Pergamon

0031-9422-(95)00091-7

*Phytochemistry*, Vol. 39, No. 4, pp. 795 800, 1995

0031-9422/95 $9.50 + 0.00

# SESQUITERPENE LACTONES, A LABDANE AND OTHER CONSTITUENTS OF *UROLEPIS HECATANTHA* AND *CHROMOLAENA ARNOTTIANA*

ADRIANA N. DE GUTIÉRREZ, CESAR A. N. CATALÁN, JESÚS G. DÍAZ* and WERNER HERZ*

Instituto de Quimica Orgánica, Facultad de Bioquímica, Química y Farmacia, Universidad Nacional de Tucumán, Ayacucho 491, 4000 S. M. de Tucumán, Argentina; *Department of Chemistry, The Florida State University, Tallahassee, FL 32306-3006, U.S.A.

(*Received* 9 *Novemeber* 1994)

**Key Word Index**— *Urolepis hecatantha*; *Chromolaena arnottiana*; Eupatorieae; Compositae; sesquiterpene lactones; heliangolides; labdane; benzofurans; *Z*, *E*-farnesol derivative; flavonoids.

**Abstract**—Aerial parts of *Urolepis hecatantha* afforded several heliangolides, a new labdane, the oleate of 9-hydroxy-*Z*, *E*-farnesol, a new toxol and isopentenylacetophenone derivatives as well as a number of common plant constituents. Aerial parts of *Chromolaena arnottiana* contained 5,3'-dihydroxy-6,7,4'-trimethoxyflavone, 5-hydroxy-6,7,3',4'-teramethoxyflavone, 5-hydroxy, 6,7,3',4',5'-pentamethoxyflavone, other common plant constituents and a derivative of 3,4-dihydroxyacetophenone.

## INTRODUCTION

*Urolepis* (DC.) R. King and H. Robins. is a monotypic genus of Eupatorieae, subtribe Gyptidinae, earlier subsumed in *Eupatorium* as section *Urolepis* [1]. In the present paper we describe the chemistry of a collection of *Urolepis hecatantha* (DC.) R. King and H. Robins. from Bolivia. Isolated were the sesquiterpene lactones eupaformosanin (**1**) [2], eucannabinolide (**2a**) [3, 4], hyodorilactone C (**2b**) [5, 6], a mixture of **2c** [7,8] and **2d** [6, 8], a mixture of **3** and **4**, the new labdane **5**, the oleic acid ester **6**, the benzofuran derivatives **7a**, **b** and the methyl ether **8**. Other substances identified in the extract were grandifloric acid, the flavonoids retusin (5-hydroxy-3,7,3',4'-tetramethoyflavone) and oxyayanin B (5,6,3'-trihydroxy-3,7,4'-trimethoxyflavone), euparin, 6-methoxyeuparin, vomifoliol, pinoresinol and stigmasterol.

*Chromolaena arnottiana* (Griseb.) R. King and H. Robins. has been studied twice previously. The roots of a collection from Bolivia furnished furanocadinanes and a norcadinane [9] while the roots of a collection from an unspecified location in Argentina contained common chromanes and a benzofuran [10]. Aerial parts of the former afforded only common terpenoids and a *p*-hydroxycinnamate ester, while aerial parts of the latter gave a cadinane. Our own collection from Catamarca Province, Argentina, furnished eupatorin (5,3'-dihydroxy-6,7,4'-trimethoxyflavone), eupatilin (5-hydroxy-6,7,3',4'-tetramethoxyflavone) and 5-hydroxy-6,7,3',4',5',-pentamethoxyflavone as well as the 3,4-dihydroxyacetophenone derivative **11**, loliolide, α- and β-amyrin, stigmasterol and sitosterol.

