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ABSINTHIFOLIDE, A SESQUITERPENE GLYCOSIDE FROM *BAHIA ABSINTHIFOLIA* VAR. *ABSINTHIFOLIA**

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Key Word Index—*Bahia absinthifolia* var. *absinthifolia*; Bahiinae; Heliantheae; Compositae; flavone; heliangolide; glucoside.

Abstract—The isolation of eucannabinolide, jaceidin and the new glycoside absinthifolide from *Bahia absinthifolia* var. *absinthifolia* is reported. The structure and stereochemistry of the new compound was established by chemical and spectroscopic means.

INTRODUCTION

The genus *Bahia* [1, 2] of the tribe Heliantheae subtribe Bahiinae is a small american genus (13 species) well represented in Central Mexico. Of the five species which have so far been examined chemically [3–6], three have furnished guaianolides [3–5] and one afforded a heliangolide and the flavonoid jaceidin [6].

RESULTS AND DISCUSSION

Chemical examination of the aerial part of *Bahia absinthifolia* var. *absinthifolia* collected in the Mexican state of San Luis Potosi, showed the presence of the new compound absinthifolide (**1a**) in addition to jaceidin [6] and eucannabinolide [7]. The same species collected in the state of Guanajuato afforded the above mentioned compounds except eucannabinolide.

Absinthifolide (**1a**) $C_{23}H_{32}O_9$, yellow gum $[\alpha]_D$ −18.27° possesses an α-methylene-γ-lactone as indicated by the IR band at 1755 cm^{-1} and the UV absorption at λ_{max} 255 nm, ε 12656. It contains free hydroxyl groups (strong band at 3400 cm^{-1}) and an ester function (band at 1735 cm^{-1}). The mass spectrum showed a molecular ion at *m/z* 453 $[M+1]^+$ (CIMS) and subsequent loss of an acetyl sugar moiety to give the parent peak $[M - \text{acetylglucopyranosyl} - 0]^+$ at *m/z* 231. This peak and the $[\text{acetylpyranosyl}]^+$ ion peak at *m/z* 205 indicated that the acetyl group is attached to the glucosyl moiety.

The ^{13}C NMR spectrum of absinthifolide (Table 1) is in complete agreement with a molecular formula of $C_{23}H_{32}O_9$ since it showed 23 C-atom signals. The α-methylene-γ-lactone was confirmed by a singlet at δ171.44 (lactone carbonyl) and two low field signals (singlet at δ140.48 and triplet at δ121.70) arising from the exocyclic methylene group. Two singlets at δ127.49 and 139.5 correspond to tetrasubstituted double bond at C-4. The signals corresponding to the acetylglucose moiety are in good agreement to those reported for other partially acetylated glycosides [8].

The ^1H NMR spectrum supports the above conclusions and helps to assign positions and stereochemistry of the

Table 1. ^{13}C NMR data of compounds **1a** and **1b** (20 MHz, $CDCl_3$, TMS as internal standard)*

	1a	**1b**
C-1	36.89 *t*	37.12 *t*
C-2	18.55 *t*	18.50 *t*
C-3	28.85 *t*	28.41 *t*
C-4	127.49	127.22
C-5	139.52	139.42
C-6	27.64 *t*	27.73 *t*
C-7	41.74 *d*	41.82 *d*
C-8	76.25 *d*	75.98 *d*
C-9	42.55 *t*	42.53 *t*
C-10	34.05	34.04
C-11	140.48	140.53
C-12	171.44	170.42
C-13	121.70 *t*	121.42 *t*
C-14	26.99 *c*	27.06 *c*
C-15	68.64 *t*	68.42 *t*
C-1′	101.04 *d*	99.19 *d*
C-2′	74.09 *d*	71.61 *d*
C-3′	76.57 *d*	73.05 *d*
C-4′	70.39 *d*	68.82 *d*
C-5′	73.66 *d*	72.12 *d*
C-6′	63.63 *t*	62.06 *t*
OAc	170.75	170.17
	20.90 *c*	169.35
		169.12
		20.54 *t*

*The assignment of the signals was based on published data [15]. Unmarked signals are singlets.

