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GLAUCOLIDES, HIRSUTINOLIDES AND OTHER SESQUITERPENE LACTONES FROM *VERNONANTHURA PINGUIS*

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Key Word Index—*Vernonanthura pinguis*; Vernoniinae; Vernonieae; Compositae; glaucolides; hirsutinolides; sesquiterpene lactones.

Abstract—Aerial parts of *Vernonanthura pinguis* contained nine known and five new glaucolides, two known and five new hirsutinolides, two new 1-deoxyhirsutinolides, one vernomargolide analogue and one eudesmanolide. The possibility that the hirsutinolides are artifacts of the isolation procedure is discussed. Copyright © 1997 Elsevier Science Ltd

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INTRODUCTION

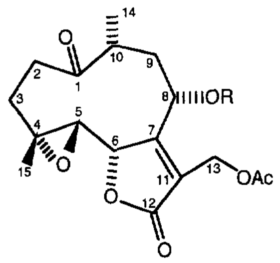
In continuation of our study of Vernoniinae of northern Argentina and adjacent regions [1–8] we have examined *Vernonanthura pinguis* (Griseb.) H. Robinson (syn. *Vernonia pinguis* Griseb. [9]) which is found in the selvas of southern Bolivia and extreme northwestern Argentina [10]. The chloroform extract of the aerial parts contained the lactones **1a** [11, 12], **1b** [11, 12], **1c**, **2** (glaucolide A) [13, 14], **3a** [15], **3b**, [6], **3c**, **4a** [16], **4b** [17], **4c** [5], **5a** [12], **5b**, **6a**, **6b**, **7a**, **7b**, **7c** [11, 12], **7d–f**, **8**, **9a** [2], **9b** and **10**, all identical with, or closely related to, lactones previously isolated from South American Vernoniinae. Another sesquiterpene lactone was isolated in a very small amount to which we tentatively ascribe formula **12**.

RESULTS AND DISCUSSION

The new glaucolide-type lactones **1c**, **3c** and **5b**, the latter obtained only in admixture with **7a**, differed from their previously known congeners **1a**, **1b**, **3a**, **3b** and **5a** only in the nature of the ester side chain on C-8, as was evident from the ^1H NMR spectra listed in Table 1. The structures of **6a** and **6b**, the 5*Z*-isomers of type **5** lactones, were deduced from their ^1H NMR spectra; the chemical shifts of H-5 and H-15 compared with those of the 5*Z*-glaucolides **3a–c**, but not with those of the 5*E*-analogues **5a** and **5b**. Furthermore NOE spectrometry, e.g. irradiation of **6b** at the frequency of H-5 which enhanced the signals of H-8 (19.3), H-14 (14.8) and H-15 (15.9), was consonant only with one of the favourable conformations of a 5*Z*-isomer.

The ^1H NMR spectrum of hirsutinolide **7a** (Table 1) differed from that of the previously known **7c** only in the upfield shifts of the H-13a,b signals: the corresponding tiglate **7b** was a contaminant in one of the fractions containing **7c**. Hirsutinolides **7d** and **7e** differed from **7c** only in the ester group attached to C-8, while **7f** lacked the C-8 function, with H-8 exhibiting the appropriate upfield shift from near δ 6.3 to δ 5.15. Hirsutinolide **8** contained an extra acetate which on the basis of the ^1H NMR spectrum had to esterify the usual hydroxyl group at C-1. The corresponding C-8 acetate has been reported from *Lessingianthus saltensis* (Hieron.) H. Robinson [12, 18] (syn. *Vernonia saltensis* [9]). Lactone **9b** was the new senecioate analogue of the previously known **9a** [2]; decoupling was carried out in C_6D_6 at elevated temperature, although some of the signals remained broadened even then.

