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TOVAROL AND OTHER GERMACRANE DERIVATIVES FROM *THAPSIA VILLOSA*

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Key Word Index—*Thapsia villosa*; *Thapsia villosa* var. *minor*; Umbelliferae; germacrane derivatives; tovarol, shiromodiol and epoxytovarol esters, 1(10),4-bulgaradiene-8-ol.

Abstract—Four tovarol, two epoxytovarol (= shiromodiol) and one diepoxytovarol esters were the new germacrane esters isolated from the roots of *Thapsia villosa* var. *minor*. The structures of these substances were assigned on the basis of spectral data and chemical correlations with shiromodiol. The acid catalysed rearrangement of tavarol yielded 1(10),4-bulgaradiene-8-ol.

INTRODUCTION

We have continued the phytochemical study on the umbelliferous plants *Thapsia villosa* L. var. *villosa* and *Thapsia villosa* L. var. *minor* (Hoff. & Link) Cout. [1].† Both plants are morphologically very alike, but their chemical components are quite different; for example, we have not been able to identify phenylpropanoids or sesquiterpene lactones (guaianolides) in *T. villosa* var. *minor*, substances which are very abundant in *T. villosa* [1, 2]. The only major metabolites which are present in both plants are some germacrane esters whose structures will be discussed in this paper.

RESULTS AND DISCUSSION

The benzene extract from the roots of *Thapsia villosa* var. *minor* was disolved in ether and washed with 4% aq. sodium hydroxide. From the neutral fraction two hydroxyesters **1** and **2** were isolated, and the phenols **3** and **4** were purified from the alkaline phase. Total hydrolysis of these four products gave a neutral material **5**, with mp 161–163° and $[\alpha]_D$ −64.5°.

The mass spectrum of **5** showed a small molecular ion $[M]^+$ at *m/z* 238, in accord with the molecular formula $C_{15}H_{26}O_2$. Further fragments appeared at *m/z* 220 $[M-H_2O]^+$, 202 $[M-2H_2O]^+$, 177 $[M-i\text{-}Pr-H_2O]^+$ and 159 $[M-2H_2O-i\text{-}Pr]^+$.

Compound **5** has two hydroxyl groups (MS, IR). It showed in the ^{1}H NMR spectrum two signals at δ4.70 (1H, *d*, *J* = 7 Hz) and 4.20 (1H, *m*) assigned to geminal protons to hydroxy groups. Acetylation of **5** gave the diacetate **6** which displayed two sharp methyl singlets at δ2.08 and 1.98.

The ^{1}H NMR spectrum of compound **5** also showed signals of two independent olefinic protons [δ5.20 (1H, *d*, *J* = 7 Hz) and 4.90 (1H, *m*); ν_{max} 1640, 840 cm^{-1}], two methyl groups on double bonds [δ1.70 (3H, *s*) and 1.50 (3H, *s*)] and one isopropyl group [δ1.15 (6H, *d*, *J* = 6 Hz)]. The mass spectrum showed ions at *m/z* 177 and 159, also consistent with the presence of an isopropyl group. The molecular formula of this compound, the above data and the signal at 2.20 (4H, *br s*, =C–CH_2–CH_2–C=) led us to assume a germacrane skeleton for diol **5**.

The signal at δ4.70 (1H, *d*, *J* = 7 Hz) of a proton geminal to a hydroxyl group was assigned to H-6; it was coupled with the vinylic proton at δ5.20 as confirmed by double irradiation. The chemical shift and the complexity of the signal of the other proton geminal to a hydroxyl [δ4.20 (1H, *m*)] suggested that this second hydroxyl group could be placed on the C-8 homoallylic position. Consequently, we tentatively proposed for **5** the structure 1(10),4-germacradiene-6,8-diol.

