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SESQUITERPENE LACTONES, FLAVANONES AND A DITERPENE ACID FROM *VIGUIERA LACINIATA*

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Key Word Index—*Viguiera laciniata*; Asteraceae; sesquiterpene lactones; flavanones; diterpene acid; lacinolide A and B; viguieric acid; eriodictyol 3′-methyl ether; eriodictyol 7,3′-dimethyl ether.

Abstract—The leaves and flower heads of *Viguiera laciniata* yielded lacinolide A, a new benzoic acid ester of heliangolide, and a new chlorinated heliangolide, lacinolide B, along with six other sesquiterpene lactones, four of which were new, one known diterpene acid and two known flavanones. The structures of all compounds were elucidated by NMR and mass spectroscopy. Lacinolide A was established by X-ray crystallography.

INTRODUCTION

Viguiera is a large genus consisting of *ca* 170 species. Recently, Schilling has suggested that 10 species of the genus occurring in Baja California, Mexico be separated from this genus based on the flavonoid chemistry, chromosome number and other data [1–3]. However, it was noted that the taxonomic level at which to recognize the Baja California species is not clear [3]. As many members of the large genus *Viguiera* produce sesquiterpene lactones or diterpenoids, or both [4–19], it was therefore of interest to initiate an investigation of the terpenoid chemistry of these Baja California species in order to ultimately compare their chemistry with the terpenoid chemistry of species from other areas. In this connection, we now report the chemical results from *V. laciniata* A. Gray, a Baja California species. It was found to contain six new compounds, including a benzoic acid ester of heliangolide (**1**) and a chlorinated heliangolide (**2**), which we named lacinolide A and B, respectively. In addition, 1*β*,10*α*-epoxy-3*β*-hydroxy-8*β*-(2′*R*,3′*R*)-epoxyangeloyloxy-heliangolide (**3**), 1*β*,10*α*-epoxy-3*β*-hydroxy-8*β*-(2′*S*,3′*S*)-epoxyangeloyloxyheliangolide (**4**), the 1*β*,10*α*-epoxy-3*β*-acetoxy-8*β*-(2′*S*,3′*S*)-epoxyangeloyloxy-heliangolide (**5**) and 1*β*,10*α*-epoxy-3*β*-acetoxy-8*β*-(2′*R*,3′*R*)-epoxyangeloyloxy-heliangolide (**6**) were characterized as new lactones from *V. laciniata*. The five known compounds include two other sesquiterpene lactones, leptocarpin (**7**) and tirotundifolin A (**8**), the diterpene, viguieric acid (**9**) and two flavanones, namely the 3′-methyl (**10**) and 7,3′-dimethyl ethers (**11**) of eriodictyol.

RESULTS AND DISCUSSION

The dichloromethane extract of leaves and flower heads of *V. laciniata* afforded compounds **1**–**11**. Leptocarpin (**7**), which was previously reported from *Viguiera linearis* from Nopala, Hidalgo [20] and several other genera [21–23], was identified here by NMR and mass spectroscopy. Tirotundifolin A (**8**), previously reported from *Tithonia rotundifolia*, and the diterpene viguieric acid (**9**), previously reported from *Viguiera deltoidea* from Baja California, were identified by comparison of spectral data with those published [24, 7]. The 3′-methyl ether (**10**) (homoeriodictyol) and the 7,3′-dimethyl ether (**11**) of eriodictyol were identified by standard procedures [25]. Moreover, the positions of the methoxyl groups in both flavanones were confirmed by difference NOE experiments conducted at 500 MHz. Compounds **1**–**6**, to our knowledge, have not been previously reported.

The available ^{1}H and ^{13}C NMR as well as MS data did not fully resolve the structure of **1**, therefore, an X-ray crystallographic analysis was conducted to establish the complete structure and stereochemistry as depicted in **1**. The structure of **1** was solved by single crystal X-ray diffraction methods. The thermal ellipsoid drawing of the molecule with the atom labelling scheme is shown in Fig. 1. The positional and equivalent isotropic thermal parameters of all non-hydrogen atoms are listed in Table 1. The absolute configuration of this compound could not be determined from the available data. However, the drawing of the molecule (Fig. 1) provided the relative configuration of all the ring substituents. Atoms H-1, H-3, O-6 and H-8 could be seen occupying one side of the 10-membered ring (below the ring) and thus were labelled *α*-substituents. Atoms O-1, O-16a, H-6 and O-8 were occupying positions on the other side of the ring (above the ring) and therefore, they were labelled *β*-substituents.