Two sesquiterpene lactones $C_{17}H_{24}O_7$ and $C_{15}H_{18}O_5$ were isolated in very small amounts. In the ^1H NMR spectrum (Table 1) of the former, to which we assigned structure **10** and which we named vernopinguisolide, the H-13a,b signals were sharp singlets indicating the presence of a substituent at C-7 while the sequence H-8 through H-10, with C-8 carrying a methacrylate in the usual α-orientation and with a secondary methyl group attached to C-10, was established by sequential decoupling in the usual way. The remaining signals, i.e. those of H-2 at low field (δ 3.29) due to deshielding by the adjacent carbonyl group and/or the hydroxyl at C-4, coupled to H-3β at δ 1.95 and H-3α at δ 1.55, and of H-5 at δ 3.07 coupled to H-6 at δ 4.59, compared in shifts and coupling constants with the signals of a substance from *Vernonia marginata* assigned formula **11** [1]. The NOE data presented in Table 2 confirmed that H-2, H-6, H-8 and H-8 were *cis* while the absence of an NOE between H-2 and H-5 indicated that H-15 was α-oriented.



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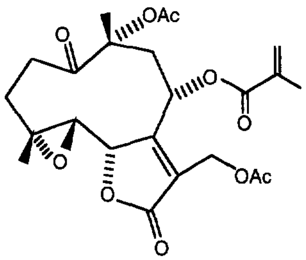

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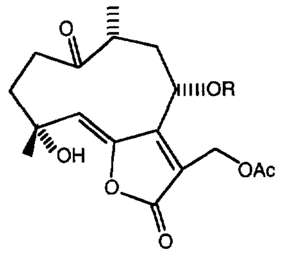

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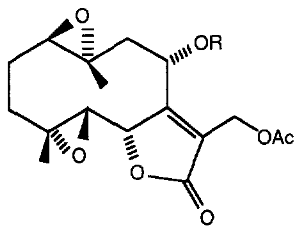

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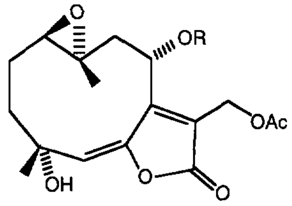

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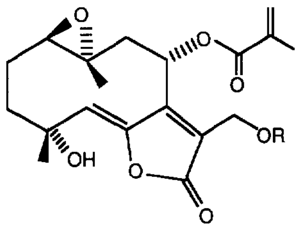

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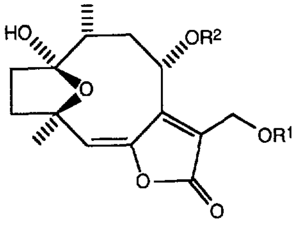
b R = Ac



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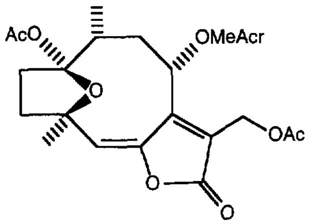
b R' = H, R2 = Tig

c R' = Ac, R2 = MeAcr

d R' = Ac, R2 = Tig

e R' = Ac, R2 = Sen

f R' = Ac, R2 = H



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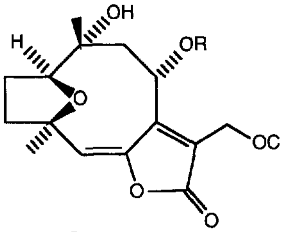
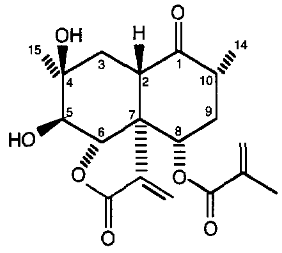


9 a R = MeAcr

b R = Sen



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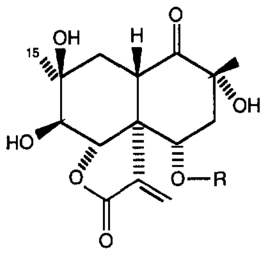

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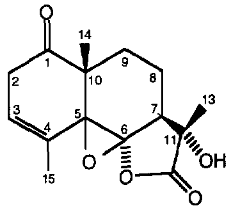

12

Table 1. ^{1}H NMR spectra of compounds **1c**, **3c**, **5b**, **6a** **6b**, **7a**–**f**, **8**, **9b** and **10** ($CDCl_3$, 500 MHz)