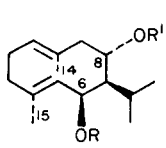
The natural compound **1** showed in its spectra characteristic signals of an angelic ester: EIMS *m/z*: 220 $[M-100]^+$, 83, 55; IR ν_{max}: 1700, 1654 cm^{-1}; ^{1}H NMR: δ6.00 (1H, *q*, *J* = 7 Hz), 2.00 (3H, *d*, *J* = 7 Hz), 1.90 (3H, *s*). Epoxidation with *m*-chloroperoxybenzoic acid‡ resulted in the formation of the 4,5-monoepoxide **9** [H-5, δ2.70 (1H, *d*, *J* = 8 Hz)]. This fact and the shielded position of H-6 in **9** [3.40 (1H, *d*, *J* = 8 Hz)] as compared with **1** and **5**, led us to conclude that the angeloxy residue is placed on C-8 and we assigned to compound **1** the structure 8-angeloyloxy-1(10),4-germacradiene-6-ol.

The epoxidation of **1** allowed us also to confirm the structure of **5**. In fact, hydrolysis and further acetylation of **9** yielded compounds **10** and **11**, substances whose physical properties were coincident with those of shiromodiol and its diacetate [3]. As the absolute stereochemistry of shiromodiol was known by X-ray crystallography [4] we assign the structure (6*S*,7*R*,8*S*)-1(10)*E*,4*E*-germacradiene-6,8-diol for **5**, for which the trivial name 'tovarol' is suggested. Consequently, the natural ester **1** must be 8-*O*-angeloyltovarol.

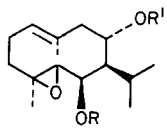
Compound **2** showed in the ^{1}H NMR spectrum signals of a senecioyl group [5.75 (1H, *br s*), 2.30 (3H, *s*), 2.00 (3H,

†Presented at the R.S.C. International Symposium on Natural Products I, Nottingham, United Kingdom, July 1982, and at the XIX Reunion Bienal de la Real Sociedad Española de Química, Santander, Spain, September 1982.

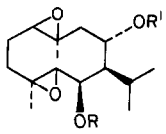
‡The same reaction could be carried out by keeping the pure substance **1** in contact with air.



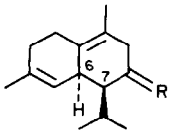
	R	R¹
1	H	Ang*
2	H	Sen*
3	H	Coum*
4	H	Fer*
5	H	H
6	Ac	Ac
7	Ac	AcCoum
8	Ac	AcFer



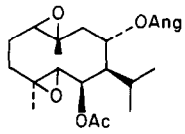
	R	R¹
9	H	Ang
10	H	H
11	Ac	Ac
12	Ac	Ang



	R	R¹
13	Ac	Ang
14	H	H



16 R=αOH
17 R=O



15

* Ang (*Z*) MeCH=CMe-CO Sen Me_2C=CH-CO Coum (*E*) 4-HO-C_6H_4-CH=CH-CO
Fer (*E*) 3-OMe-4-HO-C_6H_3-CH=CH-CO

s)] instead of the signals for the angeloxy group of **1**. The remaining signals of the ^{1}H NMR spectra of **1** and **2** were nearly identical, so this last substance must be 8-*O*-senecioyltovarol.

All attempts to separate compounds **3** and **4** as natural products failed. However, chromatography on silica gel of their diacetates **7** and **8** led us to isolate both pure substances. Partial hydrolysis of each acetate yielded the pure natural products.

Total hydrolysis of **3** and **4** gave, besides diol **5**, *p*-coumaric and ferulic acids respectively, which we assigned to position C-8 in the natural products, because of the deshielded position of the H-8 protons in both substances: **3**, 5.20 (1H, *m*); **4**, 5.30 (1H, *m*).

Compounds **1** and **9** were also isolated from the benzene extract of the roots of *T. villosa* L. var. *villosa*, as well as two new related products **12** and **13**. The IR spectra of compounds **12** and **9** were very much alike, as were their ^{1}H NMR spectra. However, **12** exhibited an acetyl group [ν1750 cm^{-1}; δ1.95 (3H, *s*)] while the hydroxyl band was absent in the IR spectrum. These data, suggested that **12** could be the acetate of **9**. To confirm this hypothesis **9** was acetylated, yielding a substance identical to **12**. The IR and ^{1}H NMR spectral traces of **12** and **13** were also quite similar. However, compound **13** had no olefinic protons in its ^{1}H NMR spectrum. This led us to conclude that the C-1 (10) double bond was epoxidized as well. In fact, reaction of **12** with *m*-CPBA afforded as expected the natural epoxide **13** together with another minor substance which must be the C-1 (10) isomeric epoxide. It is difficult to deduce the geometry of the epoxide rings from the coupling constants or from the anisotropic effects because of the flexibility of the cyclodecane ring and therefore we assigned the structures **13** and **15** in agreement with the following discussion.

