [3] and eupatolitin [4], 5-(3,4-dihydroxy-but-1-in-yl]-bithienyl-(2,2') [5] and the guaianolides anhydrocumambrin A [6], 1-desoxy-1α-peroxyrupicolin A and B-8-*O*-acetate [7], 11,13-dehydromatricarin [8] as well as **1–5** and the eudesmanolides reynosin [9], **6** and **7**. As shown by the ^{1}H NMR spectra (Table 1), **1** and **2** were hydroperoxides (*s* (*br*) 8.38 and 8.47 respectively). A pair of doublets at δ6.22 and 6.34 in the spectrum of **1** with a 6 Hz coupling clearly showed that a guaianolide with a 2,3-double bond was present. Most signals were close to those of one of the epimeric endoperoxides isolated from a *Tanacetum* species [10]. However, these compounds had no 8-*O*-acetate group. When the shifts of H-5 and H-6 were compared with those of the epimeric tanaparthin peroxides, it was obvious that **1** was the 1α,4α-isomer. NOE difference spectroscopy gave clear effects between H-14 and H-2 and H-9α, between H-5 and H-7, between H-6 and H-8 and between H-15 and H-3 and H-5, which established the proposed configurations. Models indicated however, that the orientation of H-15 cannot be assigned from these results. As the configuration of the isomeric endoperoxides from the *Tanacetum* species was established the configuration at C-4 in **1** was clear. The spectrum of **2** (Table 1) was in part similar to that of **1**. However, the olefinic signal was replaced by a pair of upfield shifted doublets which were due to epoxide protons. The β-orientation of the epoxide oxygen caused a downfield shift of the H-6 signal. Furthermore, clear NOEs were observed between H-5 and H-7, between H-6 and H-8, between H-15 and H-3 and H-5 as well as between H-14 and H-9α and H-9β. Inspection of models indicated that these effects required the proposed stereochemistry, while the couplings observed showed that the conformations of **1** and **2** were slightly different. Compound **1** we have named bishopantholide. The ^{1}H NMR spectra of **3** and **5** (Table 1) were again in part very similar. Both compounds were transformed by reduction with triphenylphosphine to the lactone **4** which also was present in the extract. Its ^{1}H NMR spectrum (Table 1) differed from that of **1** by the presence of exomethylene proton signals. As the H-9 signals were shifted downfield a 10(14)-double bond was proposed. Compound **3** showed clear NOEs between H-6 and H-8, between H-15 and H-6 and H-3, between H-14 and H-2 and between H-14' and H-9α. These results required the proposed configuration for **3–5** and the relative position of the hydroperoxide groups followed from the downfield shift of H-5 in the spectrum of **5** if compared with that of **3** and **4**. The lactone without an

