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GLAUCOLIDES AND RELATED SESQUITERPENE LACTONES FROM *VERNONIA CHAMAEDRYS*

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Key Word Index—*Vernonia chamaedrys*; Vernonieae; Compositae; glaucolides; piptocarphins; sesquiterpene lactones.

Abstract—Chemical investigation of the aerial parts of *Vernonia chamaedrys* resulted in the isolation of 15 glaucolides and related sesquiterpene lactones, six of them new, as well as a number of common plant constituents. The C-8 stereochemistry of the piptocarphins is corrected.

INTRODUCTION

Glaucolides and related sesquiterpene lactones containing a 7(11)-double bond and an acyl group on C-12 are characteristic constituents of the large genus *Vernonia* and its relatives. In continuation of our work on Argentine *Vernonia* species [1, 2] we hereby report the isolation from *Vernonia chamaedrys* Less. of a number of such lactones or substances derived from them, *viz* **1a, 1b** (glaucolide A) [3, 4]‡, **2a, b, 3, 4a, b, 5, 6a, 7a, 8a, b, 9, 10a,** and **11a**. Other substances identified in the extract were α- and β-amyrin, lupeol, stigmasterol, sitosterol, myristic acid, dotriacontanol, vanillin and the flavone chrysoeriol.

RESULTS AND DISCUSSION

Lactone **1a** (desacetylglaucolide A) is new. Like **1b** and other lactones of this type, its NMR spectrum in deuterated chloroform at room temperature exhibited broad signals due to conformational equilibrium, hence measurements were carried out in benzene at elevated temperature (Table 1). Comparison with the ^{1}H NMR spectrum of glaucolide A and the mass spectrum clearly established the gross structure and the relative stereochemistry as (4*R**, 5*R**, 6*S**, 8*S**, 10*R**)§.

Lactone **2a** was first found in *Stilpnopappus tomentosus* [6] and subsequently in *Critoniopsis bogotana* [7]; the stereochemistry originally assigned to it and to **2b** from *V. patens* has been changed recently [8] from (4*R**, 5*R**, 6*S**, 8*S**, 10*S**) to (4*R**, 5*R**, 6*S**, 8*S**, 10*R**), a conclusion with which we concur. Lactone **3** is the previously unreported methacryl analogue of a tiglate recently isolated from *Vernonia marginata* [8] as shown by the mass and ^{1}H NMR spectrum (Table 1); the NOE data in Table 2 confirm the postulated stereochemistry. Lactones **4a** (vernonataloide) (for X-ray analysis see [10]) and **4b** have been reported previously from *Vernonia natalensis* [11], *patens* [8], *jalcana* [8], and *Critoniopsis bogotana* [8] and lactone **5**, an analogue of marginatin and glaucolide G [12, 13], has been found previously in *V. arkansana* [14].

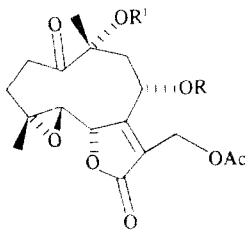
Lactone **6a** is a previously undescribed methacryl analogue of **6b** from *V. compactiflora* [15] and **6c** from *V. patens* [8], as was evident from the mass and NMR spectra (Table 1). As has been pointed out earlier [16, 17] and agreed to in [8], the C-10 stereochemistry of such compounds, including the so-called hirsutinolides of type **12**, is 10*R**, not 10*S** as frequently wirtten in the literature.‖

Lactone **7a** now found in *V. chamaedrys* was isolated earlier from *V. hirsuta* and *angulifolia* [8]. As a result of an X-ray analysis of **7b** [8] its relative stereochemistry and that of related compounds has been revised to (1*S**, 4*R**, 8*S**, 10*R**) as shown in the formula. Using Dreiding models it is difficult to reproduce the conformation of **7b** depicted in Fig. 1 of [8]. From the relatively rigid model, $J_{8,9a}$ and $J_{8,9b}$ should both be very small, whereas in fact one of these coupling constants is quite large in compounds of type **6, 7** and **12**, thus indicating considerable distortion of the nine-membered ring. The large value of $J_{8,9a}$ and the downfield shift of H-8, the latter originally

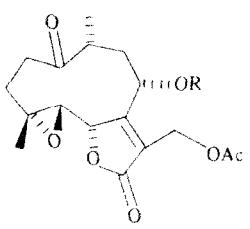
‡In our previous publication [2] the stereochemistry of the C-8 ester side chain of glaucolide A was incorrectly drawn as 8β.