Crystalline shiromodiol (**10**) [4] exhibited a conformation $_{15}D^5$, $^1D_{14}$ [5] in which only the *re,re* face of the double bond is suitably placed for an *exo*-attack by the electrophile *m*-chloroperoxybenzoic acid. If we accept that the same conformation is the prevailing one in solution, the major reaction product will have the structure **13**. As mentioned above, the main epoxidation product was identical to the natural diepoxide, for which we assigned the structure **13**.* Moreover, the ^{1}H NMR spectra of the natural diepoxide **13**, the epoxide **12** and shiromodiol diacetate (**11**), are more alike than that of the synthetic diepoxide **14**. In particular, the H-8 signal is nearly identical in **11**, **12** and **13**, but different from the H-8 multiplet of **15**. This is in agreement with the proposed structures because the C-1 (10) epoxide in **15** must point out of the ring and a conformation change to $_{15}D^5$, $_1D^{14}$ is required.

Before the chemical correlation of **1** with shiromodiol was done, we tried to deduce the relative stereochemistry of the secondary hydroxyl groups. Compound **5** was treated with 2,2-dimethoxypropane and *p*-TsOH acid but we could not get the isopropylidene derivative (1,3-*trans* hydroxyl groups). However, another rearranged product was obtained for which the structure **16** was proposed on the basis of its IR and NMR spectra and analogous rearrangements previously reported [7]. To confirm this formula and to deduce the stereochemistry, the alcoholic function of **16** was oxidized to the corresponding carbonylic compound **17**, which showed the expected cyclohexanone band in the IR spectrum (ν_{max} 1710 cm^{-1}).

Assuming no change in the configuration of the carbon atoms supporting the hydroxyl and isopropyl groups, only the bulgarane (6,7-*cis*,) or cadinane (6,7-*trans*) skeletons are possible. We have chosen the bulgarane structure because of the small coupling constant between H-6 and H-7 [δ2.95 (1H, *d*, J = 5 Hz)] which is against an *anti*-arrangement of both protons. Moreover, the deshielding effect observed for H-6 after the oxidation ($\Delta\delta$0.35 ppm) indicates that this proton must lie in the anisotropic deshielding cone of the carbonyl group and this can only be explained by a bulgarane geometry.

Finally, we would like to note that shiromodiol deriva-

* Bohlmann *et al.* [6] have described a substance with the same constitution as **13** but with a different stereochemistry and other NMR data.