H	**1c***	**3c**	**3c** (C_6D_6, 76°)	**5b**†	**6a**	**6b**	**7a**	**7d**	**7e**	**7f**	**8**	**9b** (60°)	**10**
1	—	—	—	3.06 *dd*	2.34 *br d* (12)	2.31 *br d* (12)						4.24 *br d* (7.5)	—
2a	2.5-	2.5 *m*	1.95 *m*	2.15 *ddt* (14, 3.5, 2)			2.1-	2.1-	2.1-	2.1-		2.08-	3.29 *br d* (12.5, 3)
2b	2.7 *c*	2.45 *m*	1.7 *m*	1.55 *m*			1.95 *c*	1.95 *c*	1.95 *c*	1.95 *c*		2.15	
3a	2.30 *m*	2.05 *m*	obsc	2.28 *ddd* (14, 11, 4.5)								2.38 broad	1.95 *dd* (B) (15, 3.5)
3b	1.74 *ddd*	obsc	1.60 *m*	2.05 *m*								obsc.	1.57 *dd* (d) (15, 13)
5	2.57 *d* (9)	5.39 *br s*	5.05 *m*	6.16 *s*	5.26 *s*	5.31 *s*	5.86 *s*	5.87 *s*	5.85 *s*	5.86 *s*	5.88 *s*	6.01 *s*	3.07 *d* (7)
6	4.83–4.93	—	—	—	—	—	—	—	—	—	—	—	4.59 *d* (7)
8		5.47 (broad)	5.53 (broad)	5.91 *br d* (10)	5.75 *br d* (10)	5.77 *br d* (10)	6.33 *br d* (8)	6.26 *br d* (7.5)	6.26 *dd* (7.5)	5.15 *dd* (6, 2)	6.28 *br d* (8)	6.15 (broad)	5.68 *dd* (12, 4)
9a	2.55 *c*	2.52 *m*	2.53 *dd* (12.5, 11)	2.62 *br d* (13.5)	2.65 *br d* (13)	2.63 *dd* (13, 2)	2.33 *dd* (16, 12.5)	2.29 *dd* (15, 12)	2.28 *dd* (16, 12, 2)	2.25 *ddd* (16, 12, 2)	2.31 *dd* (16, 2)	2.46 *dd* (15.5, 9)	2.23 *ddd* (13.5, 6.5, 4)
9b	2.21 *m*	obsc.	1.62 *dt* (12, 2)	1.86 (13.5, 10)	1.96 *m*	1.95 *dd* (13, 10)	1.86 *dd* (16, 8, 1)	1.85 *m*	1.8 *m*	1.83 *ddd* (16, 6, 2)	1.87 *ddd* (16, 8, 20)	2.03 *br d* (15.5)	1.67 *ddd* (14, 13.5, 12)
10	2.92 *ddq* (11, 2.5, 7)	2.9 (broad)	2.15 *ddq* (11, 2, 7)	—	—	—	1.9 *m*	1.9 *m*	1.9 *m*	1.94 *ddq* (12, 2, 7)	1.90 *ddq* (12, 2, 7)	—	2.68 *ddq* (13, 7.5, 6.5)
13a	4.87 *s*	5.02 *br d* (12)	5.21 *br d* (12.5)	5.02 *d* (13)	4.87 *s*	5.01 *d* (12.5)	4.63 *d* (13.5)	5.09 *d* (13)	5.03 *d* (13)	4.90 *d* (13)	5.10 *d* (12.5)	5.08 *br d* (12.5)	6.46 *s*
13b	4.87 *s*	4.99 *br d* (12)	5.18 *br d* (12.5)	4.90 *d* (13)	4.87 *s*	4.88 *d* (12.5)	4.55 *d* (13.5)	5.09 *d* (13)	5.00 *d* (13)	4.87 *d* (13)	5.00 *d* (12.5)	4.96 *d* (12.5)	5.32 *s*
14‡	1.12 *d* (7)	1.07 *d* (7)	0.69 *d* (7)	1.49 *s*	1.49 *s*	1.49 *s*	0.96 *d* (6.5)	0.95 *d* (7)	0.94 *d* (7)	0.98 *d* (7)	0.95 *d* (7)	1.18 *s*	1.09 *d* (6.5)
15‡	1.61 *s*	1.50 *s*	1.30 *s*	1.78 *s*	1.44 *s*	1.45 *s*	1.47 *s*	1.48 *s*	1.55 *s*	1.50 *s*	1.48 *s*	1.48 *s*	1.29 *s*
Ac‡	2.07 *s*	2.06 *s*	2.07 *s*	2.05 *s*	—	2.04 *s*	—	—	2.07 *s*	2.08 *s*	2.07 *s* 2.07 *s*	2.06 *s*	—
2′	5.62 *br s*	5.69 *br s*	5.85 *br t* (1.5)	5.71 *br s*	—	—	—	—	5.66 *br s*		—	5.68 *br s*	—
3′a	—	—	—	—	6.24 *br s*	6.18 *br s*	6.30 *br s*	7.00 *qq* (7, 1)	—			—	6.04 *br s*
3′b	—	—	—	—	5.75 *br s*	5.73 *br s*	5.64 *br s*	—	—			—	5.62 *br s*
4′‡	2.14 *br s*	2.17 *br s*	1.80 *br s*	2.07 *br s*	1.98 *br s*	1.99 *br s*	1.96 *br s*	1.78 *br s* (7)	2.15 *br s*			2.16 *br s*	1.90 *br s*
5′‡	1.92 *br s*	1.94 *br s*	1.62 *br s*	1.96 *br s*				1.82	1.88 *br s*			1.92 *br s*	