§Because of the confusion engendered by various representations of the formulas of these and similar germacranolide sesquiterpenes in the plane, it is desirable to specify relative stereochemistry as recommended in [5].

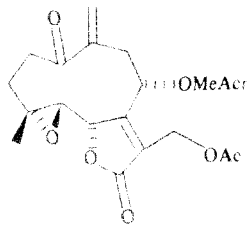
‖However it is difficult to understand the arguments adduced in ref.[8] to make this point in the case of **6c** which are based on NOE difference spectrometry. The conformational flexibility of, *inter al.* compounds of type **6** at room temperature which produces broadening of ^{1}H NMR signals requires that NMR measurements be carried out at elevated temperature. Under these conditions the very rapid interchange of conformations precludes the drawing of inferences about stereochemistry from nuclear Overhauser effects. Moreover, inspection of the NMR data given for compound **6c** (**8a** of ref.[8]) in Table 1, ref.[8], where signals of H-14 and H-15 are labelled as 'interchangeable' and where the signals of H-2α and H-^{2}β are superimposed, raises doubts about the conclusions reached in Table 8 and column 1, p. 148.



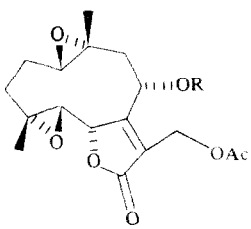
1a R = MeAcr, R^1 = H
1b R = MeAcr, R^1 = Ac
1c R = Ac, R^1 = Ac



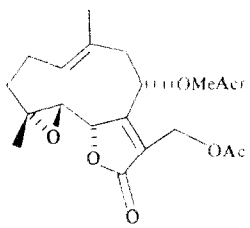
2a R = MeAcr
2b R = Ang



3



4a R = MeAcr
4b R = Ang



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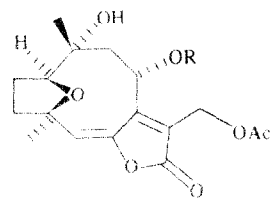
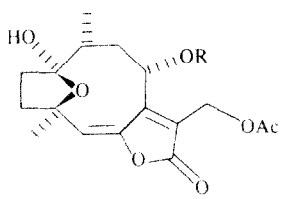
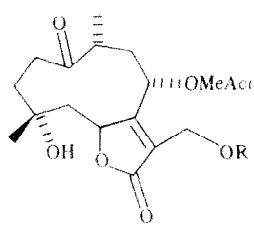


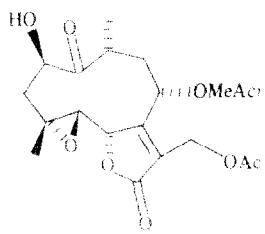
6a R = MeAcr
6b R = CO_{Pr}
6c R = Ang



7a R = MeAcr
7b R = Ang



8a R = Ac
8b R = Et



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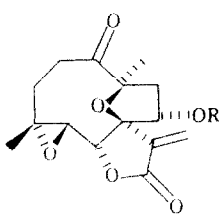
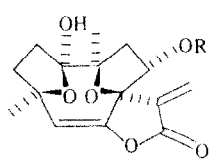


10a R = MeAcr
10b R = Tig



11a R = MeAcr
11b R = Ac

attributed to the ether oxygen but apparently due to deshielding by the 7,11-double bond, led earlier workers to the erroneous deduction of 8*R** configuration for the so-called piptocarphins [16, 17]. In view of the X-ray analysis of **7b**, the formulae of the piptocarphins A–F from *Piptocarpha chontalensis* [16], two piptocarphol esters from *Piptocarpha opaca* [17] and a new piptocarphol ester from *Vernonia mollissima* [2] must be corrected to **12a–i**. This has now been confirmed as follows. Reaction of glaucolide A (**1b**) with potassium carbonate–dioxane at 80° gave in 22% yield based on recovered material compound **12c** which on acetylation furnished piptocarphin A (**12a**) identical in all respects with the material isolated from *V. squamulosa* [2].

