GERMACRANOLIDES AND OTHER CONSTITUENTS FROM *AGERATINA* SPECIES

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Abstract—The aerial parts of *Ageratina anisochroma* gave several thymol derivatives including five new ones, a hydroxypiperitol glucoside, some substituted benzyl benzoates and several germacranolides related to provincialin. From *A. ligustrina* similar germacranolides, an oplopanone derivative and a further geranyl nerol derivatives were isolated. The structures were elucidated by high field NMR techniques.

INTRODUCTION

The large genus *Ageratina* (tribe Eupatorieae) is placed in the subtribe Oxylobinae [1]. Several species have been studied chemically. In addition to thymol derivatives prenylated *p*-hydroxyacetophenone derivatives are widespread while sesquiterpene lactones are rare [2–5]. We have studied *A. anisochroma* (Klatt.) K. et R., subgenus Klattiella [1] and *A. ligustrina* (DC) K. et. R. placed in the subgenus Neogreenella [1], where sesquiterpene lactones have been reported [2–6]. The results are discussed in this paper.

RESULTS AND DISCUSSION

The aerial parts of *A. anisochroma* afforded, in addition to widespread compounds (Experimental), the thymol derivatives 1a [7], 1b, 1c, 2a, 2b [8], 2c [9], 2d [9], 2e, 2f [2], 3a and 3b [9], the hydroxypiperitol-glucopyranoside 4, the benzyl benzoates 5a [10], 5b [2] and 5c, the germacranolides 6a [6] and 6c [11] as well as the closely related lactones 6b and 6d.

The structure of 1b could be deduced easily from its ¹H NMR spectrum (Table 1) which showed the typical signals of a cinnamate and of thymol, only one methyl doublet being replaced by a pair of double doublets. The ¹H NMR spectrum of 1c (Table 1) showed that this cinnamate was the Δ^8 derivative of 1b, the second methyl signal being replaced by a pair of broadened singlets at δ 5.53 and 5.32.

The spectral data of 2a (Table 1) showed that again a cinnamate was present. Comparison of the chemical shifts of H-10 with those of 2b indicated that 2a was a 10-cinnamoyloxy derivative. The ¹H NMR spectrum of 2e (Table 1) was very similar to that of 2a. An additional methoxy signal indicated that this cinnamate was the 6-methoxy derivative of 2a. The structure of cinnamate 3a followed from comparison of the ¹H NMR spectrum with that of 3b, the corresponding 6-hydroxy derivative.
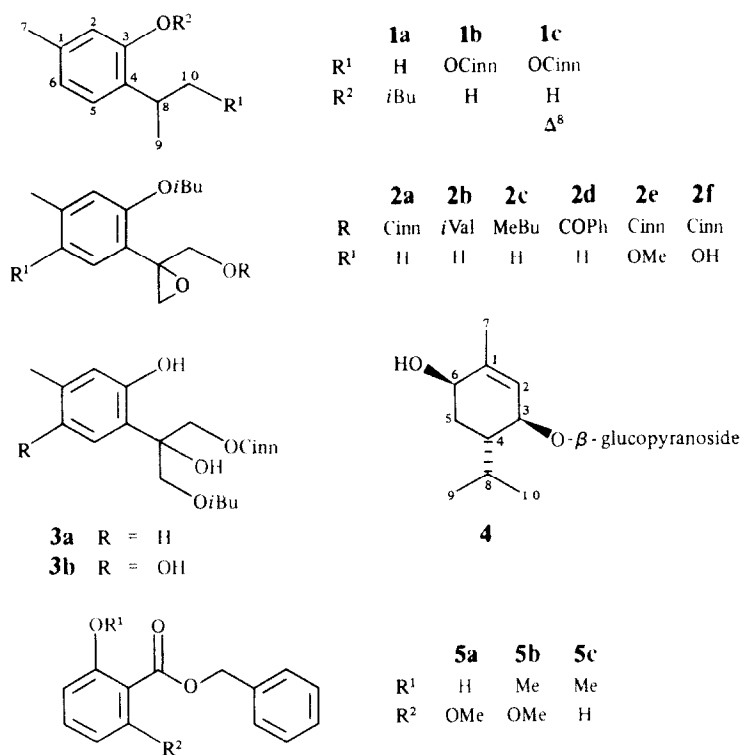
The ¹H NMR spectrum of compound 4 (Experimental) showed that a glycoside was present. Most signals could be assigned by spin decoupling and the observed NOE's indicated that a glucoside of an allylic alcohol was present as followed from the clear effect between H-1', H-2 and H-3. After acetylation, all the signals in the resultant penta acetate could be assigned by spin decoupling. The sequences showed that we were dealing with the penta acetate of 6-hydroxypiperitol-β-glucopyranoside. The observed couplings of H-6 required an axial oxygen function.