*At 250 MHz.

†From mixture of **5b** and **7a**.

‡Intensity three protons.

Table 2. NOE difference spectrum of compound **10**

Irradiated	Observed (% enhancement)
H-2	H-3β (9.5), H-6 (3.5), H-8 (11.6), H-10 (7.8)
H-3β	H-2 (2.1), H-6 (0.9), H-15 (1.1)
H-5	H-6 (3.1), H-15 (2.9)
H-6	H-2 (2.3), H-5 (2.4), H-8 (6.0)
H-8	H-2 (10.2), H-6 (8.8), H-9β (3.8), H-10 (3.8), H-3′ (3.5)
H-10	H-2 (5.5), H-8 (3.2), H-9β (2.4), H-14 (4.3)
H-13a	H-13b (27.3)
H-13b	H-13a (33.7)
H-14	H-10 (5.1)
H-15	H-5 (3.4), H-6 (1.0)

We provisionally formulate the second lactone as **12**. H-2α and H-2β at δ 2.91 and 1.13 were vicinally coupled to H-3 at δ 5.42; the latter was allylically coupled to the protons of a vinylic methyl group while H-7 was coupled vicinally to the protons of a methylene group (H-8a,b) which were in turn coupled to those of a second methylene (H-9a,b). Two methyl singlets at relatively low field, one deshielded by a carbonyl at C-1, the second by a geminal hydroxyl, completed the assignments. Because of the absence of a signal of a proton under a lactone oxygen the fourth oxygen of the empirical formula was sited between C-5 and C-6. Chemical shifts and coupling constants were not compatible with alternative formulas such as a Δ^3-1(10),5,6- or a Δ^3-1,5,6,10-diepoxyguaianolide. Irradiation at the frequency of H-7 produced no enhancement of the H-13 signal; hence the 13-hydroxyl was α-orientated.

It has been suggested [19, 20] that hirsutinulides such as **7a–f** might be artifacts formed from glaucolides of type **1** and **2** on exposure to slightly acidic silica gel during chromatography. To explore this possibility our isolation procedure involved extraction of the crude chloroform extract with benzene followed by extraction with methylene dichloride and then with methanol. The benzene extract which contained most of the organic constituents was divided into three portions. Portion 1 chromatographed on Florisil gave lactones **2**, **5a**, **5b**, **6a**, **6b**, **7a–e**, **8**, **9a**, **9b**, **10** and **12**. Portion 2 chromatographed over silica gel gave lactones **3a–c**, **4c**, **5a**, **6b**, **7b**, **7c** and **9a** and portion 3, submitted directly to HPLC and of necessity considerably smaller, afforded lactones **1a**, **1c** and **4a**. At first glance this supports the notion that the absorbents, silica gel and the slightly less acidic Florisil, were responsible for formation of the hirsutinolides. On the other hand HPLC of the methylene dichloride extract afforded not only lactones **1a**, **1b**, **4b**, **4c**, **5a**, **9a** and **9b**, but also **7c**, which suggests that at least **7c** was originally present in the extract.