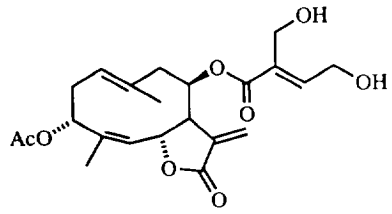
## DISCUSSION

The components of the mixture of **3** and **4** were identified by their $^1$H NMR spectra (Table 1) and extensive decoupling. In particular the NMR spectrum of **4** closely resembled the spectra of **9a** (calbenolide C) [11], **9b** (jamaicolide C) [12] and **9c** [13]* if allowance is made for the absence of an esterifying group on the C-8 hydroxyl of **4**. This resulted in an upfield shift of H-8 as compared with H-8 of **9a** and **b**, while the coupling constants remained constant. On the other hand, the coupling constants involving H-3 of **4** (12.5 and 4 Hz) differed considerably from those involving H-3 of **9a–c** (*ca* 5 and 3 Hz) indicating that the C-3 stereochemistry was inverted, while the chemical shift was close to H-3 of **9c** and 1 ppm downfield from H-3 of **9a** and **b**. The small values of $J_{7,13}$ (2.5 and 2 Hz) and $J_{6,7}$ (2.5 Hz) indicate the presence of a heliangolide while the values of $J_{7,8}$, $J_{8,9a}$ and $J_{8,9b}$ indicate β-orientation of the substituent on C-8.

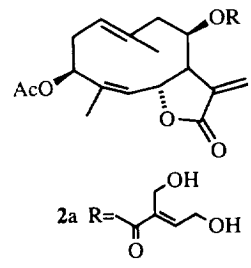
Lactone **4** may be an artefact as prolonged exposure of the lactone mixture to chloroform-*d* followed by removal of solvent resulted in essentially complete conversion of lactone **3** to lactone **4**. Other than conversion of the methyl singlet of **3** to a pair of slightly broadened olefinic singlets the transformation was accompanied by a significant diamagnetic shift of H-1, changes in the coupling constants involving H-1 and H-2a,b as well as smaller changes in the chemical shifts of H-9a,b.

The structure of **5** was deduced from the mass and $^1$H NMR spectra (Table 2). Decoupling permitted assignment of all signals. Two hydroxyl groups were located at

*The C-2 stereochemistry of **9c** from *Stevia alpina* was incorrectly represented on the formula page of ref. [13].



**1**

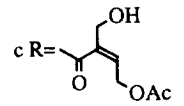


**2a** R=

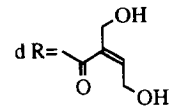


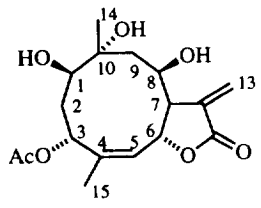
b R=H

c R=

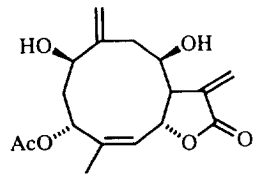


d R=

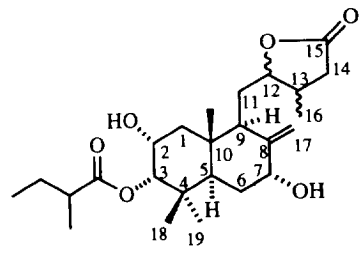




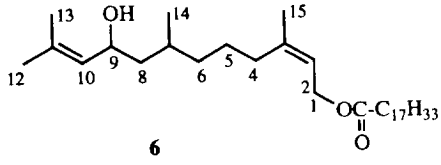
**3**



**4**



**5**

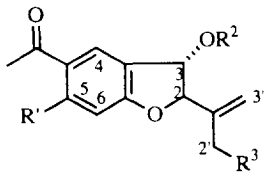


**6**

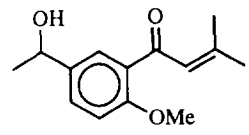
C-2 and C-7 while a 2-methylbutyrate was attached to C-3. The coupling constants involving H-2 and H-3 showed that both substituents were α-orientated, i.e. equatorial at C-2 and axial at C-3, while the coupling constants involving H-7 showed that the C-7 hydroxyl was α-orientated and axial. These assignments were verified by the NOE data listed in Table 3. A further oxygen substituent was situated at C-12; the chemical shift ($\delta$4.08) and further decoupling, which showed that a neighbouring proton (H-13) was spin-coupled to a methyl group (H-16) and to two mutually coupled protons (H-14a,b) obviously adjacent to a carbonyl function ($J_{14a,b}$ = 17 Hz), led to completion of the side chain attached to C-9.