Lactone **8a** from *V. chamaedrys* has very recently been isolated from *Critoniopsis kuatrecana* [7]; the structure of

Table 1. ^{1}H NMR spectra of compounds **1a**, **3**, **4a**, **6a**, **8b** and **9** (270 MHz)

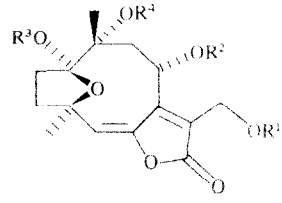
H	1a*	3†	4a†‡	6a§	6a*	8b†**	9
1	—	—	2.69 *br d* (10)	4.20 *dd* (10, 6)	3.95 *dd* (10, 6)	—	—
2a		3.24 *ddd* (14, 8, 2.5)	2.12 *br dd* (14, 2)	~2.25 *m*	1.59 *m*		4.56 ,
2b	1.93–	2.63 *ddd* (14, 10.5, 8)	1.58 *m*			1.80-	—
3a	2.20 *c*	2.38 *ddd* (13, 8, 2.5)	2.29 *ddd* (13, 5, 2)			2.45 *c*	2.35 *dd* (14, 3.5)
3b		1.60 *ddd* (13, 10.5, 8)	1.30 *m*				1.82 *dd* (14, 3.5)
5	2.24 *d* (9)	2.44 *brd* (9.5)	2.58 *d* (8.5)	5.95 *br*	5.60 *br*	5.37 *br*	2.43 *d* (9.5)
6	4.64 *d* (9)	4.81 *d* (9.5)	4.96 *br d* (8.5)	—	—	—	4.89 *d* (9.5)
8	5.02 *dd* (6, 2)	5.08 *dd* (12, 4)	5.24 *br d* (9)	6.35 *m*	6.34 *br dd* (9, 2)	5.56 *m*	4.95 *br d* (7)
9a	2.40 *dd* (15, 6)	3.52 *ddd* (12, 4, 1.5)	2.74 *br d* (15)	2.50 *dd* (14, 9)	2.32 *br dd* (15, 9)	~2.40	2.80 *ddd* (15, 11, 7)
9b	1.93- 2.20 *c*	2.91 *t* (12)	2.01 *dd* (15, 9)		1.75 *dd* (15, 2)		2.12 *br dd* (15, 1.5)
10	—	—	—	—	—		3.80 *ddd* (11, 7, 1.5)
13a	5.01 *d* (12)	5.08 *d* (12)	4.90 *d* (12)	5.17 *d* (12.5)	5.17 *d* (12.5)	4.40 *d* (12.5)	4.92 (centre
13b	4.86 *d* (12)	4.82 *d* (12)	4.78 *d* (12)	4.95 *d* (12.5)	5.02 *d* (12.5)	4.30 *d* (12.5)	of AB system, JAB = 12)
14	0.94 *s*‖	5.98 *d*(1.5) 5.96 *br*	1.51 *s*‖,¶	1.24 s‖	1.11 *s*‖,¶	1.06 *d*‖ (6)	1.12 *d*‖ (7)
15‖	1.40 *s*	1.43 *br*	1.47 *s*¶	1.48 *s*	0.92 *s*¶	1.52 *br*	1.72 *br*
OH-	3.60 *br*	—	—	—	—	—	2.28 *br*
3'a	6.10 *br*	6.14 *q* (1)	6.12 *br*	6.27 *br*	6.20 *br*	6.21 *br*	6.10 *br*
3'b	5.25 *br*	5.68 *q*(1)	5.68 *br*	5.64 *br*	5.24 *q*(1)	5.68 *br*	5.64 *br*
4'‖	1.79 *br*	1.92 *br*	1.91 *br*	1.94 *br*	1.85 *br*	1.96 *br*	1.90 *br*
Ac‖	1.75 *s*	2.06 *s*	—	2.04 *s*	1.68 *s*	—	2.06 *s*

*Run in C_6D_6, 75°.
†Run in $CDCl_3$, room temp.
‡Earlier [11] NMR data for 4a were reported in C_6H_6.
§Run in $CDCl_3$, 55°.
‖Intensity three protons.
**OEt-3.5 *m* (2H), 1.18 *t* (7).
¶Assignments may be interchangeable.