The structure of 5c could be deduced easily from the spectral data (Experimental). This benzyl ester seems to be new.

The ¹H NMR spectrum of 6b (Table 2) was similar to that of the acetate 6a. However, the chemical shift of H-3 indicated a free hydroxy group while the C-25 hydroxy group was acetylated as followed from the observed downfield shift of H-25. Furthermore, the hydroxy group in the ester side chain was shifted from C-24 to C-19 as could be deduced from the differences in the spectra of 6a and 6b. The ¹H NMR spectrum of 6d (Table 2) clearly showed that the 4*E*-isomer of the lactone 6c was present.

The extract of the aerial parts of *Ageratina ligustrina* afforded, in addition to widespread compounds (Experimental), the guaianolide 8β-hydroxykauniolide [12], the germacranolides 7a [13], 7b [14], 7c [11], 7d [11], 7e [6] and 7f [15], the oplopanone derivative 8 and the geranyl nerol derivative 9. The structure of 8 followed from the molecular formula ($C_{24}H_{32}O_4$) and from its ¹H NMR spectrum (Experimental) which was very similar to that of oplopanone, apart from the typical cinnamate signals and the replacement of the methyl ketone singlet by a pair of doublets at δ 4.91 and 4.81.

The ¹H NMR spectrum of 9 (Table 3) was similar to that of the isomeric 19-acetoxy-20-hydroxygeranyl nerol isolated from *Ageratina tristis* [6]. However, the chemical shifts of H-2 differed characteristically being more upfield in the case of acetate 9. Furthermore, on irradiation of H-

	1a	**1b**	**1c**
R^1	H	OCinn	OCinn
R^2	iBu	H	H
			Δ^8

	2a	**2b**	**2c**	**2d**	**2e**	**2f**
R	Cinn	iVal	MeBu	COPh	Cinn	Cinn
R^1	H	H	H	H	OMe	OH

3a R = H
3b R = OH

4

	5a	**5b**	**5c**
R^1	H	Me	Me
R^2	OMe	OMe	H

Table 1. ^{1}H NMR spectral data of compounds **1b**, **1c**, **2a**, **2e** and **3a** (400 MHz, CDCl$_3$, δ-values)

H	1b	1c	2a	2e*	3a
2	6.71 *br s*	6.80 *br s*	6.90 *br s*	6.85 *br s*	6.64 *br s*
5	6.90 *d*	7.03 *d*	7.41 *d*	6.96 *s*	6.86 *d*
6	6.76 *br d*	6.73 *br d*	7.08 *br d*	—	6.59 *br d*
7	2.30 *s*	2.35 *s*	2.36 *s*	2.21 *s*	2.28 *s*
8	3.44 *m*	—	—	—	—
9	1.41 *d*	{ 5.53 *br s* 5.32 *br s*	{ 3.10 *d* 2.85 *d*	{ 3.11 *d* 2.87 *d*	4.59 *s*
10	{ 4.42 *dd* 4.06 *dd*	4.90 *br s*	{ 4.63 *d* 4.40 *d*	{ 4.67 *d* 4.40 *d*	{ 4.53 *d* 4.49 *d*
OCOR	7.72 *d*	7.78 *d*	2.88 *qq*	2.86 *qq*	2.57 *qq*
	6.47 *d*	6.54 *d*	1.34 *d*	1.36 *d*	1.16 *d*
	7.54 *m*	7.56 *m*	7.66 *d*	7.66 *d*	7.61 *d*
	7.40 *m*	7.42 *m*	6.41 *d*	6.44 *d*	6.35 *d*
			7.51 *m*	7.51 *m*	7.42 *m*
			7.39 *m*	7.39 *m*	7.30 *m*

*OMe: 3.84 *s*

J[Hz]: 5,6 = 8; OC inn: 7′,8′ = 15; OiBu: 2′,3′ = 2′,4′ = 7; compound **1b**: 8,9 = 7; 8,10 = 5; 8,10′ = 8; 10,10′ = 10.5; compounds **2a** and **2e**: 9,9′ = 5; 10,10′ = 12; compound **3a**: 10,10′ = 12.