The ^{1}H NMR data had clearly indicated that **1** was a *trans*-fused heliangolide: a pair of well separated doublets appeared at δ6.43 and 5.82 (H-13, $J = 2$ Hz). A downfield double doublet at δ6.28 was attributed to H-6, ($J = 2$, 11 Hz), and the signal at δ5.41 was attributed to H-5 (*dq*, $J = 1.5$, 11 Hz). The presence of a C-1, C-10 epoxy group was evident by two ^{13}C NMR signals at around δ60 (see Table 2, because of the lack of a proton attached to them, exact assignments for the C-10 and C-2′ signals could not be made), an H-1 signal appearing at δ2.98, as well as the downfield shift of the H-14 signal at δ1.42 (singlet). Chemical shifts for H-3 (δ5.58) and H-8 (δ5.27) in the ^{1}H NMR spectrum of **1** suggested that the C-3 and C-8

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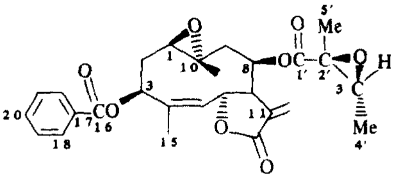

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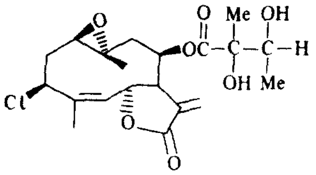

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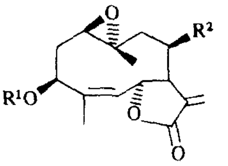
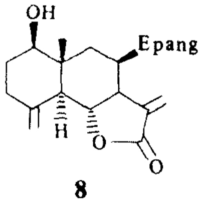


	R^1	R^2
3	H	2'*R*,3'*R* - Epang
4	H	2'*S*,3'*S* - Epang
5	Ac	2'*S*,3'*S* - Epang
6	Ac	2'*R*,3'*R* - Epang
7	H	Ang



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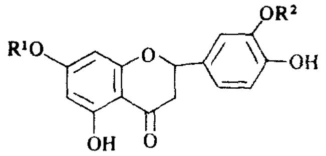
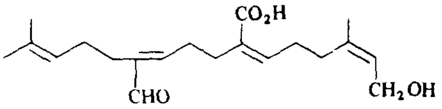


	R^1	R^2
10	H	Me
11	Me	Me



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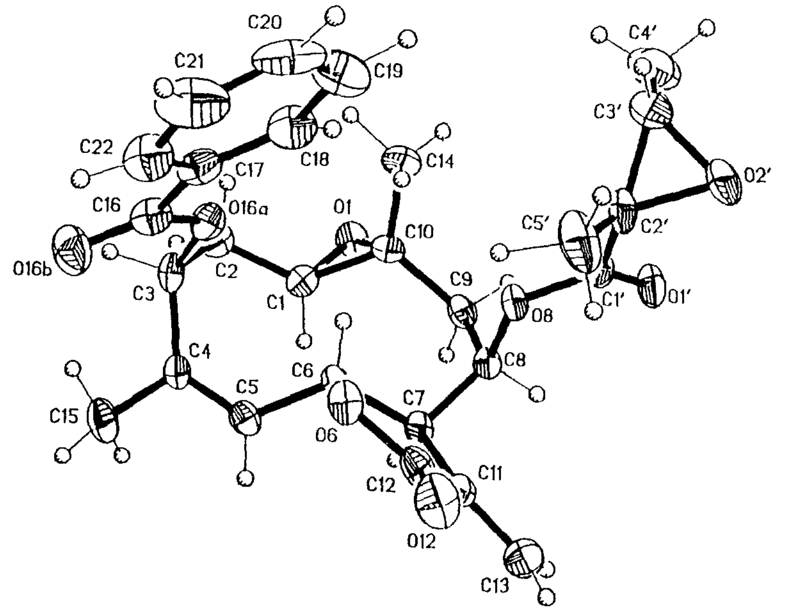

Fig. 1. Thermal ellipsoids view and atom labelling scheme of compound **1**.

positions were substituted. These were in accord with the presence of a benzoate and an epoxyangelate sidechain. The latter was indicated by signals at δ2.98 (1H, *q*, *J* = 5.4 Hz), 1.18 (3H, *d*, *J* = 5.4 Hz), and 1.39 (3H, *s*), and the former by another group of signals at δ8.11 (2H, *dd*, *J* = 1, 8 Hz), 7.48 (2H, *br t*, *J* = 8, 8 Hz), and 7.59 (1H, *br t*, *J* = 8, 8 Hz). A 2D COSY spectrum recorded at 500 MHz allowed all proton signals assignments but nevertheless