Table 2. NOE difference spectrum of compound **3**

Saturation	Observed NOE (%)
H-8	H-6 (10)
	H-9a (5)
	H-15 (5)
H-9a	H-9b (20)
	H-14b (6)
H-9b	H-8 (8)
	H-9b (16)
H-15	H-6 (6)
	H-8 (3)

the β-ethoxy analogue **8b** which is new and possibly an artefact was deduced by comparing its ^{1}H NMR spectrum (Table 1) with that of **8a**. The structure of lactone **9** which is also new was deduced by comparing its ^{1}H NMR spectrum (Table 1) with that of **2a** and **2b**. The extra oxygen atom revealed by the empirical formula was present in the form of a hydroxyl group (extra multiplet at δ4.56 coupled to broad OH signal at δ2.28 and to the protons of a methylene group at δ2.35 and δ1.82) whose location on C-2 rather than C-3 and axial orientation (β or 2*R*) was indicated by the chemical shift of the proton under the hydroxyl and the paramagnetic shifts of H-10 and H-15 (δ3.80 and δ1.70 compared with δ2.95 and δ1.60 in **2a, b**).



	R^1	R^2	R^3	R^4
12a	Ac	MeAcr	H	H
12b	Ac	Tig	H	H
12c	H	MeAcr	H	H
12d	Ac	H	H	H
12e	Ac	MeAcr	Et	H
12f	Et	MeAcr	H	H
12g	Tig	H	H	H
12h	MeAcr	H	H	H
12i	Et	Ac	H	H
12j	Ac	Ac	Ac	Ac

Structures **10a** and **10b** which possess (4*R**, 5*R**, 6*R**, 7*S**, 8*S**, 10*R**) stereochemistry, as expected from attack on C-7 of an alcoholate anion in a compound of type **1a**, have been ascribed to two diepoxy lactones, **10a** from *Pseudoelephantopus spicatus* [8] and **10b** from *Vernonia marginata* [9]. Although it has been stated [9] that the NMR spectrum of the supposed tiglate **10b** "was close to that of the corresponding methacrylate", the NMR spectra of the two compounds which are reproduced in Table 3 differ somewhat more than would be expected in exchanging a methacrylate for a tiglate moiety. The data (Table 3) for a methacryl derivative we have isolated from *V. chamaedrys* agree more closely with those of the presumed **10a**, although the chemical shifts of H-6 differ significantly. In an attempt to reproduce the proposed mode of formation of **10a**, desacetylglaucolide A (**1a**) was heated with potassium carbonate in dioxane; the product, however, obtained in 20% yield was another substance **11a** which was identical with the remaining lactone isolated from the *V. chamaedrys* extract.

Lactone **11a** is the methacryl analogue of an acetate (**11b**) prepared recently [8] by reaction of **1c** or **12j** with potassium carbonate–dioxane although, as mentioned earlier in this report, the same treatment of **1b** in our hands furnished only **12c**. Nevertheless synthesis of these compounds from **1a** in the case of **11a** and from **12j** in the case of **11b** dictates their (1*S**, 4*R**, 7*S**, 8*S**, 10*R**) stereochemistry.

EXPERIMENTAL

General. For separation of mixtures Waters HPLC equipment (M 45 pump, U6K injector and R-401 differential refractometer) was used. The column employed was an ALTEX Ultrasphere ODS column (5 μm, 10 mm i.d. × 25 cm). R_fs were measured from the injection point.

Plant material. Aerial parts of *V. chamaedrys* Less. were collected in Dec. 1983 and 1985 at the end of the flowering stage (seed formation) by Mr J. M. Retamal, IPNAYS-Facultad de Ingenieria Química, Universidad Nacional del Litoral, in 'Los Arenales', Paraná, Entre Rios Province, Argentina, and identified by Ing. J. M. Jozami (voucher No. 260, IPNAYS).