Table 1. ^{1}H NMR data for tovarol derivatives **1–15***

H	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15
1	5.10	5.10	5.80	5.30	4.90	5.40	5.20	5.15	5.15	5.21	5.36	5.30	3.10	2.80	3.00
	m	*m*	*m*	*m*	*m*	*m*	*m*	*m*	*m*	*m*	*m*	*m*	*m*	*m*	*m*
2,3	2.25	2.25	2.15	2.20	2.20	2.25	2.25	2.20							
	br s	*br s*	*br s*	*br s*	*br s*	*br s*	*br s*	*br s*							
5	5.27	5.27	5.70	5.30	5.20	5.15	5.15	5.15	2.70	2.79	2.83	2.88	3.15	2.90	2.90
	d (7)	*d* (7)	*d* (7)	*m*	*d* (7)	*d* (7)	*m*	*m*	*d* (8)	*d* (7.2)	*d* (7.2)	*d* (7)	*d* (7)	*d* (8)	*d* (8)
6	5.10	5.10	4.90	4.60	4.70	5.60	5.60	5.60	3.40	3.70	4.90	4.90	4.90	3.65	4.90
	m	*m*	*d* (7)	*d* (8)	*d* (7)	*d* (7)	*m*	*m*	*d* (8)	*dd*	*dd*	*d* (7)	*d* (7)	*d* (7)	*d* (9)
										(7.2, 1.5)	(7.2, 1.1)				
8	4.47	4.47	5.20	5.30	4.20	5.40	5.60	5.60	5.15	4.27	5.40	5.45	5.58	4.33	5.50
	m	*m*	*m*	*m*	*m*	*m*	*m*	*m*	*m*	*dd*	*dd*	*dd*	*dd*	*m*	*m*
										(11.5, 5)	(11.5, 5)	(12, 5)	(12, 5)		
12,13	1.05	1.10	1.35	1 15	1.15	1.15	1.25	1.20	1.05	1.10	1.11	1.16	1.20	1.10	1.05
	d (6)	*d* (6)	*d* (6)	*d* (6)	*d* (6)	*d* (6)	*d* (6)	*d* (6)	*d* (6)	*d* (6.5)	*d* (6.5)	*d* (6.5)	*d* (6)	*d* (6)	*d* (6)
	1.00	1.10	1.25	1.05	1.15	1.00	1.05	1.01	0.90	0.95	0.94	0.95	1.05	0.97	0.95
	d (6)	*d* (6)	*d* (6)	*d* (6)	*d* (6)	*d* (6)	*d* (6)	*d* (6)	*d* (6)	*d* (6.5)	*d* (6.5)	*d* (6.5)	*d* (6)	*d* (6)	*d* (6)
14	1.70	1.70	1.70	1.70	1.70	1.70	1.74	1.70	1.71	1.75	1.77	1.77	1.45	1.45	1.40
	s	*s*	*s*	*s*	*s*	*s*	*s*	*s*	*s*	*s*	*s*	*s*	*s*	*s*	*s*
15	1 40	1.50	1.50	1.50	1.50	1.55	1.55	1.54	1.10	1.14	1.19	1.22	1.28	1.22	1.22
	s	*s*	*s*	*s*	*s*	*s*	*s*	*s*	*s*	*s*	*s*	*s*	*s*	*s*	*s*
Acyl	6.15	5.70	7.90	7.70		2.08	7.70	7.60	5.97		2.06	6.05	6.00		6.00
	q (7)	*br s*	*d* (16)	*d* (16)		*s*	*d* (8)	*d* (16)	*q* (7)		*s*	*q* (7)	*q* (7)		*q* (7)
	2.05	2.20	7.70	7.00		1.98	7.60	7.10	2.00		1.99	1.99	2.00		1.95
	d (7)	*br s*	*d* (8)	*m*		*s*	*d* (8)	*m*	*d* (7)		*s*	*d* (7)	*d* (7)		*d* (7)
	1.90	1.90	7.20	6.30			7.15	6.35	1.90			1.96	1.93		1.90
	s	*br s*	*d* (8)	*d* (16)			*d* (8)	*d* (16)	*s*			*s*	*s*		*s*
			6.70	3.90			6.45	3.85				1.94	1.90		1.88
			d (16)	*s*			*d* (16)	*s*				*s*	*s*		*s*
							2.26	2.28							
							s	*s*							
							1.95	1.91							
							s	*s*							

*Recorded at 60 MHz except **10** and **11** at 200 MHz. δ scale in ppm; TMS as internal reference. Solvents: $CDCl_3$ except **3** (in C_5D_5N), **13** and **15** (in CCl_4).

tives could be artefacts formed in the course of the extraction and purification processes, because of the easy oxidation of tovarol esters (found in both plants studied) when exposed to air, although we think that **9**, **12** and **13** are natural metabolites.

EXPERIMENTAL

Mps were determined in a Kofler apparatus and are uncorr. ^{1}H NMR spectra were recorded in a 60 MHz instrument (**10** and **11**, 200 MHz) with TMS as internal standard and chemical shifts given as δ values. EIMS were measured at 70 eV at 180°.