The relative stereochemistry of the lactone ring remains in some doubt. Irradiation at the frequency of H-16 produced an enhancement in the signals of H-13 and H-14b which partially overlap but had no effect on the signals of H-11α or H-11b, whereas irradiation at the frequency of H-12 produced a small enhancement in the signal of H-16. This suggests that C-11 and C-16, and, therefore, H-12 and H-13, are *trans* with respect to each other on the lactone ring, a suggestion which may conceivably be accommodated by the large value of $J_{12,13}$ (11 Hz). A somewhat similar lactone, **10**, whose stereochemistry was established by X-ray crystallography has been isolated from *Koanophyllon villosum* (Sw.) R. King and H. Robins. (old synonym *Eupatorium villosum* Sw.) [14].

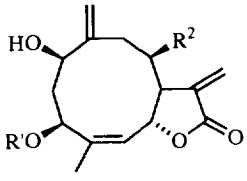
The structure of **6** was deduced from the mass and $^1$H NMR spectra listed in the Experimental. The *Z*-configuration of the 2,3-double bond was evident from the chemical shift of H-15, $\delta$1.76 and *cis* with respect to H-2 at $\delta$5.43, while assignment of the hydroxyl to C-9 was based on H-9 at $\delta$4.51 being vicinally coupled to two geminally coupled protons (signals at $\delta$2.24 and 2.18) as well as to a vinylic proton (signal at $\delta$5.18) which in turn was allylically coupled to the two terminal methyl groups



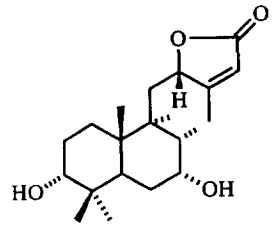
7 a R'=OH, $R^2$, $R^3$=H
b R'=H, $R^2$=Ang, $R^3$=OH



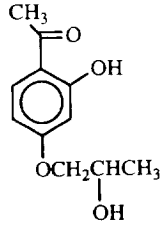
8



9 a R'=H, $R^2$=OTig
b R'=H, $R^2$=OAng
c R'=Ac, $R^2$=H



10



11

Table 1. $^1$H NMR spectra of compounds **3** and **4** ($CDCl_3$, 500 MHz)

| H | 3* | 4 |
|---|---|---|
| 1 | 4.98 *t* (8) | 3.95 *dd* (12.5, 4) |
| 2a | 2.77 *ddd* (11, 8, 4.5) | 2.73 *ddd* (12.5, 12.5, 4) |
| 2b | 2.03*m* | 2.22 *ddd* (12.5, 12.5, 4) |
| 3 | 5.58 *dd* (12.5, 5) | 5.75 *dd* (12.5, 4) |
| 5 | 5.20 *dq* (11, 1) | 5.36 *dq* (10.5, 1) |
| 6 | 5.28 *br d* (11, 2) | 5.52 *dd* (10.5, 2.5) |
| 7 | 2.84 *m* | 2.84 *m* |
| 8 | 4.20 *br t* (2.5) | 4.13 *br t* (2.5) |
| 9a | 2.47 *dd* (14, 2.5) | 2.43 *br dd* (14, 2.5, 1) |
| 9b | 2.33 *dd* (14, 2.5) | 2.76 *dd* (14, 2.5) |
| 13a | 6.40 *d* (2.5) | 6.42 *d* (2.5) |
| 13b | 5.69 *d* (2.5) | 5.73 *d* (2) |
| 14 | 1.26†*s* | 5.86 *br s* |
| | | 5.56 *br s* |
| 15† | 1.77 *br s* | 1.82 *2d* (1) |
| Ac† | 2.08 *s* | 2.09 *s* |

*From mixture with **4**.
†Intensity three protons.

on C-11. NMR signals of **7b**, **8** and **11**, the latter from *Chromolaena arnottiana*, which appear to be new are also given in the Experimental. In the case of **8**, NOE spectrometry showed that the methyl ether was on the aromatic ring and not on the hydroxyethyl side chain. In the case of **11**, the presence of bonded hydroxyl signal in the $^1$H NMR spectrum showed that the ether function was located on C-4.

