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PHENYLPROPANOIDS AND OTHER DERIVATIVES FROM *THAPSIA VILLOSA*

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Key Word Index—*Thapsia villosa*; Umbelliferae; roots; phenylpropanoids; hemanticine; guaianolides; thapsivillosin K.

Abstract—Five phenylpropanoids related to hemanticine have been obtained from *Thapsia villosa* roots. We propose for these substances the trivial names isohelmanticine, neohelmanticine, isoneohelmanticine, epoxyhelmanticine and epoxyhelmanticine angelate. All these substances are based on (1*S*,2*R*)1-(3-methoxy-4,5-methylenedioxyphenyl)-1,2-propanediol, which is esterified variously by acetic, angelic, epoxyangelic and/or (2*R*,3*S*)2,3-dihydroxy-2-methylbutyric acids. We also report three C_6-guaianolides and their hydrolysis products. The name thapsivillosin K is proposed for a new guaianolide.

INTRODUCTION

The extracts from *Thapsia villosa* have been studied previously and the presence of some guaianolides, germacrane esters and phenylpropanoids was reported [1–3]. The phenylpropane ester helmanticine (**1**) is one of the most abundant components of the benzene extract from the roots of the plant [2]. We now report the isolation of five new phenylpropanoids **2–6** related to helmanticine, and also latifolone, thapsivillosin C and K, thapsitranstagin, falcarindiol and 6-methoxy-7-geranyloxycoumarin.

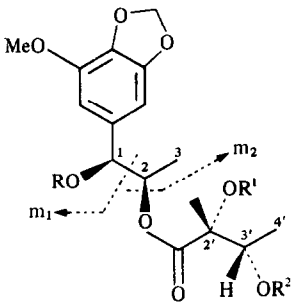
RESULTS AND DISCUSSION

The natural compound isohelmanticine (**2**) was the least polar of the new phenylpropanoids isolated from the benzene extract of *T. villosa* roots. It was a thick oil which showed IR bands corresponding to hydroxyl (3500 cm^{-1}), aromatic ring (1605, 1505 cm^{-1}) and ester group absorbances (1715 cm^{-1}). Alkaline hydrolysis of **2** gave the same products as those isolated from helmanticine: the aromatic diol **8**, 2,3-dihydroxy-2-methylbutyric and angelic acids. The ^1H NMR spectra of isohelmanticine (**2**) and **1** were very alike; however, the new compound showed a signal at δ2.98 (1H, *q*, J = 6 Hz, H-3′) corresponding to a proton geminal to a hydroxyl group which can be easily acetylated to yield **7** [δ5.25 (1H, *q*, J = 6 Hz, H-3′), 1.98 (3H, *s*, Ac)]. Taking into account these data and the molecular formula $C_{28}H_{36}O_{11}$ deduced from the MS of **7** (m/z = 548 $[M]^+$) we propose for isohelmanticine structure **2**.

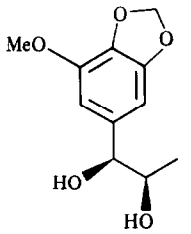
The phenylpropanoids which we have named neohelmanticine (**3**) and isohelmanticine (**4**) are isomers with the molecular formula $C_{23}H_{30}O_{10}$ (m/z = 466 $[M]^+$). Both substances contain a tertiary hydroxyl group (ν3500 cm^{-1}), one acetyl group [**3**: δ1.95 (3H, *s*); **4**: 1.99 (3H, *s*)], a single angeloxy residue [**3**: δ6.10 (1H, *q*, J = 6.5 Hz); **4**: 5.83 (1H, *q*, J = 4.5 Hz)], the characteristic signals of the aromatic diol **8** (esterified) and the 2,3-dihydroxy 2-methylbutyric ester. Neither compound could be acetylated with acetic anhydride and pyridine. The similarity of the IR and ^1H NMR spectra of neohelmanticine (**3**) and **1**, the almost coincident chemical shift of H-1 in both compounds and the presence of the mass fragments m_1 at m/z 263 and m_2 m/z 290 amu, led us to propose structure **3** for neohelmaticine. On the other hand, the benzylic proton H-1 appears at higher fields in isoneohelmanticine than in the preceding phenylpropanoids and the fragments m_1 and m_2 can be found at m/z 223 and 250 amu respectively. In this case, the acetoxy group must be placed at the benzylic position and the angeloxy residue has to be linked to the dihydroxymethylbutyric group (Dhmb), as shown in structure **4**.