Table 2. ^{1}H NMR spectral data of compounds **6b** and **6d** (400 MHz, CDCl$_3$, δ-values)

H	6b	6d
1	5.22 m	4.94 br dd
3	4.51 t	4.35 dd
5	5.22 br d	4.82 m
6	6.37 d	5.18 dd
7	2.96 br s	2.90 m
8	5.22 m	5.84 m
9	2.78 dd	2.85 dd
9'	2.41 dd	2.35 m
13	6.34 d	6.27 d
13'	5.76 d	5.60 d
14	1.74 br s	1.49 br s
15	1.74 br s	1.85 d
18	7.06 br t	7.10 t
19	4.46 d	4.54 dd / 4.47 dd
20	4.97 d / 4.90 d	5.02 d / 4.97 d
23	7.12 q	7.07 q
24	1.93 d	1.95 d
25	4.83 br s	4.81 br s
OAc	2.03 s	2.03 s

J[Hz]: Compound **6b**: 2,3 = 2',3 = 3.5; 5,6 = 10.5; 7,13 = 2.5; 7,13' = 2; 8,9 = 3.5; 8,9' = 3; 9,9' = 14.5; compound **6d** 1,2 = 13; 1,2' = 4; 2,3 = 6; 2',3 = 10; 5,6 = 9.5; 6,7 = 8.5; 7,13 = 3.5; 7,13' = 3; 8,9 = 4; 9,9' = 13; OCOR: 18,19 = 6; 20,20' = 12; 23,24 = 7; (compound **6d**: 19,19' = 15).

Table 3. ^{1}H NMR spectral data of compounds 9 and 9a (400 MHz, δ-values)

H	9 (CDCl$_3$)	9 (C$_6$D$_6$)	9a (C$_6$D$_6$)
1	4.09	5.13 br d	9.90 d
2	5.44	5.51 br t	5.84 br d
4	2.10	1.97 br t	2.17 br t
5	2.19	2.08 br q	2.00 br q
6	5.40	5.38 br t	5.05 br t
8	2.10	1.97 m	2.00 m
9	2.10	1.97 m	2.33 br q
10	5.28	5.34 br t	6.03 br t
12	2.10	1.97 m	2.24 m
13	2.04	1.84 br t	2.35 br q
14	5.10	5.32 br t	5.24 br t
16	1.67	1.54 br s	1.71 br s
17	1.59	1.44 br s	1.61 br s
18	4.11	4.18 br s	10.11 s
19	4.59	4.68 br s	4.45 br s
20	1.73	1.47 br s	1.45 d
OAc	2.06	1.58 s	1.73 s

J[Hz]: 1,2 = 4,5 = 5,6 = 9,10 = 12,13 = 13, 14 ~ 7; (compound **9a**: 1,2 = 7,8; 2,20 = 1).

the chemical shifts of H-1 and H-18 in the spectrum of the dialdehyde.

Previously some flavone glycosides [16] and the guaianolide ligustrin, an isomer of 8β-hydroxykauniolide [17] were reported from this species.

The chemistry of these two *Ageratina* species shows relationships to that of *A. tristis* (subgenus Neogreenella) by the co-occurrence of very similar germacranolides and of epoxy thymol derivatives. However, benzyl benzoates were not reported from the latter species which also contains some guaianolides. Therefore the placement of *A. anisochroma* in a separate small subgenus next to Neogreenella and *A. ligustrina* in the latter is supported by the chemistry. So far sesquiterpene lactones with 8β-acyloxy groups have been reported from *A. petiolaris* [2], *A. deltoideum* [3], *A. rhomboideum* [4] and *A. tristis* [6], all members of the subgenus Neogreenella. The latter also contain a diterpene closely related to **9**. Thymol derivatives like **2a–2f** are common in the whole genus and from some species also benzyl benzoates were reported. However, the large amounts of **5a** and **5b** in *A. aniso-chroma* as well as of the epoxides **2a** and **2e** are very unusual.