The chemistry of *Urolepis* displays affinities with the chemistry of members of subtribes Eupatorieae and Gyptidinae but not with the chemistry of those members of subtribe Hebecliniinae for which information is available [15–22].

## EXPERIMENTAL

*General.* For sepn of mixts, HPLC with a differential refractometer was used. The columns employed were (A) a phenomenex Ultremex 5C18 (5 $\mu$, 250 × 10 mm) and (B) a Phenomenex Maxsil 10C8 (10 $\mu$, 500 × 10 mm). Retention times were measured from the solvent peak.

Table 2. $^1$H NMR spectrum of compound **5** ($CDCl_3$, 500 MHz)

| H | | H | |
|---|---|---|---|
| 1α | 1.46 *dd* (12, 12) | 14a | 2.73 *dd* (17.8) |
| 1β | 1.75 *dd* (12, 4) | 14b | 2.17 *dd* (17, 8) |
| 2β | 4.18 *ddd* (12, 4, 2.5) | 16 | 1.16 *d* (7) |
| 3β | 4.92 *d* (2.5) | 17a | 5.15 *br* |
| 5α | 2.07 *dd* (14, 3) | 17b | 4.83 *d* (1.5) |
| 6α | 1.80 *ddd* (11, 3, 3) | 18 | 0.92 *s** |
| 6β | 1.60 *ddd* (14, 11, 3) | 19 | 0.95 *s** |
| 7β | 4.43 *br t* (3) | 20 | 0.74 *s** |
| 9α | 2.42 *br dd* (11, 2.5) | 2′ | 2.52 *sext* (7) |
| 11a | 1.92 *ddd* (14.5, 11, 5) | 3′a, b | 1.74 *m* |
| 11b | 1.77 *ddd* (14.5, 8, 2.5) | 4′ | 0.96 *t* (7)* |
| 12 | 4.08 *ddd* (11, 8, 5) | 5′ | 1.20 *d* (7)* |
| 13 | 2.24 *dtq* (11, 8, 7) | | |

*Intensity three protons.

Table 3. NOE difference spectrum of compound **5**

| Irradiated | Observed (%) |
|---|---|
| H-2β | H-3β (5.8), H-18 (3.8), H-20 (5) |
| H-3β | H-2β (8.1), H-18 + H-19 (5.4) |
| H-5α | H-9α (4.9), H-19 (2.6) |
| H-7β | H-6β (7.3 ), H-6α (1.9), H-17a (7.6), |
| H-9α | H-5α (5.4) |
| H-12 | H-16 (1.4), H-17b (1.6) |
| H-13, H-14b | H-14a (9.9), H-16 (1.6), H-9 (4.9) |
| H-16 | H-13 + H-14b (3.3) |
| H-17a | H-6β (3), H7β (6.8), H-17b (18.9) |
| H-17b | H-11a (6.4), H-17a (21. 4) |
| H-20 | H-2β (2.6), H-18 (2.4) |

*Plant material.* Aerial parts of *Urolepis hecatantha* (DC.) R. King and H. Robins. were collected at the flowering stage on 19 October 1992 at Las Maras, Santa Cruz de la Sierra, Bolivia. Aerial parts of *Chromolaena arnottiana* (Griseb.) R. King and H. Robins. were collected on 5 March 1989 on the road to las Estancias, Catamarca Province, Argentina. Voucher specimens are on deposit in the herbarium of the Instituto Miguel Lillo, Tucumán (C. Catalán No. 584 resp. Slanis-Catalán Lil No. 72).

*Extraction and isolation.* (a) Flowers and leaves of *Urolepis hecatantha* (600 g) were extracted with $CHCl_3$ (3 × 8 l) at room temp. for 5 days to give 96 g of crude extract a portion of which (50 g) was suspended in EtOH(860 ml) at 55°, diluted with $H_2O$ (640 ml) and extracted successively with hexane (3 × 500 ml) and $CHCl_3$ (3 × 500 ml).