Epoxyhelmanticine (**5**) also contains a free tertiary hydroxyl group (ν3500 cm^{-1}, and fails to react with Ac_2O–pyridine). Its ^1H NMR spectra showed the same proton signals as helmanticine but one of the angeloxy residues must be epoxidized as suggested by the shielding of two methyl groups at δ1.45 (3H, *s*) and 1.25 (3H, *d*, J = 6 Hz), and by one of the proton quartets which absorbs at δ2.95 (1H, *q*, J = 6 Hz). The empirical formula deduced from the MS, $C_{26}H_{34}O_{11}$ (m/z 522, $[M]^+$) and the observed fragment at m/z 406 ($[M-EpoxyAngOH]^+$) also confirms the presence of an epoxyangelic ester. The m_1 and m_2 peaks appear at the same m/z as in helmanticine (263 and 290 amu) and consequently, the epoxyangelic acid must be attached to the dihydroxymethylbutyric residue, as shown in **5**.

The spectroscopic characteristics of the phenylpropanoid epoxyhelmanticine angelate (**6**), are very similar to those of helmanticine. Alkaline hydrolysis led to **8**, angelic and 2,3-dihydroxy-2-methylbutyric acids (trapped as their 4-phenylphenacyl derivatives [4]). In this compound however, the molecular formula $C_{31}H_{42}O_{13}$ (m/z 622 $[M]^+$) indicates the presence of one further dihydroxymethylbutyric acid residue, by comparison with helmanticine. The new Dhmb fragment has to be placed at the C-3′ position, as shown in structure **6**, in agreement



	R	R¹	R²
1	Ang	H	Ang
2	Ang	Ang	H
3	Ang	H	Ac
4	Ac	H	Ang
5	Ang	H	Epoxy Ang
6	Ang	H	Dhmb Ang
7	Ang	Ang	Ac



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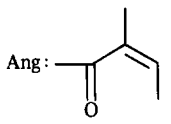
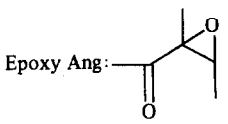
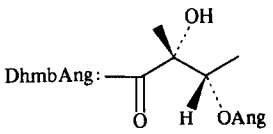
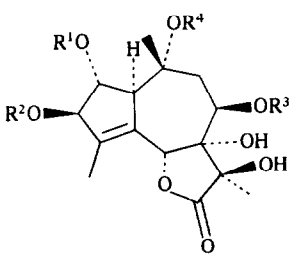
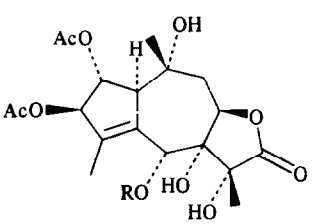




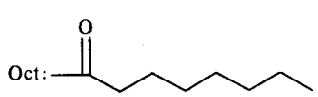


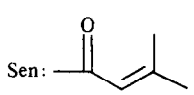


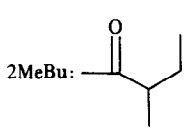
	R¹	R²	R³	R⁴
9	Oct	Ang	2MeBu	Ac
10	3MeBu	Ang	2MeBu	Ac
11	Sen	Ang	2MeBu	Ac
12	Ac	Ac	Ac	H

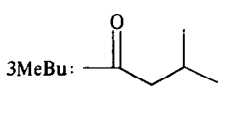


13 R = Ac
14 R = H









with the signals in the mass spectra at *m/z* 406 ([M − AngDhmbOH]$^+$, m_3), 290 (m_2) and 263 (m_1).

