Phytochemistry, Vol 29, No 1, pp 205–208, 1990
Printed in Great Britain

0031-9422/90 $3 00+0 00

A HELIANGOLIDE, 3-HYDROXYUMBELLIFERONE DERIVATIVES AND DITERPENES FROM *BAHIA AMBROSIOIDES*

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(*Received* 31 *May* 1989)

Key Word Index—*Bahia ambrosioides*, Compositae; sesquiterpene lactones, germacranolides, heliangolides, 3-hydroxyumbelliferone derivatives; diterpenes, kauranes; rosane

Abstract—The aerial parts of *Bahia ambrosioides* afforded several germacranolides and heliangolides one of which has not been reported previously Furthermore, in addition to widespread compounds, four 3-hydroxyumbelliferone derivatives were present as well as two new diterpenes, an *ent*-kaurane diol and an *ent*-rosane diol The structures were elucidated by high field NMR spectroscopy The chemotaxonomic aspects are discussed briefly.

INTRODUCTION

The small genus *Bahia* traditionally was placed in the artificial tribe Heleniеae, its genera now being distributed over several natural tribes. A recent revision of the Heliantheae has placed *Bahia* and the genus *Picradeniopsis*, previously part of the former, in the subtribe Chaenactidinae [1] together with other genera from the old tribe Heleniеae Chemical investigations have shown that *Bahia* can be characterized by the occurrence of guaianolides which are reported from three species [2–4]. However, a variety of *B absinthifolia* contains the heliangolide eucannabinolide (**6**) and an eudesmanolide glucoside [5]. Two *Picradeniopsis* species contained different types of sesquiterpene lactones. One species gave guaianolides [6] and the other more complex lactones, especially *seco*-compounds [7] We now have studied *B. ambrosioides* Lag, a species from Chile

RESULTS AND DISCUSSION

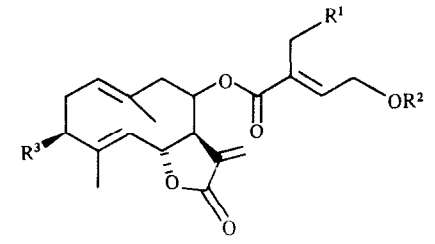
The extract of the aerial parts of *B. ambrosioides* gave, in addition to widespread compounds, the *E,E*-germacrolides **1** [8], **2** [9], **3** [10] and **4** [10] as well as the heliangolides **5** [11], **6** [12], 7 [13], **8** [14], **9** [15] and **10**. Furthermore, the flavone artemitin [16], *ent*-kaurenic acid, the kaurane derivatives **16** and **17** [17], the rosane derivative **18** and the substituted umbelliferones **12–15** were isolated

The structure of **10** could be deduced easily from the characteristic ^{1}H NMR spectrum (Experimental) which, as expected, was similar to that of **8** [14] Due to the presence of a free 3α-hydroxy group the H-3 signal was shifted upfield while the couplings indicated an unchanged configuration at C-3

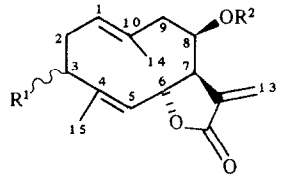
The ^{1}H NMR spectrum of **16** (Experimental) was similar to that of **17** [17] However, due to the changed configuration at C-16 some signals showed small shift differences, especially those of H-17 while those of H-18–H-20 had identical chemical shifts with those of **17**. The fragmentation pattern of the mass spectrum also supported the structure.

The molecular formula of the diacetate **18**Ac was $C_{24}H_{38}O_4$ and the ^{1}H NMR spectrum (Table 1) showed that a diterpene with four tertiary methyls and a diacetoxyethyl side chain was present. Accordingly, a pimarane or a rosane derivative with a double bond had to be proposed. As no olefinic proton signal was visible a ditertiary double bond was present. This was established by the ^{13}C NMR data (Table 1). Comparison of the chemical shifts with those of related compounds [18, 19] indicated that a rosane with a 5(10)-double bond was present. The observed NOEs allowed the assignment of the ^{1}H NMR methyl singlets as irradiation of that at δ1.01 showed effects with H-15 and H-16 (5% each) while those at δ0.97 and 0.95 gave effects with two, and that at δ0.82 with one, allylic proton The configuration at C-13 followed from the chemical shift of C-17 and from comparison of the ^{1}H NMR shifts of H-12–H-17 with those of rosanes and pimaranes with identical stereochemistry. Finally, the position of the double bond was established by selective INEPT Effects were observed between C-20, C-9 and C-10, between C-17 and C-13 as well as between C-18 and C-19 with C-4 and C-5. The absolute configuration is not established but the proposed one is very likely as *ent*-rosanes were isolated in the subtribe.