Plant material. The roots of *Thapsia villosa* var. *minor* were collected during June–July from Villar del Ciervo, Salamanca (Spain) and that of *T. villosa* var *villosa* from Villamayor (Salamanca), and were identified by Prof. Casaseca, Department of Botany, University of Salamanca, where voucher specimens were deposited.

Extraction and isolation. Dry roots of *T. villosa* var. *minor* (7.0 kg) were extracted with C_6H_6 in a Soxhlet, yielding a crude syrup (900 g, 13%). The crude material (350 g) was disolved in Et_2O (3.5 l.) and extracted three times with aq. 4% NaOH. Usual work up yielded a neutral fraction (216 g) and an acidic fraction (120 g).

The whole neutral extract was chromatographed on silica gel (1 kg) with hexane–Et_2O (95:5) and increasing slightly the polarity with Et_2O. After the less polar long chain compounds (57 g), a mixture containing mainly products **1** and **2** was obtained (58 g). CC on silica gel Merck H-60 (4 atm) with hexane–EtOAc (96:4) allowed us to isolate **1** (245 mg). Preparative HPLC (Waters Prep LC/500) on two SiO_2 LC 500 columns (500 × 40 cm) eluting with hexane–EtOAc (95.5) allowed us to purify compound **2**

The alkaline soluble substances **3** and **4** crystallized from C_6H_6–Et_2O as a mixture (4.03 g from 19.1 g of extract). All attempts to isolate them by chromatography failed. The mixture of both compounds (2.0 g) was acetylated (Ac_2O–pyridine) and the oily acetates were chromatographed on SiO_2 H-60 with hexane–EtOAc (8:2), to give pure **7** (552 mg) and **8** (193 mg). Partial hydrolysis of 290 mg of **10** in 2 ml of 2 N NaOH–MeOH for 20 min yielded after work up 45 mg of pure **3** (crystallized from Me_2CO). The same procedure was followed to hydrolyse **11** (193 mg) and pure **4** (48 mg) was isolated.

The air-dried roots of *T. villosa* var. *villosa* were extracted with C_6H_6 in a Soxhlet, obtaining a crude material (9.3%). This extract (155 g) was chromatographed on silica gel (1 kg) eluting with hexane–EtOAc (97:3) and doubling the amount of EtOAc after 10 l. of eluent. After elution of long chain compounds (9.85 g), product **1** was isolated (5 74 g) followed by latifolone (2.29) and a mixture (6.10 g) of product **12** and sitosterol. After helmanticine and isohelmanticine (35.1 g), 4 40 g of a mixture containing **9**, falcarindiol and helmanticine was separated, followed by a gum (3.03) made of **13** and falcarindiol. Dry CC on silica gel, using hexane–EtOAc (7:3) as eluent yielded pure **9**. Compounds **12** and **13** were purified by CC on silica gel with C_6H_6–EtOAc (9.1) and hexane–Me_2CO (95:5) as eluents, respectively.

8-O-*Angeloyltovarol* (**1**). Oily $[\alpha]_D$ −130.4° ($CHCl_3$; *c* 4.6). IR ν_{max}^{film} cm^{-1}: 3400 (OH), 2954, 1700 (C=O), 1654 (C=C), 1450, 1380, 1250 (C–O) 1170, 1100, 1000, 970, 850, 750. EIMS (probe) 70 eV, *m/z* (rel. int.): 220 [M − AngOH]$^+$ (5), 202 [M − AngOH − H_2O]$^+$ (10), 177 (10), 159 (30)

8-O-*Senecioyltovarol* (**2**). Oily $[\alpha]_D$ −144.0° ($CHCl_3$; *c* 1.2) IR ν_{max}^{film} cm^{-1}: 3400 (OH), 1690 (C=O), 1630 (C=C). 1210 (C–O), 1140 (C–O), 750. EIMS (probe) 70 eV, *m/z* (rel. int.): 220 [M − SenOH]$^+$ (5), 202 [M − SenOH − H_2O]$^+$ (5), 177 (30), 123 (85), 109 (80), 83 (100), 81 (60), 69 (25), 55 (20), 43 (10), 41 (10).