We also report the isolation of three guaianolides, thapsitranstagin (**9**) and thapsivillosin C (**10**), products previously reported by Christensen *et al.* [5] and thapsivillosin K (**11**). We identified the ester groups of the sesquiterpene lactones **9** and **10** by alkaline hydrolysis followed by trapping the nucleophilic carboxylate anions with 4-phenylphenacyl bromide [4]. The highly water soluble hydroxylactones were acetylated. Both lactones **9** and **10** give a crude acetylation product from which two triacetates **12** and **13** and a diacetate **14** (further acetylated to give **13**) were isolated. We assign the 8,12-lactone structure to the diacetate because of the spectroscopic

data [δ4.35 (1H, *s*, H-6)] and the hindered nature of the C-6 hydroxyl group, which made acetylation difficult. Consequently, a 6,12-lactone structure was assigned to **12**. These triacetates are in our opinion an easy way to establish the structure of the common nucleus of these guaianolides.

A further lactone **11** structurally related to **9** and **10** showed in its ^{1}H NMR spectra the characteristic signals of the 6,12-guaianolide nucleus [δ5.65 (3H, *m*, H-2, H-6, H-8), 5.49 (1H, *m*, H-3), 4.30 (1H, *m*, H-1), 1.84 (3H, *s*, Me), 1.47 (3H, *s*, Me), 1.43 (3H, *s*, Me)]. Also signals of angelic, acetic and 2,3-dihydroxy-2-methylbutyric residues could be recognised and the remaining signals correspond to a single senecioic group [δ5.65 (1H, *s*), 2.15 (3H, *s*), 1.95 (3H, *s*)]. The mass spectral conditions used to record the spectra of **9**, **10** and **11** favour an easy loss of the acyl substituents on C-2 and on C-9, so that the highest fragments appear in **9** at *m/z* 520 $[M-OctOH]^+$ and 460 $[M-OctOH-AcOH]^+$ and in **10** at *m/z* 460 $[M-2-MeBuOH-AcOH]^+$. The largest fragment from **11** at *m/z* 520 amu implies the presence of an angeloyloxy or a senecioyloxy group on C-2. Nearly all the guaianolides described from *Thapsia* species have an angelate group at C-3 and consequently we tentatively suggest for this lactone a substitution pattern as shown in **11**, with the senecioate ester attached to C-1. This type of substitution has not yet been described before; we propose the name thapsivillosin K for this last guaianolide.

EXPERIMENTAL

Mps are uncorrected, ^{1}H NMR spectra were recorded in a 60 MHz instrument with TMS as an internal standard, and chemical shift values are in δ. EI mass spectra were measured at 70 eV (temp. 180°). Silica gel 60 (Merck 7734) and 60 H (Merck 7736) were used for CC.

Plant material and isolation. The plants were collected and worked up as previously reported [2]. The crude extract (155 g) was chromatographed on silica gel with hexane–EtOAc (97:3) as eluant, doubling the amount of EtOAc every 10 l. After 23.98 g substances already described [2] containing also a 2.25 g fraction of latifolone, 35.1 g of helmanticine and isohelmanticine were obtained, followed by 7.07 g mixture and a 2.29 g fraction containing isoneohelmanticine and 4.04 g fraction containing falcarindiol. Afterwards 6-methoxy-7-geranyloxycoumarin (3.09 g) and a mixture (10.18 g) of neohelmanticine, epoxyhelmanticine and epoxyhelmanticine angelate were eluted. Finally thapsivillosin C (9.96 g), thapsitranstagin (12.59 g) and thapsivillosin K (2.25 g) were obtained.

Latifolone. Crystallized in hexane–Et_2O from the 2.25 g fraction of the main chromatography, showing the same physical constants as those previously reported [6].