Table 1. Atomic coordinates (× 10^4) and equivalent isotropic displacement coefficients of compound **1** (Å^2 × 10^3)

	X	*Y*	*Z*	*U*(eq)*
O (1)	5029 (4)	5098 (5)	4508 (3)	66 (2)
O (1′)	784 (4)	6539 (5)	4917 (3)	77 (2)
O (2′)	−994 (4)	6275 (6)	3935 (3)	83 (3)
O (6)	3127 (4)	8795 (5)	2885 (3)	63 (2)
O (8)	1915 (4)	7089 (4)	3995 (2)	51 (2)
O (12)	1891 (5)	10170 (6)	2989 (3)	93 (3)
O (16a)	4674 (4)	6462 (5)	2294 (3)	64 (2)
O (16b)	5435 (6)	7329 (6)	1312 (3)	101 (3)
C (1)	5224 (6)	6008 (7)	3997 (4)	54 (3)
C (2)	5819 (6)	5734 (7)	3295 (4)	68 (4)
C (3)	5722 (6)	6628 (8)	2691 (4)	59 (3)
C (4)	5864 (6)	7774 (8)	2982 (4)	56 (3)
C (5)	5044 (6)	8406 (7)	3236 (4)	55 (3)
C (6)	3840 (5)	8103 (6)	3366 (4)	49 (3)
C (7)	3430 (5)	8335 (7)	4163 (4)	49 (3)
C (8)	2806 (6)	7381 (6)	4522 (4)	48 (3)
C (9)	3469 (6)	6357 (7)	4769 (4)	56 (3)
C (10)	4075 (7)	5683 (6)	4195 (4)	51 (3)
C (11)	2705 (6)	9318 (7)	4083 (5)	56 (3)
C (12)	2481 (7)	9502 (9)	3284 (6)	68 (4)
C (13)	2273 (7)	9985 (8)	4598 (6)	86 (4)
C (14)	3370 (7)	4978 (7)	3679 (5)	71 (3)
C (15)	7061 (5)	8179 (8)	3001 (5)	80 (4)
C (16)	4641 (9)	6885 (7)	1604 (5)	69 (4)
C (17)	3519 (9)	6786 (7)	1270 (5)	71 (4)
C (18)	2634 (10)	6284 (9)	1599 (5)	88 (4)
C (19)	1588 (10)	6186 (10)	1248 (7)	113 (5)
C (20)	1452 (11)	6600 (10)	541 (8)	111 (6)
C (21)	2312 (13)	7136 (11)	231 (7)	130 (7)
C (22)	3337 (9)	7235 (9)	574 (6)	94 (4)
C (1′)	940 (6)	6717 (7)	4269 (5)	51 (3)
C (2′)	113 (6)	6554 (8)	3659 (5)	68 (4)
C (3′)	−355 (9)	5426 (12)	3559 (6)	95 (5)
C (4′)	−36 (9)	4443 (10)	3981 (7)	146 (7)
C (5′)	132 (7)	7370 (11)	3036 (5)	111 (5)

*Equivalent isotropic *U* defined as one-third of the trace of the orthogonalized U_{ij} tensor.

Table 2. ^{13}C NMR data for compounds **1**, **3** and **4** (125 MHz, $CDCl_3$, TMS as internal standard)*

C	**1**	**3**	**4**
1	60.18	60.59 N	60.41
2	30.61	32.45 P	32.58
3	73.66	71.79 N	71.79
4	136.72	141.84 P	141.84
5	126.77	125.85 N	125.85
6	74.58	73.96 N	74.08
7	48.25	47.84 N	47.84
8	77.13	77.26 N	76.94
9	43.67	43.54 P	43.96
10	57.98	58.38 P	58.46
11	137.45	137.02 P	137.02
12	165.67	168.81 P	168.81
13	125.51	125.20 P	125.04
14	18.93	18.70 N	18.88
15	23.25	22.84 N	22.84
OR			
16	168.93		
17	129.68		
18/22	129.68		
19/21	128.70		
20	133.30		
OR			
1′	168.93	169.40 P	168.50
2′	59.42	59.41 P	59.90
3′	59.73	59.67 N	60.41
4′	13.59	13.44 N	12.98
5′	19.59	19.87 N	20.09