8-O-*Coumaroyltovarol* (**3**). Mp 177–179° (Me_2CO), $[\alpha]_D$ −55.1° (EtOH; *c* 1.6); IR ν_{max}^{film} cm^{-1}: 3300 (OH), 3150, 2900, 1670 (C=O), 1620 (C=C), 1600 (Ph), 1500 (Ph), 1450, 1370, 1320, 1270 (C–O), 1200 (C–O), 1180 (C–O), 1160 (C–O), 960. EIMS (probe) 70 eV, *m/z* (rel. int.): 384 [M]$^+$ (1), 366 [M − H_2O]$^+$ (1), 220 [M − CoumOH]$^+$ (1), 202 [M − CoumOH − H_2O]$^+$ (25), 192 (10), 187 (10), 177 (10), 164 (30), 159 (55), 147 (85), 119 (75), 107 (30), 91 (100), 81 (55), 69 (55).

8-O-*Feruloyltovarol* (**4**). Mp 160–163° (hexane–Et_2O), $[\alpha]_D$ −117.0° ($CHCl_3$, *c* 1.4). IR ν_{max}^{film} cm^{-1}: 3500 (OH), 3400 (OH), 2900, 1680 (C=O), 1630 (C=C), 1600 (Ar), 1500 (Ar), 1450, 1420, 1370, 1250 (C–O), 1170 (C–O), 1100 (C–O), 1040, 1020, 1000, 970. EIMS (probe) 70 eV, *m/z* (rel. int.): 414 [M]$^+$ (1), 220 [M − FerOH]$^+$ (2), 193 (100), 177 (80), 159 (20), 142 (50), 117 (25), 93 (25), 81 (35), 69 (20), 55 (20).

Coumaric acid. Hydrolysis of **10** (225 mg) with 2 N NaOH–MeOH (2 ml) for 8 hr at room temp. gave after usual work up diol **5** (113 mg) and *p*-coumaric acid (95 mg). Mp 208–209° (Et_2O); IR ν_{max}^{film} cm^{-1}: 3200, 1680, 1630, 1600, 1590, 1500, 1450, 1380, 1320, 1240, 1210, 1170, 980, 830. ^{1}H NMR (60 MHz, Me_2CO-d_6): δ7.62 (1H, *d*, *J* = 15 Hz), 7.40 (2H, *d*, *J* = 9 Hz), 6.90 (2H, *d*, *J* = 9 Hz), 6.35 (1H, *d*, *J* = 15 Hz).

Ferulic acid. Hydrolysis of **11** (509 mg) in 2 N NaOH–MeOH (3 ml) gave after usual work up diol **5** (223 mg) and ferulic acid (206 mg), mp 168–169° ($CHCl_3$); IR ν_{max}^{film} cm^{-1}: 3400, 2900, 1640, 1660, 1610, 1600, 1510, 1460, 1430, 1380, 1320, 1270, 1200, 1170, 1100, 1030, 970, 950, 850, 800. ^{1}H NMR (60 MHz, Me_2CO-d_6): δ7.62 (1H, *d*, *J* = 15 Hz), 7.30 (1H, *d*, *J* = 2 Hz), 7.15 (1H, *dd*, *J* = 2 and 8 Hz), 6 85 (1H, *d*, *J* = 8 Hz), 6.40 (1H, *d*, *J* = 15 Hz), 3.95 (3H, *s*).

Tovarol (**5**). A soln of **1** and **2** (600 mg) in 2 N methanolic NaOH (5 ml) was kept at room temp for 12 hr. Usual work up yielded **5** (446 mg) Mp 161–163° (hexane–Et_2O), $[\alpha]_D$ −64.5° ($CHCl_3$, *c* 0.78). IR ν_{max}^{film} cm^{-1}: 3400 (OH), 1650 (C=C), 1450, 1380, 1220, 1050, 1000, 840. EIMS (probe) 70 eV, *m/z* (rel. int.): 238 [M]$^+$ (1), 220 [M − H_2O]$^+$ (4), 202 [M − 2H_2O]$^+$ (2), 177 (20), 159 (10), 123 (20), 119 (20), 93 (40), 83 (100), 81 (70), 69 (50), 55 (30) Diacetate (**6**): (Ac_2O–pyridine), mp 85–87° (hexane), $[\alpha]_D$ −100.5° ($CHCl_3$, *c* 7.5). IR ν_{max}^{film} cm^{-1}: 2950, 1730 (C=O), 1380, 1240 (C–O), 1140, 1010. EIMS (probe) 70 eV, *m/z* (rel. int.): 233 [M]$^+$ (1), 262 [M − AcOH]$^+$ (1), 202 [M − 2AcOH]$^+$ (20), 187 (25), 159 (100), 145 (50), 81 (50), 43 (95).