EXPERIMENTAL

The aerial parts of *A. anisochroma* (700 g) were collected in June 1986 near Cervantes, Costa Rica (voucher 116219CR, deposited in the Herbarium of the University of Costa Rica) and extracted with Et$_2$O–MeOH–petrol (1:1:1) at room temp. After defatting the extract was separated by CC (silica gel) into six fractions [1: petrol and Et$_2$O–petrol (1:2); 2: Et$_2$O–petrol (1:1); 3: Et$_2$O–petrol (7:3); 4: Et$_2$O; 5: Et$_2$O–MeOH (4:1); 6: Et$_2$O–MeOH (1:1)]. These fractions were further separated as reported previously [17] by TLC and/or by HPLC (RP 8, MeOH–H$_2$O, ca 100 bar) affording the following compounds (final purification step for each new compound is given in parenthesis): caryophyllene, germacrene D, δ-cadinene and squalene (ca 20 mg each), 1.28 g taraxasteryl acetate, 100 mg

2, an olefinic methyl singlet was sharpened (δ1.73) and saturation of the olefinic signal at δ5.10 sharpened two olefinic methyl signals. Thus oxygen functions were present at C-1, C-18 and C-19. Spin decoupling with 9 and the dialdehyde **9a** (obtained by oxidation of **9** with PCC) indicated that 19-acetoxy-18-hydroxygeranyl nerol was present. This was supported by the observed NOE's of **9a** which allowed the assignment of H-4 and H-12. Starting with these protons the sequences H-4 to H-10 and H-19 as well as H-12–H-17 could be determined. NOE's between H-20 and H-2, between H-19 and H-5 as well as between H-18 and H-9 established the configuration of the corresponding double bonds. This was supported by
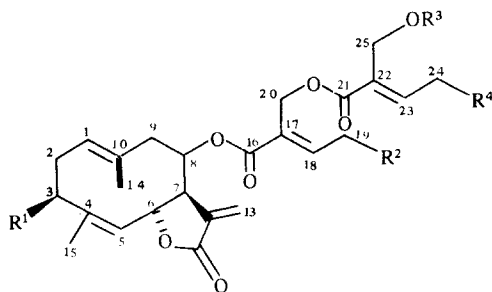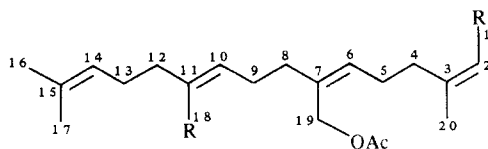
	6a	6b	6c	6d
R¹	OAc	OH	H	OH
R²	H	OH	OH	OH
R³	H	Ac	H	Ac
R⁴	OH	H	H	H
			4E	4E
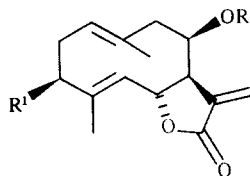
	7a	7b*	7c*	7d*	7e	7f
R	Ac	A	B	C	H	H
R¹	H	H	H	H	OAc	OAc
						4Z
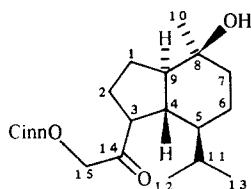
8

9 R = CH₂OH
9a R = CHO

* A = COC(Me)═CHCH₂OH(*E*); B = sarracinoyl; C = COC(CH₂OTigl)═CHCH₂OH(*E*)

cinnamic acid, 4 mg **1a**, 0.6 mg **1b** (HP 1, R_t 15.7 min), 0.6 mg **1c** (HP 1, R_t 14.7 min), 920 mg **2a** (TLC, Et₂O–petrol, 11:9, R_f 0.44), 5 mg **2b**, 12 mg **2c**, 250 mg **2d**, 4 g **2e** (HP 2, R_t 7.3 min), 82 mg **2f**, 18 mg **3a** (HP 2, R_t 8.0 min), 850 mg **3b**, 100 mg **4** (HP 3, R_t 9.8 min), 1.6 mg **5a**, 690 mg **5b**, 8 mg **5c**, 22 mg **6a**, 20 mg **6b** (HP 4, R_t 9.7 min), 5 mg **6c** and 1 mg **6d** (HP 4, R_t 6.7 min). HP 1: MeOH–H₂O (4:1); HP 2: MeOH–H₂O (17:3); HP 3: MeOH–H₂O (9:11); HP 4: MeOH–H₂O (13:7).