Falcarindiol. Rechromatography of the 4.04 g fraction of the main chromatography on silica gel (100 g) eluting with hexane–EtOAc (4:1) yielded 753 mg pure compound whose physical properties are fully consistent with those previously reported [7].

6-Methoxy-7-geranyloxycoumarin. The 3.09 fraction of the main chromatography crystallized from hexane–EtOAc, yielding 1.23 g of a product with constants fully consistent with lit. data [8].

Isohelmanticine (**2**). A part of the fraction containing **1** and **2** (2.0 g) was further chromatographed on silica gel with C_6H_6–EtOAc (97:3). The initial fractions consisted of pure **2**, $[\alpha]_D^{25}$ +9.0° ($CHCl_3$; *c* 0.55); IR ν_{max}^{film} cm^{-1}: 3500, 2870, 1715, 1605, 1505, 1230, 1100. ^{1}H NMR (60 MHz, $CDCl_3$): δ6.55 (2H, *s*, Ar), 6.00 (2H, *m*, 2 Ang), 5.95 (2H, *s*, O–CH_2–O), 5.90 (1H, *d*, *J* = 4.5 Hz, H-1), 5.25 (1H, *dq*, *J* = 4.5 and 6 Hz, H-2), 3.90 (3H, *s*, OMe), 2.98 (1H, *q*, *J* = 6 Hz, H-3'), 2.05–1.80 (12H, *m*, 2 Ang), 1.47 (3H, *s*, Me-2'), 1.30 (3H, *d*, *J* = 6.5 Hz, Me-3), 1.20 (3H, *d*, *J* = 6.5 Hz, Me-4'). *Acetate* (**7**). A portion of the fraction containing **1** and **2** (628 mg) was acetylated (Ac_2O–pyridine room temp.) to give 684 mg of a crude material. Dry CC on silica gel (C_6H_6–EtOAc, 9:1) of the crude reaction product gave helmanticine (**1**, 551 mg [2]) and pure **7** (94.5 mg); IR ν_{max}^{film} cm^{-1}: 2870, 1735, 1715, 1605, 1505, 1225. ^{1}H NMR (60 MHz, $CDCl_3$): δ6.55 (2H, *s*, Ar), 6.00 (2H, *m*, 2 × Ang), 5.95 (2H, *s*, O–CH_2–O), 5.90 (1H, *d*, *J* = 4.5 Hz, H-1), 5.25 (1H, *dq*, *J* = 4.5 and 6 Hz, H-2), 5.25 (1H, *q*, *J* = 6 Hz, H-3'), 1.98 (3H, *s*, Ac), 2.00–1.80 (12H, *m*, 2 × Ang), 1.55 (3H, *s*, Me-2'), 1.30 (3H, *d*, *J* = 6.5 Hz, Me-4'), 1.15 (3H, *d*, *J* = 6.5 Hz, Me-3). EIMS (probe) 70 eV, *m/z* (rel. int.): 548 $[M]^+$ (10), 448 $[M-AngOH]^+$ (4), 405 (4), 311 (6), 290 (70), 261 (12), 208 (11), 191 (25), 179 (70), 43 (100).