8-O-*Angeloylshiromodiol* (**9**). A soln of **1** (240 mg) in $CHCl_3$ (5 ml) and some crystals of K_2CO_3 was reacted with 1 eq. of *m*-CPBA. Usual work up and chromatography on silica gel (10 g) with hexane–Et_2O (8.2) yielded 199 mg of an oily product identical with **9** isolated from *T. villosa*. $[\alpha]_D$ −47.7° ($CHCl_3$, *c* 3.6). IR ν_{max}^{film} cm^{-1}: 3400 (OH), 2950, 1710 (C=O), 1650 (C=C), 1460, 1400, 1250 (C–O), 1170 (C–O), 1080, 1050, 780. EIMS (probe) 70 eV, *m/z* (rel. int.): 236 [M − AngOH]$^+$ (20), 218 [M − AngOH − H_2O]$^+$ (15), 175 (40), 149 (100).

Shiromodiol (**10**). Hydrolysis of **9** (190 mg) in 2 N NaOH–MeOH (1 ml) yielded shiromodiol (133 mg), mp 87–89°, $[\alpha]_D$ +74.5° ($CHCl_3$, *c* 0.9). Lit. mp 86–89° [3]. Diacetate (**11**): (Ac_2O–pyridine), mp 109–112° (hexane–Me_2CO), $[\alpha]_D$ −64.0° ($CHCl_3$, *c* 1.6) Lit. mp 109–112° [3], $[\alpha]_D$ −61.9° ($CHCl_3$, *c* 1.06) IR and ^{1}H NMR spectra of **10** and **11** in agreement with those previously reported [3].

6-O-*Acetyl*-8-O-*acetoxycoumaroyltovarol* (**7**). Oily, $[\alpha]_D$ −58 0° ($CHCl_3$, *c* 3.6). IR ν_{max}^{film} cm^{-1}: 2900, 1770 (C=O), 1750 (C=O), 1710 (C=O), 1650 (C=C), 1610 (Ar), 1520 (Ar), 1450, 1330, 1250, 1210, 1170, 1030, 1000, 920, 850. EIMS (probe) 70 eV, *m/z* (rel. int.): 468 [M]$^+$ (0.5), 195 (5), 91 (15), 81 (10), 79 (8), 65 (8), 55 (10), 43 (100).

6-O-*Acetyl*-8-O-*acetoxyferuloyltovarol* (**8**). Mp 136–138° (hexane), $[\alpha]_D$ −57.4° ($CHCl_3$, *c* 3.9). IR ν_{max}^{film} cm^{-1}: 2900, 1760

(C=O), 1730 (C=O), 1700 (C=O), 1600 (Ar), 1500 (Ar), 1450, 1370, 1250 (C–O), 1230 (C–O), 1200 (C–O), 1150 (C–O), 1020, 1000, 900. EIMS (probe) 70 eV, *m/z* (rel. int.): 498 $[M]^+$ (1), 456 (4), 438 (2), 381 (10), 262 (1), 202 (20), 194 (15), 177 (50), 159 (50), 43 (100).

6-O-*Acetyl*-8-O-*angeloylshiromodiol* (**12**). Oily; IR ν_{max}^{film} cm^{-1}: 2950, 1750 (C=O), 1720 (C=O), 1240 (C–O), 1160, 1050.