The extract of the aerial parts of *A. ligustrina* (1 kg, collected in May 1987 in Costa Rica, voucher RMK 9694, deposited in the US National Herbarium, Washington) was worked-up as above. The CC fractions were combined into three [Et₂O–petrol (1:9); Et₂O–petrol (1:1) and Et₂O–MeOH (4:1)]. Fraction 1 gave by TLC (Et₂O–petrol, 1:19) 17 mg caryophyllene and 14 mg caryophyllenepoxide. TLC of fraction 2 (C₆H₆–CH₂Cl₂–Et₂O, 9:9:2) yielded 30 mg spathulenol, 30 mg lupeol and 7.5 mg **5b**. TLC of fraction 3 (C₆H₆–CH₂Cl₂–Et₂O, 2:2:1) gave 7.5 mg cirsimaritin and five further bands (3/2–3/6) which were sepd by repeated TLC. Finally 25 mg 8β-hydroxykauniolide, 5 mg **7a**, 3 mg **7b**, 2 mg **7c**, 46 mg **7d**, 20 mg **7e**, 20 mg **7f**, 300 mg sarracinic acid, 10 mg pinoresinol, 4 mg **8** (TLC, Et₂O–petrol, 7:3), 3 mg liliolide and 180 mg **9** (TLC, C₆H₆–CH₂Cl₂–Et₂O–MeOH, 20:20:10:1)

were obtained. Known compounds were identified by comparing the 400 MHz ¹H NMR spectra with those of authentic material.

10-Cinnamoyloxythymol (**1b**). Colourless oil; IR $v_{max}^{CCl_4}$ cm⁻¹: 3530 (OH), 1715 (C═CCO₂R); MS m/z (rel. int.): 296.141 [M]⁺ (5) (calc. for C₁₉H₂₀O₃: 296.142), 148 [M − RCO₂H]⁺ (92), 131 [RCO]⁺ (100), 103 [131 − CO]⁺ (28).

10-Cinnamoyloxy-8,9-dehydrothymol (**1c**). Colourless oil; IR $v_{max}^{CCl_4}$ cm⁻¹: 3530 (OH), 1715 (C═CCO₂R); MS m/z (rel. int.): 294.125 [M]⁺ (11) (calc. for C₁₉H₁₈O₃: 294.126), 146 [M − RCO₂H]⁺ (73), 131 [RCO]⁺ (100), 103 [131 − CO]⁺ (23).

10-Cinnamoyloxy-8,9-epoxythymol isobutyrate (**2a**). Colourless oil; IR $v_{max}^{CCl_4}$ cm⁻¹: 1760 (PhOCOR), 1715 (C═CCO₂R); MS m/z (rel. int.): 380.162 [M]⁺ (1) (calc. for C₂₃H₂₄O₅: 380.162), 232 [M − RCO₂H]⁺ (8), 145 [232 − OCOR]⁺ (26), 131 [RCO]⁺ (100), 105 [131 − CO]⁺ (38), 71 [RCO]⁺ (32).

10-Cinnamoyloxy-6-methoxy-8,9-epoxythymol isobutyrate (**2e**). Colourless oil; IR $v_{max}^{CCl_4}$ cm⁻¹: 1750 (PhOCOR), 1710 (C═CCO₂R); MS m/z (rel. int.): 410.172 [M]⁺ (7) (calc. for C₂₄H₂₆O₆: 410.173), 340 [M − O═C═CMe₂]⁺ (3), 262 [M − RCO₂H]⁺ (3), 192 [262 − O═C═CMe₂]⁺ (26), 131 [RCO]⁺ (100), 103 [131 − CO]⁺ (18), 71 [RCO]⁺ (17).

10-Cinnamoyloxy-8-hydroxy-9-isobutyryloxythymol (**3a**).

Colourless oil; IR $v_{max}^{CCl_4}$ cm^{-1}: 3600 (OH), 1735 (CO$_2$R) 1715 (C=CCO$_2$R); MS m/z (rel. int.): 398.173 [M]$^+$ (1) (calc. for C$_{23}$H$_{26}$O$_6$: 398.173), 251 [M − OCinn]$^+$ (6), 131 [RCO]$^+$ (72), 105 [131 − CO]$^+$ (56), 71 [RCO]$^+$ (100).