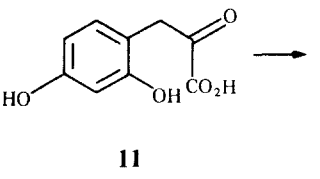
The ^{1}H NMR spectra of **12–15** (Table 2) indicated the presence of aromatic compounds which differed in the substitution pattern. While compounds **12–14** were obviously substituted with a prenyl unit, in the case of **15** a changed C-5 side chain was present Spin decoupling and the molecular formula as well as the base peak (*m/z* 178, $C_9H_6O_4$) showed that a hydroxy-dihydroprenyl group was very likely Due to the chiral centre at C-3′ a complex set of signals for H-1′ and H-2′ was observed (A, A′, X, Y-system). The $C_9H_6O_4$-fragment indicated that a dihydroxycoumarin derivative may be present, one hydroxy obviously being at C-7 and the second at C-3 or C-4. In the case of **14** the latter was methylated (3 87 *s*). The



	1	2	3	4
R¹	H	OH	OA*	OB*
R²	H	Ac	H	H
R³	H	OH	H	H



	5	6	7	8	9	10
R¹	αOAc	αOAc	βOAc	αOAc	βOAc	αOH
R²	A	C*	C	H	H	H



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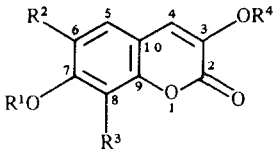
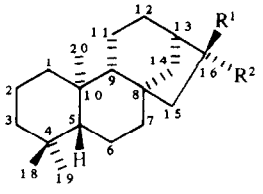
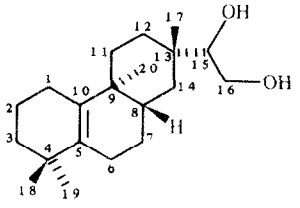


	12	13	14	15
R¹	H	H	H	D*
R²	H	H	E	H
R³	F*	E	H	H
R⁴	H	Me	Me	H



	16	17
R¹	OH	CH_2OH
R²	CH_2OH (17)	OH



18

17Ac is the 17-monoacetate, 18Ac the diacetate

* A = Tigl-5-OH, B = Tigl, C = Tigl-4,5-diOH
D = $CH_2CH_2CH(Me)CH_2OH$ (1′ 2′ 3′ 4′ 5′), E = $CH_2CH{=}CMe_2$

Table 1 NMR spectral data of compound **18**Ac (400 and 100.6 MHz respectively, $CDCl_3$, δ-values)

H		C		C	
1	2.03 *m*	1	25.8 *t*	12	31.0 *t*
6	1.88 *m*	2	19.8 *t*	13	37.1 *s*
15	4.92 *dd*	3	39.7 *t*	14	31.0 *t*
16	4.42 *dd*	4	33.9 *s*	15	79.3 *d*
16′	4.04 *dd*	5	133.4 *s*	16	63.2 *t*
17	1.01 *s*	6	25.1 *t*	17	19.3 *q*
18	0.97 *s*	7	29.3 *t*	18	28.9 *q*
19	0.95 *s*	8	37.2 *d*	19	27.8 *q*
20	0.82 *s*	9	36.6 *s*	20	16.9 *q*
OAc	2.09 *s*	10	136.0 *s*	OAc	21.0, 20.3 *q*
	2.03 *s*	11	25.2 *t*		171.0, 170.8 *s*

J [Hz] 15,16 = 2.5, 15,16′ = 9, 16,16′ = 12

Table 2 ^{1}H NMR spectral data of compounds **12**–**15** ($CDCl_3$, 400 MHz, δ-values)

H	12	13	14	15*
4	7.01 *s*	6.80 *s*	6.79 *s*	7.02 *s*
5	7.16 *d*	7.16 *d*	7.12 *s*	7.30 *d*
6	6.80 *d*	6.78 *d*		6.87 *dd*
8			6.82 *s*	6.86 *br s*
1′	3.62 *br d*	3.62 *br d*	3.37 *br d*	3.57 *d*
2′	5.26 *br t*	5.26 *br t*	5.31 *br t*	1.98 *ddt*; 1.69 *ddt*
4′	1.86 *br s*	1.85 *br s*	1.79 *br s*	1.02 *d*
5′	1.76 *br s*	1.76 *br s*	1.76 *br s*	4.12; 4.06 A, A′, X, Y
OH	5.93 *s*	5.70 *s*		5.97 *s*
	5.63 *s*			
OMe		3.88 *s*	3.87 *s*	