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substituents. The low field signals of an exocyclic methylene group (Experimental) appeared as two broad singlets, suggesting a *cis*-fused lactone ring. The position of the ring closure was impossible to ascertain at this stage, since the region of δ4–4.5 was overcrowded as is usual in glycosides, nevertheless it was cleared on acetylation (**1b**) and a lactone closure toward C-8 was shown by a multiplet at δ4.45.

The signals of the C-15 and C-6′ oxymethylenes appeared overlapped at δ4.2 forming a multiplet which was simplified on irradiation at the frequency of H-5′ (δ3.6); conversely, irradiation at δ4.2 collapsed the signal of H-5′ into a doublet (J = 8 Hz).

Catalytic hydrogenation of **1a** reduced the exocyclic double bond, affording **1d** whose ^{1}H NMR spectrum exhibited a doublet at δ1.2 due to the C-11 methyl formed on saturation of the exocyclic methylene. Hydrolysis of **1d** yielded dihydroaglycone **1e** whose ^{1}H NMR spectrum exhibited the C-15 methylene as a singlet at δ4.1 and H-8 as a multiplet at δ4.45.

The ^{13}C NMR spectrum of absinthifolide peracetate (**1b**) (Table 1) permits the identification of the β-glucoside moiety since chemical shifts for every C-atom in this part of the molecule were simiar to those reported for the peracetate of iridoid glucoside eucammioside II [9].

Assignment of the acetyl group of absinthifolide to the C-6′ position was based on comparison with ^{13}C NMR data reported for multiflorin A [8], a flavonoid glycoside containing a C-6′ acetate. The chemical shifts for every C-atom in the C-6′ acetyl glucoside moiety were similar in both compounds.

Acid hydrolysis of absinthifolide (**1a**) eliminated the sugar moiety thus affording compounds **1e** and **2**. Aglycone **1e** which still shows in addition to the C-14 tertiary methyl group (singlet at δ1.1) a singlet at δ4.1 (2H) attributed to C-15 hydroxymethylene whose multiplicity and chemical shift indicated attachment to a vinylic C-atom (C-4 double bond).

Compound **2**, dehydation product of **1c**, exhibited an ^{1}H NMR spectrum identical to that reported for the 3-dehydroalantolactone [10], thus establishing the skeleton of absinthifolide as a eudesmane and its structure as 15-*O*-(6′-acetyl-β-D-glucopyranosyl)-eudesman-4,11(13)-dien-8β,12-olide (**1a**).

The genus *Bahia* and the genera *Schkuhria* and *Picradeniopsis* [1, 11, 12] are members of the subtribe Bahiinae (tribe Heliantheae). The three genera contain sesquiterpene lactones [7, 13, 14]; nevertheless, a closer relationship exists between *Bahia* and *Picradeniopsis* since both genera have in common the guaianolides bahia II and bahifolin as well as the germacranolides woodhousin and eucannabionolide [3–7]. The presence of the glycoside of sesquiterpene lactones was reported in *Picradeniopsis* [7] and not in *Bahia*. Now, the isolation of the glycoside absinthifolide in *B. absinthifolia* var. *absinthifolia* is indicating a closer relationship between both genera.

EXPERIMENTAL

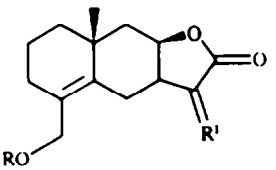
Mps are uncorr. Voucher specimens were deposited in the herbarium of the Instituto de Biologia, UNAM. Known compounds were identified by direct comparison with authentic samples.

Plant material. Above ground parts of *Bahia absinthifolia* Benth. var. *absinthifolia* were collected on October, 1983, at San Luis Potosi, Mexico, 5 km north of Matehuala, Hwy No. 57 (voucher MEXU 369281) and 5 km north of San Miguel Allende, Guanajuato, Hwy No. 49 (voucher MEXU 369278).