* Assignments for **1** and **3** were confirmed by ^{1}H–^{13}C Correlation Spectroscopy except those signals for the carbons without protons attached. N and P for **3** were Attached Proton Test results for which N = one or three protons attached to the carbon; P = none or two protons attached to the carbon.

left in question some structural features. Both CIMS and FABMS indicated that **1** had a molecular formula of $C_{27}H_{30}O_8$ (*m*/*z* at 483, 100%) accommodating a benzoate and an epoxyangelate attached to a heliangolide skeleton. The X-ray analysis established that the epoxyangelate sidechain was attached at the C-8 position and the benzoate group was attached to the C-3 position. In the ^{1}H–^{13}C NMR correlation spectrum of **1**, the ^{1}H signal at δ2.98 correlated with a ^{13}C signal at δ60.18 (C-1). Two ^{1}H signals at δ2.68 and 1.98 correlated with one ^{13}C signal at δ30.61 (C-2). The H-3 signal (δ5.58) correlated with a ^{13}C signal at δ73.66 (C-3). Signals for H-6, 7, 8 and H-9 correlated with ^{13}C signals at δ74.58, 48.25, 77.13 and 43.67, respectively. The ^{1}H signals for H-13, 14, 15, 4′ and H-5′ were correlated with relevant ^{13}C signals (Table 2). Another two ^{13}C signals at δ57.98 and 59.42, attributed to C-10 and C-2′, did not correlate with any proton signals and thus their assignments, as well as those for C-11 and C-4, are interchangeable. While ^{13}C NMR signals for C-18, 19, 20, 21 and 22 could be confirmed, signals for C-17 and C-16 could not be observed as these carbon atoms had no attached protons and their signals probably overlapped two other signals at δ129.68 and 168.93.

Compound **2**, which we named lacinolide B, was also a heliangolide. While ^{1}H NMR spectral data (Table 3) indicated that **2** also had a skeleton similar to that of **1**, the spectrum of **2** exhibited different sidechain signals, namely, signals at δ4.35 (*q*, *J* = 6.7 Hz), 1.48 (*d*, *J* = 6.7 Hz) and 1.25 (*s*) for a 2′,3′-dihydroxyangelate group. This dihydroxyangelate sidechain was assigned to C-8 by comparing the chemical shifts for H-3 and H-8. A 2D COSY spectrum recorded at 500 MHz allowed unambiguous signal assignments. The coupling pattern of H-3 at δ4.44 (*dd*, *J* = 2.6, 4 Hz) indicated that there was not a hydroxyl group at this position since an H-3 signal would have appeared as a broad singlet if a hydroxyl group had been present, as was the case for H-3 in the spectra of **3** and **4**. The absence of a hydroxyl group at C-3 in **2** was in accord with a CI mass spectrum of **2** which exhibited a

Table 3. ^{1}H NMR data for compounds **1** and **2** (500 MHz, TMS as internal standard)*

H	**1** ($CDCl_3$)	**2** (acetone-d_6)
1	2.98 *dd* (5, 10)	2.87
2α	2.68 *ddd* (5, 5, 16)	2.47
2β	1.98 *ddd* (2, 10, 16)	1.63
3	5.58 *dd* (2, 5)	4.44 *dd* (2.6, 4)
5	5.41 *dq* (1.5, 11)	5.25
6	6.28 *dd* (2, 11)	6.69
7	2.98 *br s*	3.20
8	5.27 *br s*	5.40
9α	2.72 *dd* (5, 15)	2.48
9β	1.41 *dd* (3, 15)	1.51
13a	6.43 *d* (2)	6.22
13b	5.82 *d* (2)	5.41
14 (3H)	1.42 *s*	1.55
15 (3H)	1.98 *d* (1.5)	1.78
OR		
18/22 (2H)	8.11 *dd* (1, 8)	
19/21 (2H)	7.48 *br s* (8)	
20	7.59 *br s* (8)	
OR′		
3′	2.98 *q* (5.4)	4.35 *q* (6.7)
4′ (3H)	1.18 *d* (5.4)	1.48 *d* (6.7)
5′ (3H)	1.39 *s*	1.25

*Coupling patterns and coupling constants (value in Hz in parenthesis) are not repeated if identical with the preceding column.