Epoxyhelmanticine angelate (**6**). The 10.18 g fraction of the main chromatography was further chromatographed on silica gel H-60 (*p* = 6 atm, 150 g) with C_6H_6–Et_2O (4:1) as eluent. Earlier fractions afforded a mixture of phenylpropanoids (2.53 g). Further chromatography of this fraction yielded 551 mg of a mixture containing neohelmanticine, epoxyhelmanticine and 1.18 g of the oily epoxyhelmanticine angelate, $[\alpha]_D^{25}$ +48.7° ($CHCl_3$; *c* 3.5); IR ν_{max}^{film} cm^{-1}: 3500, 2870, 1740, 1720, 1640, 1510, 1450, 1250, 1230, 1200, 1170, 1100, 1060, 950, 850, 750. ^{1}H NMR (60 MHz, $CDCl_3$): δ6.35 (2H, *s*, Ar), 5.90 (2H, *m*, 2 × Ang), 5.85 (2H, *s*, O–CH_2–O), 5.80 (1H, *d*, *J* = 5 Hz, H-1), 5.05 (3H, *m*, H-2, H-3', H-3''), 1.90 (12H, *m*, 2 × Ang), 1.40 (12H, *m*), 1.30 (3H, *d*, *J* = 6 Hz, Me-3). EIMS (probe), 70 eV, *m/z* (rel. int.): 622 $[M]^+$ (30), 489 (20), 406 $[M-DhmbOH-AngOH]^+$ (20), 290 $[M-2\times DhmbOH-AngOH]^+$ (15), 263 $[M-2\times DhmbOH-AngOH-C_2H_3]^+$ (2), 207 (40), 192 (20), 181 (20), 171 (40), 83 (100), 55 (60), 43 (40).

Hydrolysis and trapping of nucleophilic anions. A soln of **6** (862 mg) in 2 N NaOH–MeOH (3 ml) was kept for 1 hr at room temp. Usual work up and extraction with EtOAc yielded deacylhelmanticine (329 mg). The aqueous residue was concd to 5 ml and HCl was added until phenolphthalein change. After adding EtOH (40 mg) and 4-phenylphenacyl bromide (1.0 g) the reaction mixture was refluxed for 30 min. EtOH was evaporated *in vacuo* and the product chromatographed on silica gel with mixtures of C_6H_6–EtOAc to yield 4-phenylphenacyl angelate (352 mg, mp 89–91°) and 4-phenylphenacyl (2*R*,3*S*)2,3-dihydroxy-2-methylbutyrate (240 mg), $[\alpha]_{365}^{20}$ −97.4° ($CHCl_3$; *c* 0.27), mp 167–169°.

Neohelmanticine (**3**) *and epoxyhelmanticine* (**5**). A fraction containing **3** and **5** (550 mg) was rechromatographed on silica gel H-60 (*p* = 4 atm, 60 g) using as eluent hexane–Me_2CO (9:1). Earlier fractions contained neohelmanticine (174 mg) and afterwards epoxyhelmanticine was eluted (238 mg). *Compound* **3**. Gum, $[\alpha]_D^{25}$ +20.8° ($CHCl_3$; *c* 3.6); IR ν_{max}^{film} cm^{-1}: 3500, 2870, 1740, 1720, 1640, 1620, 1510, 1250, 1240, 1150, 840. ^{1}H NMR (60 MHz, $CDCl_3$): δ6.52 (2H, *s*, Ar), 6.10 (1H, *q*, *J* = 7 Hz, Ang), 5.92 (2H, *s*, O–CH_2–O), 5.82 (1H, *d*, *J* = 5 Hz, H-1), 5.10 (1H, *m*, H-2), 4.95 (1H, *q*, *J* = 7 Hz, H-3'), 3.87 (3H, *s*, OMe), 2.02 (3H, *d*, *J* = 7 Hz, Ang), 1.95 (3H, *s*, Ang), 1.95 (3H, *s*, Ac), 1.30 (3H, *s*, Me-5'), 1.25 (3H, *d*, *J* = 6 Hz, Me-3), 1.23 (3H, *d*, *J* = 7 Hz, Me-4'). EIMS (probe), 70 eV, *m/z* (rel. int.): 466 $[M]^+$ (4), 290 $[M-DhmbOH-AcOH]^+$ (9), 263 (3), 192 (10), 170 (20), 149 (30), 131 (10), 85 (100), 55 (20). *Compound* **5**. Gum, $[\alpha]_D^{25}$ +60.6° ($CHCl_3$; *c* 3.0); IR ν_{max}^{film} cm^{-1}: 3500, 2870, 1750, 1640, 1610, 1510, 1260, 1200, 1150, 1100, 1050, 850, 790, 760. ^{1}H NMR (60 MHz, $CDCl_3$): δ6.40 (2H, *s*, Ar), 5.90 (1H, *q*, *J* = 6 Hz, Ang), 5.86 (2H, *s*, O–CH_2–O), 5.77 (1H, *d*, *J* = 6 Hz, H-1), 5.20 (1H, *m*, H-2), 5.05 (1H, *q*, *J* = 6 Hz, Me-4'), 3.84 (3H, *s*, OMe), 2.95 (1H, *q*, *J* = 6 Hz,