6β-Hydroxypiperitol-3-O-β,D-glucopyranoside (**4**). Colourless oil; ^{1}H NMR (MeOD): δ 5.66 (*br s*, H-2), 4.11 (*br d*, H-3), 1.75 (*m*, H-5$_1$), 1.45 (*dt*, H-5$_2$), 3.92 (*br t*, H-6), 1.88 (*br s*, H-7), 2.18 (*m*, H-8), 1.93 (*d*, H-9), 1.83 (*d*, H-10), 4.40 (*d*, H-1′), 3.30 (*m*, H-2′−H-5′), 3.84 and 3.67 (*dd*, H-6′) (*J* [Hz]: 2,3 = 9; 5$_1$,5$_2$ = 14; 5,6 = 3; 8,9 = 8,10 = 7; 1′,2′ = 8; 5′,6′$_1$ = 2.5; 5′,6′$_2$ = 5.5; 6′$_1$,6′$_2$ = 12); $[\alpha]_D^{24°}$ −49 (MeOH; *c* 0.29).

Acetylation (Ac$_2$O, DMAP, CHCl$_3$) afforded the pentaacetate of **4**, colourless gum; IR $v_{max}^{CCl_4}$ cm^{-1}: 1750 (OAc); MS m/z (rel. int.): 331 (14), 169 (80), 135 (68), 109 (70), 93 (100); CIMS m/z (rel. int.): 483 (0.3) [M + 1 − HOAc]$^+$ 195 (100), 135 [C$_{10}$H$_{15}$]$^+$ (16); ^{1}H NMR (CDCl$_3$): 5.62 (*br s*, H-2), 4.03 (*br d*, H-3), 1.65 (*m*, H-4), 1.78 (*ddd*, H-5$_1$), 1.46 (*ddd*, H-5$_2$), 5.16 (*br t*, H-6), 1.69 (*br s*, H-7), 2.04 (*m*, H-8), 1.38 (*d*, H-9), 1.27 (*d*, H-10), 4.62 (*d*, H-1′), 4.96 (*dd*, H-2′), 5.06 (*t*, H-3′), 5.22 (*t*, H-4′), 3.68 (*ddd*, H-5′), 4.19 (*dd*, H-6′$_1$), 4.13 (*dd*, H-6′$_2$); OAc: 2.08, 2.06, 2.05, 2.03, 2.02 s (*J* [Hz]: **4** and 2′,3′ = 3′,4′ = 4′,5′ = 9; 5′,6′$_1$ = 5.5; 5′,6′$_2$ = 3; 6′$_1$,6′$_2$ = 12).

Benzyl-2-methoxybenzoate (**5c**). Colourless oil; IR $v_{max}^{CCl_4}$ cm^{-1}: 1740 (CO$_2$R); MS m/z (rel. int.): 242.094 [M]$^+$ (56) (calc. for C$_{15}$H$_{14}$O$_3$: 242.094), 151 [RCO$_2$]$^+$ (10), 135 [RCO]$^+$ (88), 91 [C$_7$H$_7$]$^+$ (100); ^{1}H NMR (CDCl$_3$): 6.98 (*d*, H-3), 7.48 (*ddd*, H-4), 6.98 (*dd*, H-5), 7.84 (*dd*, H-6), 7.47 (*m*, H-2′, H-6′), 7.37 (*m*, H-3′, H-4′, H-5′), 5.35 (*s*, H-7′), 3.91 (*s*, OMe) (*J* [Hz]: 3,4 = 4,5 = 5,6 = 8; 4,6 = 1.5) (assignment proven in part by the NOE's).

Desacetyl-24-desoxyprovincialin-25-O-acetate (**6b**). Colourless gum; IR $v_{max}^{CHCl_3}$ cm^{-1}: 3520 (OH), 1760 (γ-lactone), 1720 (C=CCO$_2$R); MS m/z (rel. int.): 518 [M]$^+$ (1.5), 458.194 [M − HOAc]$^+$ (8) (calc. for C$_{25}$H$_{30}$O$_8$: 458.194), 246 [M − RCO$_2$H]$^+$ (30), 228 [246 − H$_2$O]$^+$ (30), 141 [RCO]$^+$ (73), 99 [141 − ketene]$^+$ (41), 81 [99 − H$_2$O]$^+$ (100).

3β-Hydroxy-8β-[5-O-acetylsarracinoyloxy-4-hydroxytigloyloxy]costunolide (**6d**). Colourless gum; CIMS m/z (rel. int.): 159 [RCO$_2$H + 1]$^+$ (100), 141 [159 − H$_2$O]$^+$ (36), 99 [141 − ketene]$^+$ (8).