Table 3. ^{1}H NMR spectra of compounds **10a**, **b** and **11a** ($CDCl_3$)

H	**10a***	**10b†**	**10a‡**	**11a‡**
2a	2.18 *m*	2.58 *m*	3.33 *m*	2.02 *m*
2b	3.36 *m*	2.15 *m*	2.22 *m*	2.68 *m*
			1.80 *m*	
3a	2.34 *m*	1.85 *m*		
3b	1.80 *m*			
5	3.14 *d*	4.07 *d*	3.38 *d*	5.31 *s*
	(9.5)	(10.5)	(9)	
6	4.80 *d*	4.80 *d*	4.59 *d*	—
		(10.5)	(9)	
8	5.23 *dd*	5.36 *dd*	5.22 *t*	5.04 *dd*
	(7.5, 7.5)	(8)	(7)	(10, 2.5)
9a	3.17 *dd*	2.98 *dd*	3.16 *dd*	2.76 *dd*
	(13.5, 7.5)	(13.5)	(14, 7)	(14, 2.5)
9b	2.18 *dd*	1.91 *dd*	2.17 *dd*	2.26 *dd*
	(13.5, 7.5)	(13.5)	(14, 7)	(14, 10)
13a	6.65 *s*	6.45 *s*	6.62 *s*	6.43 *s*
13b	5.99 *s*	5.73 *s*	5.98 *s*	5.84 *s*
14§	1.46 *s*	1.41 *s*	1.45 *s*	1.43 *s*‖
15§	1.35 *s*	1.39 *s*	1.33 *s*	1.40 *s*‖
3'a	6.07 *dq*	6.79 *qq*	6.04 *br*	6.17 *br*
3'b	5.62 *dq*	—	5.61 *br*	5.60 *br*
4'§	1.88 *dd*	1.75 *dq*	1.87 *br*	1.90 *br*
5'§	—	1.77 *dq*	—	—

*400 MHz, taken from ref. [8]
†400 MHz, taken from ref. [9]
‡270 MHz, this work
§Intensity three protons
‖Assignments may be interchangeable

Extraction of V. chamaedrys. Flowers and seeds (620 g) of the 1983 collection were extracted with 2 × 10 l of $CHCl_3$ at room temp. for 7 days to give 43.9 g of extract which was suspended in 500 ml of EtOH at 50–55°, diluted with 375 ml of H_2O and extracted successively with hexane (3 × 300 ml) and $CHCl_2$ (3 × 300 ml). Evapn of the hexane extract gave 25.9 g of residue. A portion of this residue (3.2g) was dissolved in hexane–EtOAc (2:1), decolourized with charcoal, filtered, evapd and saponified with dil KOH. The unsaponifiable material (2.45 g) was chromatographed over silica gel (96 g) using hexane and increasing amounts of Et_2O (from 10 to 50%), all fractions being monitored by TLC. This gave 1.108 g waxes, 1.079 pentacyclic triterpenes, 0.116 g sterols and 0.041 g of a fraction with lower R_f than the sterol fraction. Reverse-phase HPLC separation of a small portion (76 mg) of the triterpene fraction (eluting solvent MeOH, flow rate 2 ml/min) gave 231 mg lupeol, 18.1 mg β-amyrin, 21.4 mg α-amyrin, 1.3 mg dotriacontanol and 0.8 mg of a mixture of dotriacontanol and homologues (NMR, MS). The triterpenes were identified by co-injection with authentic material in HPLC and GC, mp, mmp, and ^{1}H NMR. Dotriacontanol, $Me(CH_2)_{30}CH_2OH$, ^{1}H NMR: δ3.52 (*q*, CH_2OH), 2.32 (*t*, $-CH_2-CH_2OH$), 1.64 (*quin*, $-CH_2$), 1.25 (–CH_2–) 0.87 (*m*, CH_2Me), was identified by computer matching of its MS with mass spectra of similar compounds. A small portion (38 mg) of the sterol fraction was separated by reversed phase HPLC into 12.4 mg stigmasterol and 11.9 mg sitosterol which were identified in the manner described for the triterpenes. Separation of the lowest R_f fraction by reversed phase HPLC (MeOH, flow rate 1.2 ml/min) gave 13.2 mg myristic acid, mp 57–59°; ^{1}H NMR: δ7.92 (OH), 2.37 (*t*,

J = 7 Hz, 2H), 1.64 (*quin*, J = 7, 2H), 1.25 (*m*, approx 20H), 0.87 (*m*, Me).