Evapn of the hexane fr. gave 21 g of residue. A 10 g portion was submitted to CC (silica gel, 300 g) using hexane with increasing amounts of $Et_2O$ (0–30%) all frs being monitored by TLC. This gave 300 mg of material with the same $R_f$ as β-amyrin. A portion of this material was processed by HPLC (column A, MeOH, 2.0 ml min$^{-1}$) to give undefined material, ($R_t$ 7.0 min), 7.9 mg of hydrocarbons (51 min) and a number of partially resolved peaks which were rechromatographed on column A (MeCN–EtOAc, 3:1, 2.0 ml min$^{-1}$) to give hydrocarbons ($R_t$ = 15.2 min), and 0.9 mg of **6** ($R_t$ 22.9 min) followed by hydrocarbons ($R_t$ 24.9 and 28.9 min) and 0.9 mg of stigmasterol ($R_t$ 3.4 min).

The residue from the $CHCl_3$ extract (17 g) was subjected to CC (silica gel, 600 g) using $CHCl_3$ with increasing amounts of EtOAc (0–30%), 153 frs being collected. Frs 15–16 were combined; trituration of the residue with $Et_2O$ afforded 4.0 mg of euparin, mp 118–120° identified by mass and $^1$H NMR spectrometry. Frs 17–24 (260 mg) were subjected to flash chromatography (florisil, hexane–$Et_2O$, 2:1) to give 8 frs. Frs 1 and 2 (23 mg) on processing by HPLC (column A, MeOH–$H_2O$, 3:2, 2.0 ml min$^{-1}$) afforded unidentified mixtures while frs 3–8 decomposed extensively during processing. Frs 25–28 of the original chromatogram (210 mg) also decomposed. Trituration of fr. 46 with $Et_2O$ gave 1 mg of a mixture of retusin and oxyayanin B; the ethereal washings contained unidentified material. Frs 47–54 (300 mg) were combined, decolorized with charcoal and processed by HPLC (column A, MeOH–$H_2O$, 4:3, 2.0 ml min$^{-1}$) to give 12 mg of grandifloric acid ($R_t$ 4.3 and 15.8 min) identified by MS and $^1$H NMR spectrometry. Frs 64–66 on combination and processing by HPLC (column A, MeOH–$H_2O$, 2.0 ml min$^{-1}$) gave 7.7 mg of **7a** ($R_t$ 12.4 min) identified by mass and $^1$H NMR spectrometry and, after rechromatography, 0.6 mg of **8**. Frs 67–70 on combination and flash chromatography (silica gel, $CHCl_3$–EtOAc, 7:1) gave 5 mg of retusin identified by MS and $^1$H NMR spectrometry, 2.5 mg of a flavonoid mixture containing mainly retusin, and a mixture which on processing by HPLC (column A, MeOH–$H_2O$ 3:2, 2.0 ml min$^{-1}$) furnished 0.9 mg of 6-methoxyeuparin ($R_t$ 15.6 min) identified by mass and $^1$H NMR spectrometry.

Frs 71–75 were also processed by HPLC (column B, MeOH–$H_2O$, 4:3, 2.0 ml min$^{-1}$) to give 3 mg of pinoresinol ($R_t$ 7.7 min) identified by comparison with authentic material, 7.6 mg of **2b** ($R_t$ 10.5 min), 2.0 mg of the mixture of heliangolides **3** and **4** ($R_t$ 12.6 min), 1.4 mg of **7b** ($R_t$ 21.9 min) and 6.6 mg of a mixture of flavonoids ($R_t$ 36.7 min). Frs 76–89 gave unidentifiable mixtures. Frs 90–92 on processing by HPLC (column B, MeOH–$H_2O$, 4:3, 2.0 ml min$^{-1}$) gave 8.1 mg of labdane **5** ($R_t$ 10.2 min) and 3.7 mg of a mixture of **2c** and **d** ($R_t$ 18.5 min).