EpoxyAng), 1.78 (3H, *d*, $J = 6$ Hz, Ang), 1.46 (3H, *s*, Ang), 1.45 (3H, *s*), 1.25 (*m*, 12H). EIMS (probe) 70 eV *m/z* (rel. int.): 522 $[M]^+$ (5), 406 $[M - EpoxyAng]^+$ (10), 290 $[M - DhmbOH - EpoxyAng)]^+$ (4), 263 (3), 235 (10), 208 (40), 192 (20), 171 (30), 119 (15), 83 (100), 55 (30), 43 (10).

Isoneohelmanticine (**4**). The 2.29 g fraction of the main chromatography was further chromatographed on silica gel (100 g) eluting with hexane–Me_2CO (9:1), yielding a mixture which was rechromatographed on silica gel H-60 ($p = 4$ atm, 40 g) with $CHCl_3$–Et_2O (9:1) to give 111 mg of **4** as an oil, $[\alpha]_D^{25}$ +39.5 ($CHCl_3$, *c* 1.9); IR ν_{max}^{film} cm^{-1}: 3500, 2870, 1745, 1720, 1650, 1620, 1520, 1450, 1250, 1150, 1100, 850, 760. ^1H NMR (60 MHz, CCl_4): δ6.38 (2H, *s*, Ar), 5.83 (2H, *s*, O–CH_2–O), 5.83 (1H, *q*, $J = 6$ Hz, Ang), 5.65 (1H, *d*, $J = 5$ Hz, H-1), 4.95 (1H, *m*, H-2), 4.95 (1H, *m*, H-3'), 3.83 (3H, *s*, OMe), 2.00 (3H, *d*, $J = 6$ Hz, Ang), 1.99 (3H, *s*, Ac), 1.78 (3H, *s*, Ang), 1.25 (3H, *d*, $J = 6$ Hz, Me-4'), 1.24 (3H, *s*, Me-5'), 1.18 (3H, *d*, $J = 6$ Hz, Me-3). EIMS (probe) 70 eV, *m/z* (rel. int.): 466 $[M]^+$ (10), 406 $[M - AcOH]^+$ (9), 250 $[M - DhmbOH - AcOH]^+$ (23), 223 (4), 192 (40), 181 (80), 171 (15), 153 (15), 123 (20), 119 (30), 117 (30), 95 (20), 91 (20), 83 (100), 55 (80), 43 (40).

Thapsivillosin C (**9**). A 10.18 g fraction containing **9** was further purified by chromatography on silica gel H-60 ($p = 4$ atm, 100 g), eluting with C_6H_6–Et_2O (4:1). The less polar fraction was a gum (7.18 g), which crystallized from C_6H_6–Et_2O affording a product whose physical properties were fully consistent with those described for thapsivillosin C [5]. Hydrolysis of **9** (1.02 g) under the above mentioned conditions, followed by chromatography, led to the following 4-phenylphenacyl derivatives: acetate (108 mg, mp 110–122°), angelate (111 mg, mp 89–91°), dihydroangelate (100 mg, mp 70–72°), octanoate (54 mg, mp 47–50°). Once the phenacyl derivatives were removed, the aqueous soln was basified and kept for 8 hr at room temp. It was then acidified with aqueous HCl, the soln was heated for 5 min and evaporated to dryness. Pyridine (4 ml) and Ac_2O (2 ml) were added and the suspension was kept at room temp. overnight. Usual work up yielded 515 mg of a crude material which could be resolved by chromatography on silica gel with Et_2O–EtOAc (9:1) to give **12** (195 mg), **13** (125 mg) and **14** (26 mg). Further acetylation of **14** (Ac_2O–pyridine) gave triacetate **13**.