EXPERIMENTAL

General. For sepn of mixts, HPLC with a differential refractometer was used. Columns employed were (A) a Beckman Ultrasphere C8 (5 μm, 10 × 250 mm) and (B) a Phenomenex C18 (5 μm, 10 × 250 mm). Retention times were measured from the solvent peak.

Plant material. Aerial parts of *V. pinguis* (Griseb.) H. Robinson were collected at the flowering stage in October 1992 near Rio Piray, Departamento Santa Cruz, Bolivia. A voucher specimen, LIL No. 595772, is on deposit in the Herbarium of the Fundación Miguel Lillo, Tucumán.

Extraction and isolation. Flowers and leaves (1195 g) were extracted with EtOAc (free of HOAc) (2 × 2 l.) at room temp. for 7 days to give 37 g (3.13%) of residue which was suspended in 320 ml of EtOH at 55°, diluted with 240 ml of H_2O and extracted successively with hexane (2 × 200 ml), C_6H_6 (2 × 200 ml), CH_2Cl_2 (2 × 200 ml) and EtOAc (2 × 150 ml). Evapn of the C_6H_6 extract at red. pres. gave 10.48 g of residue which was divided into three portions processed as follows. Portion 1 was subjected to CC over Florisil (see below); the frs obtained were processed by HPLC. Portion 2 was submitted to CC over silica gel (see below); the frs obtained were also processed by HPLC. Portion 3 was stirred with MeOH and the MeOH soln was processed directly by HPLC.

Portion 1 (4 g) on chromatography over Florisil (120 g) using C_6H_6 with increasing amounts of EtOAc (0–100%) gave 41 frs. Frs containing sesquiterpene lactones as indicated by IR absorption at *ca* 1765 cm^{-1} were further purified by HPLC. Frs 15–20 (300 mg) on HPLC (column B, MeOH–H_2O 4:3, 2 ml min^{-1}) (procedure 1) gave **12** (2.8 mg, R_t 10 min), **6b** (1.8 mg, R_t 14 min), a mixture of **5b** and **8** (2.1 mg, R_t 16 min), **7b** (90 mg, R_t 21 min), a lactone mixture (2.8 mg, R_t 28 min), **7d** (4.8 mg, R_t 32 min) and **7c** (25 mg, R_t 35 min). Frs 21–25 (300 mg) on HPLC (procedure 1) gave a lactone mixture (2.5 mp, R_t 23 min) and six additional peaks (mixtures by TLC) each of which was again subjected to HPLC to give a lactone mixture (3.8 mg, R_t 26 min), **5a** (5.8 mg, R_t 29 min), a second lactone mixture (3 mg, R_t 31 min), glaucolide A (**2**, 1.3 mg, R_t 31 min), **9a** (13 mg, R_t 46 min), **7b** (4 mg, R_t 56 min), **7d** (8 mg, R_t 49 min), **9b** (9 mg, R_t 47 min) and **7c** (4 mg, R_t 53 min). A 200 mg portion of frs 26–31 (445 mg) on HPLC (procedure 2) gave **6b** (5.9 mg, R_t 25 min), **7a** (1 mg, R_t 28 min) and 3 mg of a complex lactone mixture. HPLC (procedure 2) of frs 32–35 (324 mg) gave **7e** (1 mg, R_t 22 min), **6a** (6 mg, R_t 20 min), **10** (2.3 mg, R_t 25 min) and 2.6 mg of **3b** containing some **3a** (R_t 30 min).

Portion 2 (3 g) on chromatography over silica gel gave 21 frs. HPLC of frs 6–11 (300 mg, procedure 1) gave 60 mg of a lactone mixture containing mainly **7b** and **7c** (R_t 25 min), **4a** (20 mg, R_t 37 min), **7d** (9.4 mg, R_t 48 min),**7c** (7.4 mg, R_t 54 min) and **4c** (20 mg, R_t 40 min). Frs 12–21 (210 mg) on HPLC (procedure 1) gave **3a** (1 mg, R_t 16 min), **6b** (9 mg, R_t 20 min), **5a** (7.2 mg, R_t 24 min), 7 mg of a mixture of **3a** and **3b** (R_t 26 min), **3c** (7.9 mg, R_t 28 min) and **9a** (15.6 mg, R_t 52 min).