15-Cinnamoyloxyoplopanone (**8**). Colourless oil; IR $v_{max}^{CHCl_3}$ cm^{-1}: 3590 (OH), 1720 (C=O, C=CC=$_2$R); MS m/z (rel. int.). 384.230 [M]$^+$ (0.5) (calc. for C$_{24}$H$_{32}$O$_4$: 384.230), 236 [M − RCO$_2$H]$^+$ (21), 223 [M − CH$_2$OCinn]$^+$ (46), 205 [223 − H$_2$O]$^+$ (6), 177 [205 − CO]$^+$ (54), 131 [RCO]$^+$ (100); ^{1}H NMR (CDCl$_3$): δ 2.71 (*ddd*, H-3, *J* = 11.5, 9, 5.5 Hz), 1.73 (*dt*, H-3, *J* = 5.5, 11.5), 1.97 (*m*, H-5), 1.20 (*s*, H-10), 1.47 (*m*, H-11), 0.92

and 0.69 (*d*, H-12, 13), 4.91 and 4.81 (*d*, H-15, *J* = 17).

19-Acetoxy-18-hydroxygeranyl nerol (**9**). Colourless oil; IR $v_{max}^{CHCl_3}$ cm^{-1}: 3570 (OH), 1725 (OAc); MS m/z (rel. int.). 346 [M − H$_2$O]$^+$ (2), 286 [346 − HOAc]$^+$ (4), 268 [286 − H$_2$O]$^+$ (3.5), 69 [Me$_2$C = CHCH$_2$]$^+$ (100). 20 mg **9** in 3 ml CH$_2$Cl$_2$ were stirred for 6 hr with 40 mg PCC. TLC (Et$_2$O−petrol, 4:1) gave 5 mg **9a**; MS m/z (rel. int.): 300 [M − HOAc]$^+$ (1.5), 271 [300 − CHO]$^+$ (2.5), 69 [Me$_2$C = CHCH$_2$]$^+$ (100).

REFERENCES

1. King, R. M. and Robinson, H. (1987) *The Genera of the Eupatorieae*, Monographs in Systematic Botany, Missouri Botanical Garden, Vol. 22, 428.
2. Bohlmann, F., Jakupovic, J. and Lonitz, M. (1977) *Chem. Ber.* **110**, 301.
3. Quijano, L., Calderon, J. S., Gomez, F., Garduno, J. T. and Rios, T. (1980) *Phytochemistry* **19**, 1975.
4. Guerrero, C., Diaz, E., Martinez, M., Taboada, J., Plata, S. M., Diddi, M. G. and Tellez, J. (1977) *Rev. Latinoam. Quim.* **8**, 123.
5. Romo, J., Rios, T. and Quijano, L. (1968) *Tetrahedron* **24**, 6087.
6. Bohlmann, F., Banerjee, S., Wolfrum, C., Jakupovic, J., King, R. M. and Robinson, H. (1985) *Phytochemistry* **24**, 1319.
7. Rinn, M. (1970) *Planta Med.* 147.
8. Bohlmann, F. and Abraham, W. R. (1979) *Phytochemistry* **18**, 868.
9. Bohlmann, F. and Zdero, C. (1978) *Phytochemistry* **17**, 1135.
10. Bohlmann, F., Zdero, C. and Kapteyn, H. (1969) *Chem. Ber.* **102**, 1682.
11. Bohlmann, F., Zdero, C. and Turner, B. L. (1985) *Phytochemistry* **24**, 1263.
12. Bohlmann, F., Zdero, C., King, R. M. and Robinson, H. (1982) *Phytochemistry* **21**, 2021.
13. Dolejs, L. and Herout, V. (1962) *Coll. Czech. Chem. Commun.* **27**, 2654.
14. Bohlmann, F., Jakupovic, J. and Schuster, A. (1983) *Phytochemistry* **22**, 1637.
15. Takahashi, T., Eto, H., Ichimura, T. and Murae, T. (1978) *Chem. Letters* 1345.
16. Quijano, L. Malanco, F. and Rios, T. (1970) *Tetrahedron* **26**, 2851.
17. Bohlmann, F., Zdero, C., King, R. M. and Robinson, H. (1984) *Phytochemistry* **23**, 1979.