2,3,8-*Triacetoxy*-7,10,11-*trihydroxyguaian*-6,12-*olide* (**12**). Mp 218–220° (Et_2O–EtOAc); $[\alpha]_D^{25}$ +30.0° ($CHCl_3$; *c* 0.8). IR ν_{max}^{film} cm^{-1}: 3400 (OH), 2950, 1790 (C=O), 1730 (Ac), 1450, 1380, 1250 (C–O), 1150 (C–O), 1040 (C–O), 930. ^1H NMR (60 MHz, DMSO-d_6): δ7.28 (1H, *s*), 5.95 (1H, *s*) 5.76 (1H, *m*), 5.35 (1H, *m*), 5.15 (2H, *m*), 4.94 (1H, *s*), 2.95 (1H, *m*), 2.12 (3H, *s*, Ac), 2.05 (3H, *s*, Ac), 2.04 (3H, *s*, Ac), 1.55 (3H, *s*), 1.36 (3H, *s*), 1.10 (3H, *s*). EIMS (probe) 70 eV, *m/z* (rel. int.): 336 $[M - AcOH - H_2O]^+$ (2), 276 $[M - 2AcOH - H_2O]^+$ (3), 206 (2), 114 (10), 90 (7), 79 (100), 52 (35), 43 (25).

2,3,6-*Triacetoxy*-7,10,11-*trihydroxyguaian*-8,12-*olide* (**13**). Oil, $[\alpha]_D^{20}$ −37.0° ($CHCl_3$; *c* 1.5), IR ν_{max}^{film} cm^{-1}: 3400 (OH), 2950, 1780 (C=O), 1740 (Ac), 1380, 1250 (C–O), 1110 (C–O), 1050 (C–O), 1000, 950. ^1H NMR (60 MHz, DMSO-d_6): δ8.15 (1H, *s*), 7.25 (1H, *s*), 5.95 (1H, *s*), 5.85 (1H, *s*), 5.40 (3H, *m*), 2.10 (3H, *s*, Ac), 2.02 (3H, *s*, Ac), 1.97 (3H, *s*, Ac), 1.75 (3H, *s*), 1.27 (3H, *s*), 1.04 (3H, *s*). EIMS (probe) 70 eV, *m/z* (rel. int.): 336 $[M - AcOH - H_2O]^+$, 318 $[M - AcOH - 2H_2O]^+$ (5), 276 $[M - 2AcOH - H_2O]^+$ (25), 258 $[M - 2AcOH - 2H_2O]^+$ (2), 206 (20), 188 (55), 145 (30), 137 (30), 125 (50), 111 (50), 108 (50), 95 (50), 91 (75), 83 (95), 78 (100), 43 (95).

2,3-*Diacetoxy*-6,7,10,11-*tetrahydroxyguaian*-8,12-*olide* (**14**). Oil, $[\alpha]_D^{20}$ −84.4° (MeOH; *c* 1.0). IR ν_{max}^{film} cm^{-1}: 3500 (OH), 2900, 1790 (C=O), 1730 (Ac), 1470, 1380, 1270, 1100, 1060, 1040, 1000, 830, 730. ^1H NMR (60 MHz, Me_2CO-d_6): δ5.75 (1H, *br s*, H-3), 5.55 (1H, *t*, $J = 2$ Hz, H-8), 5.30 (1H, *t*, $J = 4$ Hz, H-2), 4.35 (1H, *s*, H-6'), 3.55 (1H, *br s*, H-1), 2.10 (3H, *s*, Ac), 2.00 (3H, *s*, Ac), 1.78 (3H, *s*), 142 (3H, *s*), 1.19 (3H, *s*). EIMS (probe) 70 eV, *m/z* (rel. int.): 294 $[M - AcOH - H_2O]^+$ (10), 276 $[M - AcOH - 2H_2O]^+$ (3), 205 (5), 170 (13), 141 (20), 125 (20), 108 (70), 77 (60), 60 (70), 55 (30), 43 (100).