Portion 3 (500 mg) was stirred with cold MeOH. The MeOH solution on HPLC (procedure 1) gave only three pure substances, **4a** (10 mg, R_t 16 min), **1a** (9.9 mg, R_t

18 min) and **1c** (5 mg, R_t 29 min).

Evapn of the CH_2Cl_2 extract at red. pres. followed by HPLC of the residue (400 mg) using procedure 1 gave **5a** (5 mg, R_t 13 min), **7a** (2.4 mg, R_t 12 min) purified further by radial chromatography, **9a** (3.2 mg, R_t 12 min) purified further by radial chromatography, **9a** (3.2 mg, R_t 21 min) also purified by radial chromatography, **4c** (2.5 mg, R_t 25 min) and other peaks which represented mixts by TLC. These were further purified by HPLC (procedure 2) to give **4a** (20 mg, R_t 15 min), **1a** (5 mg, R_t 18 min), **4b** (3 mg, R_t 19 min), **1b** (3 mg, R_t 22 min), **8b** (30 mg, R_t 25 min), **7c** (1 mg, R_t 38 min) and **9b** (1.8 mg, R_t 45 min). Evapn of the EtOAc extract at red. pres. gave 100 mg of residue which on HPLC (procedure 1) gave 4 mg of a mixture containing **9a** as one of the constituents.

(4R*,5S*,6S*,8S*,10R*) - 1 - *Oxo* - 4,5 - *epoxy* - 8 - *senecioyloxy*-13-*acetoxy*-7 (11)-*germacren*-6,12-*olide* (**1c**). Gum; EI-MS *m/z* (rel. int.): 420 [M^+, $C_{22}H_{28}O_8$] (1), 360 (1), 260 (5), 83 (100). IR $\nu_{\max}^{\text{film}}$ cm^{-1} 1765, 1650 (unsatd lactone), 1730, 1230 (Ac), 1710 (ketone). ^{1}NMR spectrum in Table 1.

(4R*,8S*,10R*)-1-*Oxo*-4-*hydroxy*-8-*senecioyloxy*-13-*acetoxy*-5Z,7(11)-*germacradien*-6,12-*olide* (**3c**). Gum; CI(NH_3) MS *m/z* (rel. int.): 438 [100, M + NH_4^+, $C_{22}H_{28}O_8$). ^{1}H NMR spectrum in Table 1.

(1R*,4R*,8S*,10R*)-1(10)-*Epoxy*-8-*methacryloxy*-13-*hydroxy*-5Z, 7(11)-*germacradien*-6,12-*olide* (**6a**). Gum; ^{1}H NMR spectrum in Table 1. ^{13}C NMR spectrum (62.85 MHz, $CDCl_3$) with tentative assignments δ 167.1 (C-12), 16.55 (C-1′), 150.9, 146.6 (C-7, C-11), 135.3 (C-2′), 127.5 (C-3′), 125.6 (C-6), 120.5 (C-5), 72.6 (C-4), 67.3, 65.9 (C-1, C-8), 58.8 (C10), 55.0 (C-13), 45.8 (C-9), 42.5 (C-3), 28.2 (C-14), 23.9 (C-2), 18.0 (C-4′), 16.5 (C-15).

(1R*,4R*,8S*,10R*)-1(10)-*Epoxy*-8-*methacryloxy*-13-*acetoxy*-5Z, 7(11)-*germacradien*-6,12-*olide* (**6b**). Gum; PCI (isobutane) MS *m/z* (rel. int.): 407 (89.1, M + H^+, $C_{21}H_{26}O_8$), 389 (100), 347 (26.9), 210 (50.4). ^{1}H NMR spectrum in Table 1. ^{3}C NMR spectrum (62.85 MHz, ($CDCl_3$) δ 170.2*s* (Ac C=O), 167.1*s* (C-12), 165.9*s* (C-1′), 153.5*s* (C-6), 120.9*d* (C-5), 72.7*s* (C-4), 67.1*d*, 65.8*d* (C-1, C-8), 56.5*s* (C-10), 55.0*t* (C-13), 45.7*t* (C-9), 42.6*t* (C-3), 28.4*q* (C-14), 23.7*t* (C-2), 20.5*q* (Ac · Me), 18.1*q* (C-4′), 16.8*q* (C-15).