Evaporation of the $CHCl_3$ fraction gave a residue (15.8 g) which was worked-up in the usual-manner [19] to give 13.8 g of gum. A portion (6.1 g) was chromatographed over silica gel partially deactivated with EtOAc (6:1, 286 g, 230–400 mesh) using $CHCl_3$ and increasing amounts of Et_2O (0–20%), as partial decomposition of some components of the mixture was observed in a trial run with normally activated silica gel. Twenty-eight fractions were collected. Fr. 1 (9 mg) gave a small amount of a complex mixture which was not analysed further. Frs 2–5, each of which showed the same four major spots, were combined (0.772 g); a small portion was sepd by HPLC (MeOH–H_2O 2:1, flow rate 1.5 ml/min) to give vanillin (1.8 mg, R_t 10.3 min), **2a** (9.1 mg, R_t 17.5 min), **10a** (2.3 mg, R_t 19 min), **2b** (1.5 mg, R_t 23.3 min) and **5** (1.5 mg, R_t 30.5 min). A small portion of Frs 6–8 (combined wt 1.966 g) sepd by HPLC (MeOH–H_2O 4:3) gave **11a** (1.8 mg, R_t 27 min), **4a** (3.1 mg, R_t 28.5 min), **7a** (3.1 mg, R_t 41.5 min) and **4b** (1.2 mg, R_t 47.5 min). A small portion of frs 9–11 (combined wt 790 mg) processed in the same manner gave **2a** (4.5 mg, R_t 30 min), **3** (2.6 mg, R_t 33 min) and **1b** (7.3 mg, R_t 51 min). Frs 9 and 10 (333 mg) which showed one major spot were combined and purified by CC and finally by HPLC (MeOH–H_2O 4:3) to give **1a** (R_t 20 min). Frs 14–16 (310 mg) contained **1a** and the lactones of frs 17–19 (237 mg), a portion of which on purification by HPLC (MeOH–H_2O, 4:3) gave **8a** (15 mg, R_t 18.5 min), **1a** (55 mg, R_t 20.5 min), **9** (6 mg, R_t 25 min) **8b** (5 mg, R_t 28.5 min) and **6a** (5 mg, R_t 39 min). Purification of a small portion of frs 20 and 21 (151 mg) by HPLC gave **8a** (23 mg, R_t 18.5 min), **1a** (26 mg, R_t 21 min) and **6a** (8 mg, R_t 40 min). Fr. 22 (62 mg), was also a mixture of **8a**, **1a** and **6a**. TLC of frs 23–25 (140 mg) showed the presence of one major constituent. PTLC ($CHCl_3$–Et_2O 5:1) furnished 25 mg **8a** (gum) [7] whose ^1H NMR spectrum (C_6D_6) at room temp exhibited only broad signals, but could be studied satisfactorily in $CDCl_3$ at $-40°$, PCI MS *m/z* (rel. int.): 407 (20.4), 389 (46.6), 347 (7.8), 277 (100), 87 (3.2). Frs 25–28 (72 mg) on PTLC ($CHCl_3$–EtOAC–MeOH 6:1:1) gave 25 mg chrysoeriol, mp 323–325° (dec., MeOH), lit. mp 330–331° [20], 326–328° [21]. The substance was identified by UV spectrometry [23] which indicated the presence of 5-OH and 4′-OH groups and by its ^1H NMR spectrum (DMSO-d_6): δ 12.97 (5-OH), 10.78 (*br*, –OH), 9.96 (–OH), 7.58 (*m*, H-2′, H-6′), 6.96 (*d*, J = Hz, H-5′), 6.90 (*s*, H-3), 6.52 and 6.21 (each *d*, J = 1.5 Hz, H-6 and H-8), 3.92 (–OMe).

Analysis of the $CHCl_3$ extract from the 1985 collection of *V. chamaedrys* gave results which did not differ significantly from those described above.