Frs 102–107 on processing by HPLC (column A, MeOH–$H_2O$, 1:1, 2.0 ml min$^{-1}$) gave unidentifiable material and mixtures which on further HPLC (column B, MeOH–$H_2O$, 1:1, 2.0 ml min$^{-1}$) gave 1.8 mg of vomifoliol identified by mass and $^1$H NMR spectrometry, mixtures, 5.3 mg of **2a** ($R_t$ 13.0 min) and 5.8 mg of **1**. Frs 112–115 on processing by HPLC (column A, MeOH–$H_2O$, 1:1, 2.0 ml min$^{-1}$) gave 4.2 mg of unidentifiable material ($R_t$ 8.3 min), 21 mg of **2a** ($R_t$ 11.2 min) and a mixture which on rechromatography (column B) afforded 0.9 mg of **1**. Frs 135–139 on HPLC as above furnished an additional 3.5 mg of **1** ($R_t$ 24.0 min) and 10.5 mg of **2a** ($R_t$ 5.0 min). Frs 140–146 on HPLC (col-

umn A, MeOH–$H_2O$, 1:1, 2.0 ml $min^{-1}$) gave 11.7 mg of **2a** and a fraction which on rechromatography over column B gave 1.9 mg of **1**.

(b) Flowers and leaves of *Chromolaena arnottiana* (150 g) on extraction with $CHCl_3$ (3 × 3 l) at room temp. for 5 days gave 12 g of crude extract which was suspended in 103 ml of EtOH at 55°, diluted with 77 ml of $H_2O$ and extracted successively with hexane (3 × 100 ml) and $CHCl_3$ (3 × 100 ml). Evapn of the hexane fr. gave 4.9 g of residue which was chromatographed over silica gel using hexane with increasing amounts of $Et_2O$ (0–30 %), all frs being monitored by TLC. This gave 150 mg of material with the same $R_f$ as β-amyrin and 260 mg of material with $R_f$ close to cholesterol. HPLC (column A, MeOH, 2.0 ml $min^{-1}$) of a portion of the triterpene fr. gave 1.8 mg of β-amyrin, 4.5 mg of α-amyrin and 1.0 mg of high $M_r$ linear alcohols. HPLC of a portion of the sterol fr. in the same manner gave 7.7 mg of stigmasterol, 10.0 mg of sitosterol and 2.2 mg of long-chain linear alcohols.

The residue from the $CHCl_3$ extract (3.2 g) on chromatography over silica gel (160 g) using $CHCl_3$–$Et_2O$ mixtures (0–25%) followed by $CHCl_3$ and EtOAc (0–30%) furnished 19 frs. Fr. 2 on flash chromatography ($CHCl_3$–$Et_2O$, 25–50%) gave 9 mg of eupatorin. Frs 3–5 on flash chromatography and prep. TLC of the several frs afforded 50 mg of mixtures of eupatilin and 5-hydroxy-6,7,3′,4′,5′-pentamethoxyflavone in various proportions. Combination of frs 6–11 and rechromatography (silicia gel, $CHCl_3$–EtOAc, 0–30%) give 9 frs. HPLC of fr. 3 (column B, MeOH–$H_2O$, 3:2, 2 ml $min^{-1}$) gave 1 mg of **11** ($R_t$ 12.5 min). Trituration of fr. 4 with MeOH resulted in sepn of very polar solid material; HPLC of the solution in the same names afforded 1.2 mg of loliolide ($R_t$ 4.5 min). HPLC of frs 5–10 and 12–13 resulted in eluates containing small amounts of the flavone mixture, loliolide and unidentifiable material.

*Mixture of* (1R*, 3R*, 6R*, 7R*, 8R*, 10R*)-3-*acetoxy*-1,8,10- *trihydroxyhelianga* 4, 11 (13)-*dien*-6, 12-*olide and* (1R*, 3R*, 6R*, 7R*, 8R*)-3-*acetoxy*-4,10(14),11(13)-*trien*-6, 12-*olide* (**3** *and* **4**). Gum, PCI-MS ($NH_3$) *m/z* (rel. int.): 358 (86.9) $[C_{17}H_{24}O_7 + NH_3 + H]^+$), 340 (9.80) $[C_{17}H_{22}O_6 + NH_3 + H]^+$, 322 (100); $^1$H NMR spectrum in Table 1.