* H-3′ 1.93 *ttq*

J [Hz] 5,6 = 8, 1′,2′ = 7, compound **15** 6,8 = 2, 1′,2′ = 2′, 3′–3′, 4′ = 3′ 5′ ~ 6.5 $3'_1$, $3'_2$ = 13

position of the aromatic protons could be assigned by the observed NOEs Thus irradiation of the singlet at δ7.12 (H-5) showed effects with H-1′ (3%), H-2′ (3%) and the protons which showed a singlet at δ6.79 (H-4) (5%). Similar saturation of the latter signal gave a NOE with H-5 (7%) but also with the methoxy group (6%). Accordingly, a 3-methoxy-6-prenylcoumarin was present. This was supported by the ^{13}C NMR spectrum (Experimental) which excluded a 4-hydroxy coumarin by the observed chemical shifts

The ^{1}H NMR signals of **12** required an 8-prenyl-3-hydroxyumbelliferone and those of **13** the presence of the corresponding 3-*O*-methyl ether. Surprisingly, 3-hydroxycoumarins seem to be unknown as natural compounds Most likely they are formed from phenylpyruvates such as **11**, which are the intermediates in the formation of the corresponding amino acids.

The new results on the chemistry of *Bahia* supports its placement in the subtribe Chaenactidinae as similar germacranolides and heliangolides with oxygenated 8β-tigloyl residues are reported from typical genera of this subtribe (*Chaenactis* [20, 21], *Florestina* [22], *Schkuhria* and *Peucephyllum*) Closely related lactones are present in *Hymenothrix* [19] However, these lactones are absent in *Arnica* and *Palafoxia*. The co-occurrence of rosane derivatives in *Bahia*, *Hymenothrix* [19] and *Palafoxia* [23, 24] support the placement of these genera in one subtribe while the chemistry of *Arnica* differs from that of all the other genera of this group. Further common constituents of the genera of the subtribe Chaenactidinae are the thiarubins from the roots [25]. Again these compounds are not reported from *Arnica* where pseudoguaianolides and xanthanolides are characteristic [26] which so far have not been isolated from any other genus of the subtribe.

EXPERIMENTAL

The air-dried plant material (100 g) collected in December 1988 in Northern Chile (voucher AH 13, deposited in the Herbarium of the University of Chile) was extracted at room temp. with MeOH–Et_2O–petrol (1 1 1) The defatted extract (MeOH) gave by crystallization 20 mg artemitin and by CC (silica gel) five fractions (1 Et_2O–petrol, 1 19; 2 Et_2O–petrol, 1 3, 3 Et_2O–petrol, 1 1; 4 Et_2O, 5 Et_2O–MeOH, 9 1) TLC of fraction 1 gave caryophyllene, α-curcumene and α-zingiberene (10 mg each); fraction 2 gave 70 mg nerylacetate and fraction 3 gave 300 mg *ent*-kaurenic acid HPLC of fraction 4 (MeOH–H_2O, 4 1, always RP 8, flow rate 3 ml/min) afforded 5 mg **9** (R_t 1.0 min), 5 mg **8** (R_t 1 3 min), 2 mg **12** (R_t 1 9 min), 4 mg **13** (R_t 2 3 min), 2 mg **4** (R_t 3 0 min), 3 mg **14** (R_t 3 5 min), 20 mg **16** (R_t 30 0 min) and a mixture (4/8) (R_t 26 8 min). Fraction 4/8 showed no acetoxy methyl singlet in the ^{1}H NMR Acetylation (Ac_2O, 3 hr, 70°) gave after HPLC (MeOH–H_2O, 9·1) 5 mg **17**Ac (R_t 9 3 min) and 5 mg **18**Ac (R_t 13 7 min) HPLC of fraction 5 (MeOH–H_2O, 13.7) gave 10 mg **7** (R_t 1 3 min), 50 mg **6** (R_t 1 8 min) and three mixtures (5/3 R_t 1 1 min, 5/4 R_t 2 2 min, 5/5 R_t 3.2 min) TLC of 5/3 (MeOH–Et_2O–C_6H_6–$CHCl_3$, 1 30 30·30 = Tl) gave **2** mg **10** (R_f 0 42) and **5** mg **2** (R_f 0 30). TLC of 5/4 (Tl) gave 1 mg **15** (R_f 0 50) and 5 mg **1** (R_f 0.30) TLC of 5/5 (Tl) afforded 10 mg **5** (R_f 0 52) and 10 mg **3** (R_f 0 35). Known compounds were identified by comparison of the 400 MHz ^{1}H NMR spectra with those of authentic material