(4R*, 5R*, 6S*, 8S*, 10R*)-1-*Oxo*-4,5-*epoxy*-8-*methacryloxy*-10-*hydroxy*-13-*acetoxygermacr*-7(11)-*en*-6,12-*olide* (*desacetylglaucolide A*, **1a**). Gum, IR ν^{CHCl_3} cm^{-1}: 3480, 1775, 1750, 1730, 1715; UV (MeOH) 288 nm (weak); ^1H NMR: Table 1; PCI MS *m/z* (rel. int.): 423 $[M+1]^+$ (100), 405 (1.5), 363 (8.0), 337 (1.3), 277 (9.7), 87 (1.8).

A soln of 10 mg **1a** in 1 ml dioxane and 1 ml 0.1 N K_2CO_3 was heated at 60° for hr, diluted with 10 ml H_2O, neutralized with dil HCl and extracted with $CHCl_3$. The organic layer was dried and evapd; PTLC (C_6H_6–EtOAc, 7:3) afforded 2 mg **11a** (*vide infra*). Heating of 0.1 g glaucolide A (**1b**) at 80° for 2 hr followed by the same work-up and purification of the residue by radial chromatography afforded 30 mg of starting material and 15 mg 1*S**, 4*R**, 8*S**, 10*R**,)-1,4-epoxy-1,10,13-trihydroxy-8-meth-acryloxygermacra-5,7(11)-dien-6,12-olide (**12c**) whose acetylation (Ac_2O-Pyridine) followed by the usual work-up gave 15 mg piptocarphin A (**12a**).

(4R*, 5R*, 6S*, 8S*)-1-*Oxo*-4,5-*epoxy*-8-*methacryloxy*-13-*acetoxy*-*germacra*-7(11),10(14)-*dien*-6,12-*olide* (**3**). Gum, IR ν^{CHCl_3} cm^{-1}: 1770, 1740, 1720; UV (MeOH): 212, 292 nm (ε 11000, 1500); ^1H NMR: Table 1; PCI MS *m/z* (rel. int.): 405 $[M+1]^+$ (100), 345, (3.1), 319 (1.3), 301 (1), 275 (2.1), 259 (4.5), 87 (2.5).

(1S*, 4R*, 8S*, 10R*)-1,4-*Epoxy*-8-*methacryloxy*-10-*hydroxy*-13-*acetoxygermacra*-5*E*,7(11)-*dien*-6,12-*olide* (**6a**). Gum, IR ν^{CHCl_3} cm^{-1}: 3550, 1740, 1720; UV (MeOH) 288 nm (ε 17500); ^1H NMR Table 1. Assignments for H-14 and H-15 differ from those given for **6b, c** in refs [8, 15] and were established by irradiation at the frequencies of H-9a, which sharpened the signal at δ 1.24, and H-5 which sharpened the signal at δ 1.48; PCI MS *m/z* (rel. int.): 407 $[M+1]^+$ (100), 389 (11.8), 347 (20.8), 321 (38.8), 303 (12.5), 261 (6.2), 87 (4.5).

4(R*, 8S*, 10R*)-1-*Oxo*-4-*hydroxy*-8-*methacryloxy*-13-*ethoxy*-*germacra*-5*Z*,7(11)-*dien*-6,12-*olide* (**8b**). Gum, UV (MeOH) 286 nm (ε 17800); ^1H NMR: Table 1; PCI MS *m/z* (rel. int.) 393 (47.6), 375 (100), 347 (3.3), 307 (11.7), 289 (22.7), 261 (8.3), 87 (2.1).

(2R*, 4R*, 5R*, 6S*, 8S*, 10R*)-1-*Oxo*-2-*hydroxy*-4,5-*epoxy*-8-*methacryloxy*-13-*acetoxygermacr*-7(11)-*en*-6,12-*olide* (**9**). Gum, IR ν^{CHCl_3} cm^{-1}: 3440, 1770, 1745, 1715; ^1H NMR: Table 1; PCI MS *m/z* (rel. int.): 423 $[M+1]^+$ (100), 405 (4.3), 363 (5.1), 337 (1.5), 87 (1).