Thapsitranstagin (**10**). The fraction containing **10** (7.71 g) was further rechromatographed on silica gel H-60 ($p = 4$ atm, 100 g) with C_6H_6–Et_2O (4:1), affording 5.51 g of crude **10** which was crystallized from hexane–C_6H_6, to yield pure **10** (3.50 g) with physical data fully consistent with those previously published for thapsitranstagin [5]. Hydrolysis of the natural product (654 mg) following the above procedure led to a mixture of 4-phenylphenacyl derivatives of the dihydroangelic, angelic, acetic and isovalerianic (mp 78–80°) acids.

Thapsivillosin K (**11**). The fraction containing **11** (2.2 g) was rechromatographed on silica gel (100 g) with C_6H_6–Me_2CO (19:1) as eluent. The crude lactone (1.1) after crystallization from hexane–C_6H_6 (410 mg), had mp 119–121°, $[\alpha]_D^{25}$ −28.6° ($CHCl_3$; *c* 2.5). IR ν_{max}^{film} cm^{-1}: 3400, 2950, 1800, 1780, 1730, 1650, 1450, 1380, 1250, 1150, 1080, 1050, 1000, 850. ^1H NMR (60 MHz, $CDCl_3$): δ6.00 (1H, *q*, $J = 7$ Hz, Ang), 5.65 (4H, *m*, H-2, H-6, H-8, Sen), 5.49 (1H, *m*, H-3), 4.30 (1H, *m*, H-1), 3.85 (1H, *s*), 2.15 (3H, *s*, Sen), 2.00 (3H, *d*, $J = 7$ Hz, Ang), 1.96 (3H, *s*, Ac), 1.95 (6H, *br s*, Ang, Sen), 1.84 (3H, *s*, Me), 1.47 (6H, *s*, 2 × Me), 1.15 (3H, *d*, $J = 7$ Hz, 2-MeBu), 0.90 (3H, *t*, $J = 7$ Hz, 2 MeBu), EIMS (probe) 70 eV, *m/z* (rel. int.): 520 $[M - SenOH]^+$ (0.5), 460 $[M - SenOH - AcOH]^+$ (5), 424 $[M - SenOH - AcOH - 2H_2O]^+$ (15), 276 (3), 188 (7), 160 (12), 159 (12), 128 (10), 115 (13), 100 (12), 83 (100), 55 (60), 43 (30).

REFERENCES

1. Rasmussen, V., Christensen, S. B. and Sandberg, F. (1981) *Planta Med.* **43**, 336.
2. De Pascual Teresa, J., Pascual, M., Arias, A., Hernández, J. M., Morán, J. R. and Grande, M. (1985) *Phytochemistry* **24**, 1773.
3. De Pascual Teresa, J., Morán, J. R., Hernández, J. M. and Grande, M. (1985) *Phytochemistry* **24**, 1779.
4. Nielsen, B. E. and Lemmich, J. (1965) *Acta Chem. Scand.* **19**, 601.
5. Christensen, S. B., Norup, E., Rasmussen, U. and Madsen, J. O. (1984) *Phytochemistry* **23**, 1659.
6. Holub, M., Herout, V. and Sorm, F. (1959) *Collect. Czech. Chem. Commun.* **24**, 3934.
7. Lemmich, E. (1979) *Phytochemistry* **18**, 1195.
8. Larsen, P. K. and Sandberg, F. (1970) *Acta Chem. Scand.* **24**, 1113.