6-*Acetoxy*-8-*angeloxy*-1(10),4(5)-*diepoxygermacrane* (**13**). Oily, $[\alpha]_D$ −10.5° ($CHCl_3$, *c* 0.6). IR ν_{max}^{film} cm^{-1}: 2950, 1750 (C=O), 1720 (C=O), 1640 (C=C), 1460, 1390, 1370, 1250 (C–O), 1160, 1130, 1100, 990, 940, 900, 820, 680. EIMS (probe) 70 eV, *m/z* (rel. int.): 394 $[M]^+$ (2), 354 (2), 294 (10), 234 (10), 209 (30), 191 (30), 147 (40), 137 (40), 123 (50), 109 (50), 99 (50), 83 (100), 55 (80).

1(10),4(5)-*Diepoxygermacrane*-6,8-*diol* (**14**). Mp 188–190° (Et_2O) $[\alpha]_D$ +112.0° ($CHCl_3$, *c* 1.8). IR ν_{max}^{film} cm^{-1}: 3580 (OH), 3400 (OH), 2950, 1470, 1390, 1320, 1230 (C–O), 1105 (C–O), 1090, 1060, 1020, 940, 900, 780, 720. EIMS (probe) 70 eV, *m/z* (rel. int.): 252 $[M - H_2O]^+$ (5), 151 (3), 136 (15), 123 (25), 111 (30), 93 (100), 85 (70), 71 (60), 55 (25), 43 (100).

6-*Acetoxy*-8-*angeloxy*-1(10),4(5)-*diepoxygermacrane* (**15**). A suspension of **12** (172 mg) and K_2CO_3 (500 mg) in $CHCl_3$ (10 ml) was treated with *m*-CPBA (100 mg) and left overnight with stirring. After usual work up the crude material was chromatographed on silica gel (10 g) with hexane–Et_2O 7:3 as eluent, yielding **13** (86 mg) and **15** (44 mg), oily, $[\alpha]_D$ −51.5° ($CHCl_3$, *c* 1.9). IR ν_{max}^{film} cm^{-1}: 2900, 1750 (C=O), 1720 (C=O), 1650 (C=C), 1460, 1390, 1370, 1240 (C–O), 1170 (C–O), 1140 (C–O), 1050, 960, 900, 820. EIMS (probe) 70 eV, *m/z* (rel. int.): 334 $[M]^+$ (1), 294 (1), 234 (4), 149 (7), 109 (15), 95 (25), 83 (100), 69 (30), 55 (50), 43 (25)

Rearrangement of **5** *to yield* 1(10)-*bulgaradien*-8-*ol* (**16**). Tovarol (**5**, 2.0 g) in Me_2CO (20 ml) was treated with 2,2-dimethoxypropane (3 ml) and a small crystal of *p*-TsOH acid. After 6 hr at room temp the crude product of reaction was chromatographed on silica gel (60 mg). Elution with hexane–Et_2O (9:1) gave **16** (1.10 g), oily, $[\alpha]_D$ +17.0° ($CHCl_3$, *c* 4.1). IR ν_{max}^{film} cm^{-1}: 3400 (OH), 1660 (C=C), 1450, 1380, 1250, 1180, 1130, 1100, 1050 (C–O), 900, 850 (C=C). EIMS (probe) 70 eV, *m/z* (rel. int.): 220 $[M]^+$ (25), 205 $[M - Me]^+$ (25), 202 $[M - H_2O]^+$ (20), 159 $[M - i\text{-}Pr - H_2O]^+$ (100), 145 (20), 134 (30), 119 (80), 105 (50), 91 (50).

1(10),4-*Bulgaradien*-8-*one* (**17**). To a soln of **16** (322 mg) in CH_2Cl_2 (10 ml), PDC (300 mg) was added and the mixture was kept at room temp for 2 days. The crude suspension was chromatographed on silica gel (10 g) with hexane–Et_2O (95:5) to give **17** (111 mg) as an oily compound: $[\alpha]_D$ +120.7° ($CHCl_3$, *c* 2.9). IR ν_{max}^{film} cm^{-1}: 2900, 1710 (C=O), 1650 (C=C), 1450, 1380, 1220, 1180, 890, 840 (C=C).

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