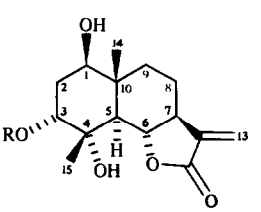


1

2 2β, 3β – epoxide



	3	4	5
R	H	H	OH
R^1	OH	H	H



6 R = iBu
7 R = Mebu

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

H	1	2	3	4	5	6* and 7†
1	—	—	—	—	—	3.79 dd
2	6.22 *d*	3.64 *d*	5.91 *d*	5.62 *d*	6.03 *d*	1.93 *m*
3	6.34 *d*	3.29 *d*	6.11 *d*	6.01 *d*	6.21 *d*	5.03 *dd*
5	2.73 *d*	2.72 *d*	2.54 *d*	2.46 *d*	2.92 *d*	2.16 *d*
6	3.74 *dd*	4.25 *dd*	4.16 *dd*	4.16 *dd*	4.16 *dd*	4.15 *dd*
7	3.67 *dddd*	3.54 *dddd*	3.45 *dddd*	3.65 *dddd*	3.47 *dddd*	2.65 *m*
8	5.15 *ddd*	5.20 *ddd*	4.90 *ddd*	4.90 *ddd*	4.90 *ddd*	2.10 *m* 1.60 *dddd*
9α	2.31 *dd*	2.39 *dd*	2.73 *dd*	2.89 *dd*	2.75 *dd*	2.07 *m*
9β	2.09 *dd*	1.83 *dd*	2.84 *dd*	2.75 *dd*	2.87 *dd*	1.40 *m*
13	6.22 *d*	6.24 *d*	6.35 *d*	6.34 *d*	6.32 *d*	6.13 *d*
13′	5.48 *d*	5.60 *d*	5.86 *d*	5.87 *d*	5.84 *d*	5.46 *d*
14	1.50 *s*	1.13 *s*	5.27 *s* (*br*) 4.97 *s* (*br*)	5.13 *s* (*br*) 4.89 *s* (*br*)	5.28 *s* (*br*) 4.99 *s* (*br*)	1.00 *s*
15	1.70 *s*	1.56 *s*	1.37 *s*	1.35 *s*	1.30 *s*	1.39 *s*
OAc	2.18 *s*	2.12 *s*	2.15 *s*	2.15 *s*	2.15 *s*	—
OOH	8.47 *s* (*br*)	8.38 *s* (*br*)	8.55 *s* (*br*)	—		

*OCOCHMe$_2$: 2.62 *qq*, 1.18 *d*, 1.19 *d*; [*J* (Hz): 2, 3 = 2, 4 = 7].

†OCOCH(Me)Et: 2.53 *tq*, 0.91 *t*, 1.16 *d*; [*J* (Hz): 2, 3 = 2, 5 = 3, 4 = 7].

J (Hz): Compound **1**: 2, 3 = 6; 5, 6 = 6, 7 = 11; 7, 8 = 10; 7, 13 = 3.5; 7, 13′ = 3; 8, 9α = 1; 8, 9β = 6; 9α, 9β = 17; compound **2**: 2, 3 = 1; 5, 6 = 6, 7 = 11; 7, 8 = 10; 7, 13 = 3.5; 7, 13′ = 3; 8, 9α = 7.5; 8, 9β = 4; 9α, 9β = 17; compounds **3**–**5**: 2, 3 = 6; 5, 6 = 12; 6, 7 = 9; 7, 8 = 11; 7, 13 = 3.5; 7, 13′ = 3; 8, 9α = 11; 8, 8β = 6; 9α, 9β = 13; compounds **6** and **7**: 1α, 2α = 5; 1α, 2β = 11; 2α, 3β = 3; 5, 6 = 6, 7 = 11; 7, 13 = 3.5; 7, 13′ = 3.

oxygen function at C-1 and C-4 we have named bishopsolicepolide.

The ^{1}H NMR spectra of **6** and **7** (Table 1) showed some similarities to that of 1β-hydroxyarbusculin A [11]. However, a double doublet at δ5.03 and the additional signals of ester groups indicated the presence of an oxygen function at C-3 whereas the couplings required an α-orientation. Spin decoupling supported this assumption and NOEs of both H-14 and H-15 with H-6 led to the assignment of the configuration shown. The nature of the ester groups followed from the typical signals. The roots only gave known compounds (see Experimental).