(1S*,4R*,8S*,10R*)-1,13-*Dihydroxy*-1,4-*epoxy*-8-*methacryloxy* - 5E, 7(11) - *germacradien* - 6,12 - *olide* (**7a**). Gum: CI(NH_3) MS *m/z* (rel. int.): 364 (100, M + NH_4^+ $-H_2O$), 346 (26.7). ^{1}H NMR spectrum in Table 1. The MS of the mixture with **5b** whose ^{1}H NMR spectrum is also listed in Table 1 had extra peaks at 414 (86.8, M of **5b** + NH_4^+), 396 (21.6).

(1S*,4R*,8S*,10R*) - 1 - *Hydroxy* - 1,4 - *epoxy* - 8 - *senecioyloxy* - 13 - *acetoxy* - 5E, 7(11) - *germacradien* - 6,12-*olide* (**7d**). Gum; CI(NH_3) MS *m/z* (rel. int.) 438 (100, M + NH_4^+, $C_{20}H_{28}O_8$), 420 (63.3), 403 (25.4), 338 (13.5); IR $\nu_{\max}^{\text{film}}$ cm^{-1} 3400, 1765, 1705, 1645; ^{1}H NMR spectrum in Table 1.

(1S*,4R*,8S*,10R*)-1,8-*Dihydroxy*-1,4-*epoxy*-13-*acetoxy* - 5E, 7(11) - *germacradien* - 6,12 - *olide* (**7e**). Gum; PCI (isobutane) MS *m/z* (rel. int.) 339 (100, M + NH_4^+, $C_{17}H_{22}O_7$), 321 (62.9), 279 (40.7), 261 (34.5). ^{1}H NMR spectrum in Table 1.

(1R*,4R*,8S*,10R*)-1,13-*Diacetoxy*-1,4-*epoxy*-8-*methacryloxy* - 5E, 11(13) - *germacradien* - 6,12 - *olide* (**8**). Gum; CI(NH_3) MS *m/z* (rel. int.) 466 (100, M + NH_4^+, $C_{23}H_{28}O_9$), 448 (80.6); IR $\nu_{\max}^{\text{film}}$ cm^{-1} 3400, 1775, 1700, 1640; H NMR spectrum in Table 1.

(1S*,4R*,8S*,10R*)-1,4-*Epoxy*-8-*senecioyloxy*-10-*hydroxy* - 13 - *acetoxy* - 5Z, 7(11) - *germacradien* - 6,12 - *olide*(**9b**). Gum; PCI (isobutane) MS *m/z* (rel. int.): 421 (76, M + H^+, $C_{22}H_{28}O_8$), 321 (100), 303 (30.8); IR $\nu_{\max}^{\text{film}}$: 1760, 1715, 1640; ^{1}H NMR spectrum in Table 1.

Vernopinguisolide (**10**). Gum; PCI (isobutane) MS *m/z* (rel. int.): 365 (100, M + H^+, $C_{19}H_{24}O_7$)), 347 (72.1); CI(NH_3) MS *m/z* (rel. int.): 382 (100, M + NH_4^+), ^{1}H NMR in Table 1, NOEs in Table 2.

5,6 - *Epoxy* - 11 - *hydroxy* - 1 - *oxoeudesm* - 3 - *en* - 6,12 - *olide* (**12**). Gum; PCI (isobutane) MS *m/z* (rel. int.): 279 (100, M + H^+, $C_{15}H_{18}O_5$ 261 (11.9), 181 (27.4); CI(NH_3) MS *m/z* (rel. int.): 296 (100, M + NH_4^+), 278 (9.1). ^{1}H NMR (500 MHz, $CDCl_3$): δ 5.41 (*ddq*, J = 12.5, 3, 1.5 Hz, H-3), 3.59 (*br*-OH), 2.91 *brdd*, J = 13, 2 Hz, H-2a), 2.29 (*dd*, J = 11, 2 Hz, H-7), 2.17 (*dddd*, J = 14, 2.5, 2.5, 2 Hz, H-8 eq), 2.10 (*ddd*, J = 14.5, 2.5, 2 Hz, H-9 eq), 2.06 (*brs*, 3p, H-15), 1.90 (*ddd*, J = 14.5, 14, 2.5 Hz, H-9ax), 1.51 (*s*, 6H, H-13, H-14), 1.38 (*dddd*, J = 14, 11, 2.5, 2.5 Hz, H-8ax), 1.13 (*dd*, J = 13, 12.5 Hz, H-2b); ^{1}H NMR (C_6D_6): δ 4.48 (*ddq*, J = 12.5, 3, 1 Hz, H-3), 2.61 (*s*, -OH), 2.4 (*dd*, J = 13, 2 Hz, H-2a), 1.90 (*dd*, J = 11, 2 Hz, H-7), 1.83 (*brs*, 3 H, H-15), 1.76 (*brdd*, J = 14.5, 14 Hz, H-9ax), 1.52 (*dddd*, J = 14, 2.5, 7.5, 2 Hz, H-8eq), 1.42 (*ddd*, J = 14.5, 2.5, 2 Hz, H-9eq), 0.83 (*s*, 3H, H-13), 0.77 (*m*, H-8ax), 0.77 (*s*, 3H, H-14), 0.66 (*dd*, J = 13, 12.5 Hz, H-2b).