2α,7α-*Dihydroxy*-3α(2′-*methylbutanoyloxy*)8(17)-*labden*-12, 15-*olide* (**5**). Gum; PCI -MS ($NH_3$) *m/z* (rel. int.): 454 (100) $[C_{25}H_{40}O_6 + NH_4]^+$; $^1$H NMR spectrum in Table 2.

2Z,6E-9-*Hydroxyfarnesyloleate* (**6**). Gum, PCI-MS ($NH_3$) *m/z* (rel. int.): 303 ($[M + NH_3 + H]^+$, 14.4), 287(46.9), 271 (100); $^1$H NMR (500 MHz, $CDCl_3$): δ5.43 (*br t*, *J* = 7 Hz, H-2), 5.34 (*m*, 2H, H-9′, H-10′), 5.18 (*dq*, *J* = 8, 1Hz, H-10),5.03 (*qq*, *J* = 6.5, 1 Hz, H-6), 4.60 (2H, *d*, *J* = 7 Hz, H-1a,b), 4.51 (*td*, *J* = 8, 5 Hz, H-9), 2.29 (2H, *t*, *J* = 8 Hz, H-4a,b), 2.24 (*dd*, *J* = 13, 8 Hz, H-8a), 2.18 (*dd*, *J* = 13, 5 Hz, H-8b), 2.05 (2H, *m*, H-5a, b), 2.0 (4H, *m*, H-8′, H-11′), 1.76 (3H, *br s*, H-15), 1.69 (3H, *d*, *J* = 1.5 Hz) and 1.68 (3H, *d*, *J* = 1 Hz, H-12 and H-13), 1.65 (4H, *m*), 1.60 (3H, *br s*, H-14), 1.33–1.27 *m*, 0.88 (3H, *t*, *J* = 7 Hz, H-18′).

2,3-*Dihydro*-trans-2-(2′-*hydroxyisopropenyl*) 3-*angelyloxy*-6-*acetylbenzofuran* (**7b**). PCI-MS (isobutane) *m/z* (rel. int.): 219 (14.3), 201 (50.5), 115 (65.5), 99 (100); $^1$H NMR (500 MHz, $CDCl_3$): δ8.07 (*d*, *J* = 1.5 Hz, H-4), 8.01 (*dd*, *J* = 8, 1.5 Hz, H-6), 6.98 (*d*, *J* = 8 Hz, H-7), 6.44 (*qt*, *J* = 7, 1 Hz, H-3 of angelate), 6.27 (*d*, *J* = 2.5, H-3), 5.15 (*br d*, *J* = 2.5, H-2), 5.09 and 4.99 (both *br s*, H-3′ a, H-3′b), 4.25 and 4.23 (both *d*, *J* = 14 Hz, H-2′a,b), 2.55 (3H, *s*, MeCO), 2.05 (3H, *br d*, *J* = 7 Hz, H-4′ of angelate), 1.77 (3H, *br s*, H-5′ of angelate).

2-(β,β-*Dimethylacrylyl*)-4-*hydroxyethylanisole* (**8**). MS (PCI, isobutane) *m/z* (rel. int.): 235 (100, $[M + H]^+$); 1H NMR (500 MHz, $CDCl_3$): δ7.54 (*d*, *J* = 2.5 Hz, H-3), 7.45 (*dd*, *J* = 8.5, 2.5 Hz, H-5), 6.93 (*d*, *J* = Hz, H-6), 6.61 (*sept*, *J* = 1.5 Hz, H-2″), 4.88 (*q*, *J* = 7 Hz, H-1″), 3.87 (3H, *s*, OMe), 2.22 and 1.96 (each 3H and *br*, H-3′ and H-4′), 1.49 (3H, *d*, *J* = 6.5, H-2″).