Bishopanthus is the most recently described of the 16 known genera of the tribe Liabeae [1] and is the only genus not covered in the recent generic review of the tribe [12]. It is probably closely related to *Cacosmia* and *Ferreyanthus* of the subtribe Liabinae which occur in the same geographical area and which have similar shrubby habits. The probability of such a relationship is strengthened by the observation of rather similar highly oxygenated guaianolides in *Cacosmia* [13] and *Ferreyanthus*, where in addition to guaianolides [14] the corresponding eudesmanolides as well as germacranolides are reported [15]. However, extensive differences in structural details between the genera raise the possibility that the similarities in both habit and chemistry are relicts of a primitive type in the subtribe. Simple sesquiterpene lactones are also present in *Liabum* [16] and *Munnozia* [17]. In addition acetylenes have also been isolated from members of the Liabeae [14]. The proposed links to the tribe Vernonieae [12] are supported by the chemistry as again highly oxygenated sesquiterpene lactones are common in Vernonieae and also similar acetylenes have been observed. The suggested evolutionary scheme for the Liabeae [12] would indicate that the capacity of formation of highly oxygenated sesquiterpene lactones is lost in the more advanced genera like *Chrysactinium*, *Munnozia*, *Liabum*, *Sinclairia* and *Paranephelius*. Further investigations of representatives of the tribe Liabeae would be of interest.

EXPERIMENTAL

The air dried plant material (collected in January 1983 in Peru, voucher RMK 9280) was extracted with Et_2O–petrol–MeOH (1:1:1), and the extracts obtained were separated as described previously [18]. The CC (silica gel) fractions of the aerial parts (260 g) obtained with Et_2O–petrol (1:1) (Fr. 1) and with Et_2O and Et_2O–MeOH (9:1) (Fr. 2), were further separated by TLC (silica gel PF 254). TLC of fraction 1 (Et_2O–petrol, 2:3, several developments) gave 1.5 mg anhydrocumambrin A, 2 mg each of 1-desoxy-1α-peroxyrupicolin A- and B-8-*O*-acetate, 2 mg ferulic acid and 10 mg pectolinarigenin. TLC of fraction 2 (Et_2O–petrol, 9:1) gave three bands (2/1–2/3). TLC of 2/1 (CH_2Cl_2–C_6H_6–Et_2O, 2:2:1) gave 1.5 mg 11,13-dehydromatricarin (R_f 0.35) and 3.7 mg **5** (R_f 0.05). TLC of 2/2 (same solvent, several developments) gave 1.9 mg **1** (R_f 0.12), 3 mg **2** (R_f 0.10), 2 mg 5-[3,4-dihydroxybut-1-inyl]-bithienyl-(2,2′), 5 mg 3-desmethoxycentaureidin and 5 mg eupatolitin. TLC of 2/3 (CH_2Cl_2–C_6H_6–Et_2O, 1:1:1, several developments) gave 1.2 mg reynosin, 1.2 mg **7** (R_f 0.17), 2 mg **6** (R_f 0.15), 2 mg **3** (R_f 0.12) and 1.4 mg **4** (R_f 0.1). CC (silica gel) of the extract of the roots (80 g) gave fractions as follows: 1 (Et_2O–petrol, 1:9), 2 (Et_2O–petrol, 1:3) and 3 (Et_2O–petrol, 1:1 and Et_2O). TLC (Et_2O–petrol, 1:9) of fraction 1 gave 50 mg lupeyl acetate. TLC of fraction 2 (Et_2O–petrol, 1:3) gave 20 mg lupeol, 5 mg stigmasterol, 5 mg taraxasterol and 10 mg sitosterol. TLC of fraction 3 (Et_2O) gave 3 mg 5-[3,4-dihydroxybut-1-inyl]-bithienyl-(2,2′), 1.5 mg

tetrahydro-3-dehydrozaluzanin C [19], 2 mg 11β,13-dihydrozaluzanin C [20] and 1 mg lidbeckia lactone [21]. Known compounds were identified by comparison of their 400 MHz ^{1}H NMR spectra with those of authentic materials and by co-TLC. The purity of the compounds was checked by TLC in different solvent mixtures and by ^{1}H NMR spectroscopy.

Bishopantholide (**1**). Colourless oil, IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3480 (OH), 1775 (γ-lactone), 1740 (OAc); MS *m/z* (rel. int.): 320 $[M-O_2]^+$ (1), 287.128 $[320-O_2H]^+$ (12) (calc. for $C_{17}H_{19}O_4$: 287.120), 227 $[287-HOAc]^+$ (100); $[\alpha]_D = +28$ ($CHCl_3$; *c* 0.19).