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REFERENCES

1. Catalán, C. A. N., Iglesias, D. I. A., Kavka, J., Sosa, V. E. and Herz, W. (1986) *J. Nat. Prod.* **49**, 351.
2. Catalán, C. A. N., Iglesias, D. I. A., Kavka, J., Sosa, V. E. and Herz, W. (1988) *Phytochemistry* **27**, 197.
3. Bardón, A., Catalán, C. A. N., Gutiérrez, A. B. and Herz, W. (1988) *Phytochemistry* **27**, 1691.
4. Bardón, A., Catalán, C. A. N., Gutiérrez, A. B. and Herz, W. (1988) *Phytochemistry* **27**, 2989.
5. Bardón, A., Catalán, C. A. N., Gutiérrez, A. B. and Herz, W. (1990) *Phytochemistry* **29**, 313.
6. Bardón, A., Kamiya, N. I., de Ponce de Leon, C., Catalán, C. A. N., Díaz, J. G. and Herz, W. (1992) *Phytochemistry* **31**, 609.
7. Bardón, A., Montanaro, S., Catalán, C. A. N., Díaz, J. G. and Herz, W. (1993) *Phytochemistry* **34**, 253.
8. Borkosky, P. S., Valdés, D. A., Bardón, A., Díaz,

J. G. and Herz, W. (1996) *Phytochemistry* **42**, 1637.

9. Robinson, H. (1992) *Phytologia* **73**, 65.
10. Cabrera, A. L. (1978) *Flora de la Provincia de Jujuy, Collección Cientifica del INTA*, Vol. 13, 42, Buenos Aires.
11. Bohlmann, F., Zdero, C., King, R. M. and Robinson, H. (1982) *Phytochemistry* **21**, 1045.
12. Schmeda-Hirschmann, G., Schuster, A., Zdero, C., Bohlmann, F., King, R. M., Robinson, H. and Pickardt, J. (1986) *Phytochemistry* **25**, 145.
13. Padolina, W. G., Yoshioka, H., Nakatani, H., Mabry, T. J., Monti, S. A., Davis, R. E., Cox, P. J., Sim, G. A., Watson, W. H. and Wu, I. B. (1974) *Tetrahedron* **30**, 1161.
14. Cox, P. J. and Sim, G. A. (1975) *J. Chem. Soc., Perkin Trans II* 455.
15. Jakupovic, J., Banerjee, S., Castro, V., Bohlmann, F., Schuster, A., Msonthi, J. D. and Keelye, S. (1986) *Phytochemistry* **25**, 1359.
16. Bohlmann, F. and Zdero, C. (1982) *Phytochemistry* **21**, 2263.
17. Jakapovic, J., Gage, D. A., Bohlmann, F. and Mabry, T. J. (1986) *Phytochemistry* **25**, 1179.
18. Bohlmann, F., Mahanta, K. and Dutta, L. N. (1979) *Phytochemistry* **18**, 279.
19. Martinez, K. M., Sanchez, F., Lopez, B. G. and Joseph-Nathan, P. (1986) *Z. Naturf. C, Biosc.* **41**, 1119.
20. Martinez-Vazquez, M., Sepulveda, S., Belmont, M. A., Rubio, M. and Joseph-Nathan, P. (1992) *J. Nat. Prod.* **55**, 884.