2-*Hydroxy*-4-(2′-*hydroxypropoxy*)-*acetophenone* (**11**). MS (PCI, isobutane) *m/z* (rel. int.): 211 (100, $[M + H]^+$); $^1$H NMR (500 MHz, $CDCl_3$): δ12.96, (*s*, bonded-OH), 7.55 (*dd*, *J* = 9, 1 Hz, H-5), 6.86 (*d*, *J* = 9 Hz, H-6), 6.70 (*d*, *J* = 1 Hz, H-3), 3.90 (*br dd*, *J* = 11, 6.5 Hz, H-1′a), 3.87 (*br dd*, *J* = 11, 5.5 Hz, H-1′b), 3.21 (*ddq*, *J* = 6.5, 5.5, 7 Hz, H-2′), 2.77 (*s*, 3H, Me of methyl ketone), 1.41 (*d*, *J* = 7 Hz, 3p, H-3′).

*Acknowledgements*—Work in Tucumán was supported by grants from Consejo Nacional de Investigaciones Cientificasy Técnicas and Consejo de Investigaciones de la Universidad de Tucumán.

## REFERENCES

1. King, R. M. and Robinson, H. (1987). *The Genera of the Eupatorieae* (*Asteraceae*), Monographs in Systematic Botany, Vol. 22, pp. 89–92. Missouri Botanical Gardens.
2. Lee, K.-H., Kimura, T., McPhail, A. T., Onan, K. D. and Huang, H.-C. (1977) *Phytochemistry* **16**, 1068.
3. Drozdz, B., Grabarczyk, H., Samek, Z., Holub, M., Herout, V. and Sorm, F. (1972) *Collec. Czech. Chem. Commun.* **37**, 1546.
4. Herz, W. and Govindan, S. V. (1980) *Phytochemistry* **19**, 1234.
5. Takahashi, T., Ibo, H., Ichimura, T. and Murae, T. (1978) *Chem. Letter* 1345.
6. Takahashi, T., Ichimura, T. and Murae, T. (1979) *Chem. Pharm. Bull.* **27**, 2539.
7. Bohlmann, F., Schmeda-Hirschmann, G. and Jakupovic, J. (1984) *Phytochemistry* **23**, 1435.
8. Calderon, J. S., Quijano, L., Gomez, F. and Rios, T. (1987) *J. Nat. Prod.* **50**, 522.
9. Bohlmann, F., Zdero, C., King, R. M. and Robinson, H. (1979) *Phytochemistry* **18**, 1177.
10. Boeker, R., Bohlmann, F. and King, R. M. (1986) *Rev. Latinoam. Quim.* **17**, 47.
11. Ober, A. G., Urbatsch, L. E. and Fischer, N. H. (1985) *Phytochemistry* **24**, 1743.

12. Ober, A. G. and Fischer, N. H. (1986) *Phytochemistry* **25**, 877.
13. De Heluani, C. S., de Lampasona, M. P., Catalán, C. A. N., Goedken, V. L., Gutiérrez, A. B. and Herz, W. (1989) *Phytochemistry* **28**, 1931.
14. Manchand, P. S., Blount, J. F., McCabe, T. and Clardy, J. (1979) *J.Org. Chem.* **44**, 1322.
15. Bohlmann, F. and Grenz, M. (1977) *Chem. Ber.* **110**, 1321.
16. Bohlmann, F., Zitzkowski, Suwita, A. and Fiedler, L. (1978) *Phytochemistry* **17**, 2101.
17. Alvarado, S., Ciccio, J. C., Calzado, J., Zabel, V. and Watson, W. H. (1979) *Phytochemistry* **18**, 330.
18. Castro, V., Ciccio, J. C., Alvarado, S., Bohlmann, F., Schmeda-Hirschmann, G. and Jakupovic, J. (1983) *Liebigs Ann.* 975.
19. Miski, M., Gage, D. A. and Mabry, T. J. (1985) *Phytochemistry* **24**, 3078.
20. Gao, F., Miski, M. and Mabry, T. J. (1986) *Phytochemistry* **25**, 1231.
21. de Luengo, D. H., Miski, M., Gage, D. A. and Mabry, T. J. (1986) *Phytochemistry* **25**, 1917.
22. Miski, M., de Luengo, D. H. and Mabry, T. J. (1987) *Phytochemistry* **26**, 199.