2β,3β-Epoxybishopantholide (**2**). Colourless oil, IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3550 (OH), 1775 (γ-lactone), 1740 (OAc); MS *m/z* (rel. int.): 336.121 $[M-O_2]^+$ (1) (calc. for $C_{17}H_{20}O_7$: 336.121); CIMS: 369 $[M+1]^+$ (4), 337 $[369-O_2]^+$ (18), 277 $[337-HOAc]^+$ (28), 259 $[277-H_2O]^+$ (25), 243 $[277-H_2O_2]^+$ (18), 181 (70), 165 (100); $[\alpha]_D = +44$ ($CHCl_3$; *c* 0.3).

1α-Peroxy-4α-hydroxybishopsolicepolide (**3**). Colourless oil, IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3620 (OH), 1770 (γ-lactone), 1740 (OAc); MS *m/z* (rel. int.): 303 $[M-O_2H]^+$ (2), 243.102 $[303-HOAc]^+$ (10) (calc. for $C_{15}H_{15}O_3$: 243.102), 215 $[243-CO]^+$ (10), 200 $[215-Me]^+$ (10), 55 (100).

To 2 mg **3** in 0.5 ml $CDCl_3$ 5 mg triphenylphosphine was added. After 5 min the ^{1}H NMR spectrum was changed to that of **4**. Usual work-up gave **4**, identical with the natural lactone (^{1}H NMR, co-TLC).

1α,4α-Dihydroxybishopsolicepolide (**4**). Colourless oil, IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3600 (OH), 1770 (γ-lactone), 1740 (OAc); MS *m/z* (rel. int.): 305 $[M-Me]^+$ (2), 260.104 $[M-HOAc]^+$ (2) (calc. for $C_{15}H_{16}O_4$: 260.104), 242 $[260-H_2O]^+$ (4), 227 $[242-Me]^+$ (3), 199 $[227-CO]^+$ (5), 55 (100); $[\alpha]_D = +44$ ($CHCl_3$; *c* 0.14).

1α-Hydroxy-4α-peroxybishopsolicepolide (**5**). Colourless oil, IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3540 (OH), 1770 (γ-lactone), 1740 (OAc); MS *m/z* (rel. int.): 336 $[M]^+$ (1), 303 $[M-O_2H]^+$ (4), 243.102 $[303-HOAc]^+$ (8) (calc. for $C_{15}H_{15}O_3$: 243.102), 215 $[243-CO]^+$ (8), 197 $[215-H_2O]^+$ (7), 55 (100); $[\alpha]_D = +57$ ($CHCl_3$; *c* 0.37).

1β-Hydroxy-3α-isobutyryloxyarbusculin A (**6**). Colourless oil, IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3600 (OH), 1775 (γ-lactone), 1730 (CO_2R); MS *m/z* (rel. int.): 352 $[M]^+$ (1), 334.178 $[M-H_2O]^+$ (6) (calc. for $C_{19}H_{26}O_5$: 334.178), 246 $[334-RCO_2H]^+$ (10), 218 $[246-CO]^+$ (5), 203 $[218-Me]^+$ (8), 71 $[C_3H_7CO]^+$ (50), 55 (100).

1β-Hydroxy-3α-[2-methylbutyryloxy]-arbusculin A (**7**). Colourless oil, IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3540 (OH), 1770 (γ-lactone), 1730 (CO_2R); MS *m/z* (rel. int.): 366 $[M]^+$ (0.5), 348.194 $[M-H_2O]^+$ (3) (calc. for $C_{20}H_{28}O_5$: 348.194), 246 $[348-RCO_2H]^+$ (1), 85 $[C_4H_9CO]^+$ (26), 57 $[85-CO]^+$ (100); $[\alpha]_D = +25$ ($CHCl_3$; *c* 0.12).

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