(4R*, 5R*, 6R*, 7S*, 8S*, 10R*)-1-*Oxo*-4,5,7,10-*diepoxy*-8-*methacryloxy*-11(13)-*en*-6,12-*olide* (**10a**). Gum; IR ν^{CHCl_3} cm^{-1}: 1775, 1730, 1725; ^1H NMR: Table 3; PCI MS *m/z* (rel. int.): 363 $[M+1]^+$ (100), 277 (53.5), 87 (10.9).

(1S*, 4R*, 7S*, 8S*, 10R*)-1-*Hydroxy*-1,4,7,10-*diepoxy*-8-*methacryloxygermacra*-5*Z*,11(13)-*dien*-6,12-*olide* (**11a**). Gum, IR ν^{CHCl_3} cm^{-1}: 3580, 1775, 1730; ^1H NMR: Table 3; PCI MS *m/z* (rel. int.): $[M+1]^+$ (27.1), 345 (16.9), 279 (20.5), 195 (100), 151 (72.3), 135 (61.1).

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REFERENCES

1. Catalán, C. A. N., Legname, P. R., Crist, B. V. and de Iglesias, D. I. A. (1985) *Phytochemistry* **24**, 2113.
2. Catalán, C. A. N., de Iglesias, D. I. A., Kavka, J., Sosa, V. E. and Herz, W. (1986) *J. Nat. Prod.* **49**, 351.
3. Padolina, W. G., Yoshiaka, 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.
4. Cox, P. J. and Sim, G. A. (1975) *J. Chem. Soc. Perkin II*, 455.
5. Rogers, D., Moss, G. P. and Neidle, S. (1972) *J. Chem. Soc. Chem. Commun.* 142.
6. Bohlmann, F., Zdero, C., King, R. M. and Robinson, H. (1982) *Phytochemistry* **21**, 1045.
7. Jakupovic, J., Banerjee, S., Castro, V., Bohlmann, F., Schuster, A., Msonthi, J. D. and Keeley, S. (1986) *Phytochemistry* **25**, 1359.
8. Jakupovic, J., Schmeda-Hirschmann, G., Schuster, A., Zdero, C., Bohlmann, F., King, R. M., Robinson, H. and Pickardt, J. (1986) *Phytochemistry* **25**, 145.
9. Jakupovic, J. Gage, D. A., Bohlmann, F. and Mabry, T. J. (1986) *Phytochemistry* **25**, 1179.
10. Zabel, V., Watson, W. H., Mabry, T. J. and Padolina, W. G. (1980) *Acta Cryst.* **B36**, 3024.
11. Bohlmann, F. and Zdero, C. (1982) *Phytochemistry* **21**, 2263.
12. Padolina, W. G., Nakatani, N., Yoshiaka, H., Mabry, T. J. and Monti, S. A. (1974) *Phytochemistry* **13**, 2225.
13. Betkouski, M., Mabry, T. J., Adams, T. W., Watson, W. H. and Jones, S. B. (1976) *Rev. Latinoam. Quim.* **7**, 111.
14. Bohlmann, F., Singh, P., Borthakur, N. and Jakupovic, J.

(1981) *Phytochemistry* **20**, 2379.
15. Bohlmann, F., Zdero, C., King, R. M. and Robinson, H. (1982) *Phytochemistry* **21**, 695.
16. Cowall, P. L., Cassady, J. M., Chang, C.-J and Kozlowski, J. F. (1981) *J. Org. Chem.* **46**, 1108.
17. Herz, W. and Kulanthaivel, P. (1983) *Phytochemistry* **22**, 1287.
18. Bohlmann, F., Brindöpke, G. and Rastogi, R. C. (1978) *Phytochemistry* **17**, 475.
19. Herz, W. and Högenauer, G. (1962) *J. Org. Chem.* **27**, 905.
20. Gripenberg, J. (1962) in *The Chemistry of Flavonoid Compounds* (Geissman, T. A., ed.) p. 422. McMillan, New York.
21. Herz, W., Chikamatsu, H., Viswanathan, N. and Sudarsanam, V. (1967) *J. Org. Chem.* **32**, 682.
22. Mabry, T. J., Markham, K. R. and Thomas, M. B. (1970) *The Systematic Identification of Flavonoids*, p. 10. Springer, New York.