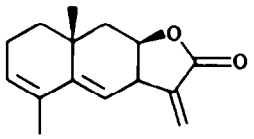
Extraction and separation. Air-dried aerial parts of *B. absinthifolia* var. *absinthifolia* (501.6 g) (collection from San Luis Potosi, Mexico) were extracted with CH_2Cl_2 and Me_2CO. The crude extract (41.4 g) was percolated over Kieselgel G and eluted with hexane, EtOAc and Me_2CO. The EtOAc–Me_2CO fractions were chromatographed over a silica gel column using a hexane–Me_2CO gradient elution system. The hexane–Me_2CO (1:1) fractions afforded 189.7 mg of jaceidin, 1.117 g of eucannabinolide and a yellow oil. The latter was percolated over Kieselgel G with hexane–Me_2CO (6:4) yielding 532.3 mg of **1a** as yellow gum. $[\alpha]_D$ = −18.27° (*c* 0.208, $CHCl_3$). UV λ_{max}^{MeOH} nm: 205, ε = 12656. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3400, 1755, 1735, 1650. CIMS (CH_4) 200 eV, *m/z* (rel. int.): 453 [M + 1, $C_{23}H_{32}O_9$]$^+$ (1.2), 233 [M + 1 − $C_9H_{12}O_7$]$^+$ (60.1), 231 [M + 1 − $C_9H_{14}O_7$]$^+$ (100), 205 [$C_9H_{13}O_6$]$^+$ (43.9), 187 [205 − H_2O]$^+$ (24.0), 145 [205 − HOAc]$^+$ (17.0), 127 [145 − H_2O]$^+$ (22.0). ^{1}H NMR (80 MHz, $CDCl_3$): δ1.13 (3H, *s*, H-14), 2.1 (3H, *s*, Ac), 2.6–3.6 (4H, overlapping signals, H-2′, H-3′, H-4′ and H-5′), 4–4.5 (4H, overlapping signals, H-8, H-15, H-1′ and H-6′), 5.65 (1H, *br s*, H-13b), 6.2 (1H, *br s*, H-13a).

Collection from Guanajuato. Aerial part of *B. absinthifolia* (1.6 kg) collected in Guanajuato was worked up as above, affording 298.6 mg of jaceidin and 789.3 mg of **1a**.

Dihydroabsinthifolide (**1d**). A soln containing 137.8 mg absinthifolide (**1a**) in 10 ml EtOAc was hydrogenated in the



1a R = A, R′ = CH_2
1b R = B, R′ = CH_2
1c R = H, R′ = CH_2
1d R = A, R′ = H, Me
1e R = H, R′ = H, Me



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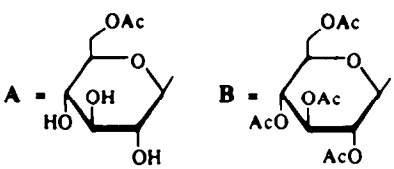

presence of 26 mg 5% Pd/C for 2.45 hr at room temp. The catalyst was filtered and the soln concd giving 128.3 mg of **1d** as a colourless oil. IR $\nu_{max}^{CHCl_3}$ cm $^{-1}$: 3596, 3450, 1764, 1740, 1601. CIMS (CH_4) 200 eV, *m/z* (rel. int.): 455 $[M+1]^+$ (0.5), 234 $[M+1-C_8H_{13}O_7]^+$ (19.5), 233 $[M+1-C_8H_{14}O_7]^+$ (100), 205 $[C_8H_{13}O_6]^+$ (25.5), 187 $[205-H_2O]^+$ (29.7), 145 [205 − HOAc]$^+$ (4.5), 127 $[145-H_2O]^+$ (4.5). ^{1}H NMR (80 MHz, $CDCl_3$): δ1.15 (3H, *s*, H-14), 1.2 (3H, *d*, J = 7.0 Hz, H-13), 2.1 (3H, *s*, Ac), 3.4 (4H, *m*, H-2', H-3', H-4' and H-5'), 4.25 (4H, *m*, H-15 and H-6'), 4.4 (2H, *m*, H-8 and H-1').

Acid hydrolysis of **1d**. Compound **1d** (125.4 mg) was dissolved in 5 ml 7% H_2SO_4 with heating and then refluxed for 0.5 hr. The reaction mixture was cooled and extracted with EtOAc, washed with aq. $NaHCO_3$ soln and dried with dry Na_2SO_4. The crude product was purified by percolation over Kieselgel G eluting with hexane–Me_2CO (95:5) yielding 8.6 mg of **1e** as colourless oil. IR $\nu_{max}^{CHCl_3}$ cm $^{-1}$: 3612, 1766. EIMS 70 eV, *m/z* (rel. int.): 250 $[M]^+$ (16.0), 232 $[M-H_2O]^+$ (83), 55 $[C_3H_3O]^+$ (100). ^{1}H NMR (80 MHz, $CDCl_3$): δ1.15 (3H, *s*, H-14), 1.2 (3H, *d*, J = 7 Hz, H-13), 4.1 (2H, *s*, H-15), 4.45 (1H, *m*, H-8).