Desacetyleupaformonin (**10**) Colourless gum, IR $\nu_{max}^{CHCl_3}$ cm^{-1}. 3600 (OH), 1765 (γ-lactone), MS *m/z* (rel int)· 264.136 $[M]^+$ (5) (calc. for $C_{15}H_{20}O_4$· 264 136), 246 $[M-H_2O]^+$ (7), 228 [246 $-H_2O]^+$ (8), 166 $[M-C_6H_{10}O]^+$ (100); ^{1}H NMR ($CDCl_3$) δ5.99 (*br t*, H-1), 2.62 and 2.09 (*m*, H-2), 4 66 (*br dd*, H-3), 5 24 (*br d*, H-5), 5 18 (*br d*, H-6), 2 83 (*br s*, H-7), 4 19 (*br t*, H-8), 2 46 and 2 33 (*br dd*, H-9), 6.41 and 5 69 (*d*, H-13), 1 93 (*br s*, H-14), 1 78 (*br s*, H-15), *J* [Hz] 1,2 = 1,2′ ~ 8, 2,3 = 5, 2′,3 = 11, 5,6 = 10, 7,13 = 2.5, 7,13′ = 2, 8,9 = 8,9′ ~ 3; 9,9′ = 14

3,7-*Dihydroxy*-8-[3,3-*dimethylallyl*]-*coumarin* (**12**). Colourless gum, IR $\nu_{max}^{CCl_4}$ cm^{-1}· 3320 (OH), 1710 (C=O); MS *m/z* (rel int.) 246 089 $[M]^+$ (92) (calc for $C_{14}H_{14}O_4$: 246 089), 191 $[M-C_4H_7]^+$ (100), 190 $[M-C_4H_8]^+$ (78), 162 (18), 135 (16), 97 (48)

7-*Hydroxy*-3-*methoxy*-8-[3,3-*dimethylallyl*]-*coumarin* (**13**). Colourless gum, IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3440 (OH), 1720 (CO), MS *m/z* (rel. int) 260 105 $[M]^+$ (100) (calc for $C_{15}H_{16}O_4$: 260.105), 205 $[M-C_4H_7]^+$ (65), 204 $[M-C_4H_8]^+$ (83), 176 (12), 161 (30)

7-*Hydroxy*-3-*methoxy*-6-[3,3-*dimethylallyl*]-*coumarin* (**14**). Colourless crystals, mp 167°, IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3600 (OH), 1720, 1710 (C=O); MS *m/z* (rel int). 260 105 $[M]^+$ (62) (calc for $C_{15}H_{16}O_4$: 260 105), 205 $[M-C_4H_7]^+$ (100), 119 (58), 69 (76), ^{13}C NMR ($CDCl_3$, C-2–C-10). δ 158 3 *s*, 142 4 *s*, 126.7 *d*, 113 5 *d*, 125.1 *s*, 149.1 *s*, 103 0 *d*, 155 1 *s*, 112.5 *s*, C-1′–C-5′ 28 8 *t*, 121 0 *d*, 135 2 *s*, 25 7 *q*, 17 8 *q*

3-*Hydroxy*-7-[4-*hydroxy*-*isopentyloxy*]*coumarin* (**15**). Colourless gum, IR $\nu_{max}^{CCl_4}$ cm^{-1} 3520 (OH), 1725 (C=O); MS *m/z* (rel int.). 264 100 $[M]^+$ (7) (calc. for $C_{14}H_{16}O_5$: 264.100), 178 $[M-C_5H_{10}O]^+$ (100), 69 (33).

ent-*Kaurane*-16,17-*diol* (**16**). Colourless crystals, mp 168°; IR $\nu_{max}^{CHCl_3}$ cm^{-1} 3440 (OH), MS *m/z* (rel. int.): 275.237 $[M-CH_2OH]^+$ (100), 257 $[275-H_2O]^+$ (29), 137 (28), 123 (31), 69 (37); ^{1}H NMR ($CDCl_3$): δ 2 07 (*br q*, H-13), 2 00 and 1 00 (*dd*, H-14), 3 47 and 3 39 (*d*, H-17), 1.02, 0 84, 0 80 (*s*, H-18–H-20), *J* [Hz]: 12, 13 = 12′, 13 = 13, 14′ ~ 3, 14, 14′ = 12, 14, 15 = 2, $[\alpha]_D^{24°}$ −51 ($CHCl_3$, *c* 0 16)

ent-*Ros*-5(10)-*ene*-15,16-*diol* (**18**). Isolated as its diacetate, colourless gum, IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3600 (OH), 1750 (OAc), MS *m/z* (rel int) 390 277 $[M-H_2O]^+$ (55) (calc. for $C_{24}H_{38}O_4$ 390 277), 375 $[390-Me]^+$ (32), 315 $[375-HOAc]^+$ (28), 255 $[315-HOAc]^+$ (100), $[\alpha]_D^{24°}$ + 53 ($CHCl_3$; *c* 0.32)

Acknowledgement—We thank the Volkswagen-Stiftung for financial support and Mrs C Fernandez, Mrs A. Hoffmann and Mr M Quezada for help in the collection and identification of the plant material

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