Acetylation of **1a**. Compound **1a** (106.7 mg) was acetylated with 1 ml of pyridine and 1 ml of Ac_2O during 50 min on a steam bath. The mixture was worked up in the usual manner and purified by percolation over Kieselgel G eluting with hexane–Me_2CO (9:1) yielding 85 mg **1b** as a colourless oil. IR $\nu_{max}^{CHCl_3}$ cm $^{-1}$: 1758, 1665. EIMS 70 eV, *m/z* (rel. int.): 578 $[M]^+$ (0.2), 458 $[M-2HOAc]^+$ (0.1), 398 $[M-3HOAc]^+$ (0.15), 331 $[C_{14}H_{19}O_9]^+$ (40.7), 271 $[C_{12}H_{15}O_7]^+$ (15.0), 230 $[C_{15}H_{18}O_2]^+$ (53.4), 169 $[C_8H_9O_4]^+$ (93.7), 109 $[C_6H_5O_2]^+$ (39.0), 43 $[C_2H_3O]^+$ (100). ^{1}H NMR (80 MHz, $CDCl_3$): δ1.15 (3H, *s*, H-14), 1.98 (3H, *s*, Ac), 2.05 (6H, *s*, Ac), 2.07 (3H, *s*, Ac), 3.0 (1H, *m*, H-7), 3.6 (1H, *m*, H-5'), 4.2 (4H, *m*, H-15 and H-6'), 4.42 (1H, *d*, J = 7.5 Hz, H-1'), 4.45 (1H, *m*, H-8), 5.0 (3H, *m*, H-2', H-3' and H-4'), 5.62 (1H, *d*, J = 1.5 Hz, H-13b), 6.22 (1H, *d*, J = 2.0 Hz, H-13a).

Acid hydrolysis of **1a**. Compound **1a** (150 mg) was dissolved in 7 ml 7% H_2SO_4 and refluxed for 10 min. The mixture was extracted with EtOAc, washed with $NaHCO_3$, dried, evaporated and purified by preparative TLC (CH_2Cl_2–Me_2CO, 8:2) yielding 9.1 mg **1c** and 20.8 mg **2** both as colourless oils.

Compound **1c**. IR $\nu_{max}^{CHCl_3}$ cm $^{-1}$: 3609, 3497, 1759, 1714, 1666. EIMS 70 eV, *m/z* (rel. int.): 248 $[M]^+$ (5.2), 230 $[M-H_2O]^+$ (28.0), 55 $[C_3H_3O]^+$ (71.4), 43 $[C_2H_3O]^+$ (88.7), 41 $[C_3H_5]^+$ (100). ^{1}H NMR (80 MHz, $CDCl_3$): δ1.12 (3H, *s*, H-14), 4.1 (2H, *s*, H-15), 4.5 (1H, *m*, H-8), 5.6 (1H, *d*, J = 2.0 Hz, H-13b), 6.2 (1H, *d*, J = 2.0 Hz, H-13a).

Compound **2**. UV λ_{max}^{MeOH} nm: 205 ε = 7072, 227, ε = 7245. IR $\nu_{max}^{CHCl_3}$ cm $^{-1}$: 1757, 1662. EIMS 70 eV, *m/z* (rel. int.): 230 $[M]^+$ (67.0), 121 $[C_7H_9O_2]^+$ (100), 119 $[C_9H_{11}]^+$ (50.5), 91 $[C_7H_7]^+$ (58.8). ^{1}H NMR (80 MHz, $CDCl_3$): δ1.05 (3H, *s*, H-14), 1.75 (3H, *br s*, H-15), 3.72 (1H, *m*, H-7), 4.85 (1H, *ddd*, J = 3, 4, 7.5 Hz, H-8), 5.32 (1H, *d*, J = 4.0 Hz, H-6), 5.6 (1H, *m*, H-3), 5.66 (1H, *d*, J = 1.5 Hz, H-13b), 6.22 (1H, *d*, J = 2.0 Hz, H-13a).

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