Table 4. ^{1}H NMR data for compounds **3**–**6** ($CDCl_3$, TMS as internal standard, data for **3** were recorded at 500 MHz, for **4** and **6** at 200 MHz and for **5** at 360 MHz)*

H	**3**	**4**	**5**	**6**
1	2.83 *dd* (4.4, 10)	2.82	2.89	2.89
2α	2.46 *dt* (4, 4, 15)	2.49	2.59	2.58
2β	1.75 *ddd* (2, 9, 15)	1.76	1.77	1.72
3α	4.50 *br s*	4.52	5.26 *dd* (2, 5)	5.26
5	5.31 *dq* (1.4, 11)	5.31	5.29	5.28
6	6.66 *dd* (2, 11)	6.66	6.15	6.16
7	2.92 *br s*	2.90	2.90	2.91
8	5.25 *br s*	5.34	5.30	5.30
9α	2.71 *dd* (2, 15)	2.73	2.77	2.72
9β	1.38 *dd* (2, 15)	1.41	1.43	1.42
13a	6.41 *d* (2)	6.36	6.36	6.42
13b	5.81 *d* (2)	5.78	5.78	5.82
14†	1.49 *s*	1.56	1.56	1.52
15†	1.81 *d* (1.3)	1.82	1.92	1.92
OR				
3′	3.07 *q* (5.4)	3.02	3.03	3.08
4′†	1.31 *d* (5.4)	1.19	1.21	1.31
5′†	1.49 *s*	1.56	1.57	1.51
OAc†			2.17	2.18

*Coupling patterns and coupling constants (value in Hz in parenthesis) were not repeated if identical with the preceding column.

†Intensity for three protons.

molecular ion at *m/z* 415 representing a molecular formula of $C_{20}H_{27}O_7Cl$. The CIMS indicated the presence of a chlorine atom by a characteristic peak at *m/z* 417 with *ca* one-third the intensity of the peak at *m/z* 415; also the peak at *m/z* 379 was in accord with the loss of a chlorine atom. On the basis of the coupling constants of H-1, H-3 and H-8 as well as the stereochemistry at C-1, C-3, C-8 in **1**, we assigned **2** to be 1β,10α-epoxy-3β-chloro-8β-2′,3′-dihydroxyangeloyloxy heliangolide. Since chlorinated sesquiterpene lactones are not usually found within the genus *Viguiera*, we could not exclude the possibility that **2** is an artifact.

Compounds **3** and **4** were isomeric heliangolides (see Table 4). A 2D COSY spectrum of **3** was recorded at 500 MHz which confirmed signal assignments. Signals at δ2.83 (*dd*, $J = 4.4$, 10 Hz), 3.07 (*q*, $J = 5.4$ Hz) and 1.31 (*d*, $J = 5.4$ Hz) allowed assignments of 1β,10α-epoxy and 2′,3′-epoxyangelate groups. A ^{1}H–^{13}C NMR correlation spectrum (500–125 MHz) as well as an attached proton test spectrum (125 MHz) confirmed the structure and all signal assignments. A CI mass spectrum also established a molecular formula of $C_{20}H_{26}O_7$ by a peak at *m/z* 379 $[M+H]^+$. Other peaks in the CI mass spectrum and also those in the EI mass spectrum were in accord with the structure assignment for **3**. The structure of **4** was easily correlated with **3**. A CI mass spectrum also indicated a $C_{20}H_{26}O_7$ formula for **4**. The only difference between **3** and **4** was the stereochemistry of the 2′,3′-epoxy group. Comparing the ^{1}H NMR signal of the sidechains in both **3** and **4**, chemical shifts of the of H-4′ and H-3′ at δ1.19 and 3.02 for **4** were similar to the signals observed for **1** (the relative stereochemistry of which was confirmed by X-ray). Therefore, we tentatively assigned a 2′*S*,3′*S*-epoxyangelate for **4** and a 2′*R*,3′*R*-epoxyangelate for **3**.

The structures of compounds **5** and **6** were readily correlated with those of **3** and **4**. The only difference was that the hydroxyl groups in **3** and **4** were acetylated to yield, respectively, **5** and **6**. The CI and EI mass spectra of both compounds (see Experimental) were in accord with these structure assignments. The relative stereochemistry at the epoxyangelate sidechains were tentatively assigned on the basis of the H-4′ and H-3′ signals as discussed for those for **3** and **4**.

When additional species from Baja California are investigated for their terpenoids, a more definitive statement can be made concerning Schilling's suggestion that *Viguiera* species from Baja California differ from those from other areas.

EXPERIMENTAL

Viguiera laciniata A. Gray was collected by E. Schilling on March 11, 1984, 36 miles west of Bahia de Los Angeles in Baja California, Mexico. The plant (Schilling 10109) was identified by E. Schilling, Department of Botany, University of Tennessee, Knoxville, where a voucher is deposited.

Leaves and flower heads (430 g) were extracted twice with CH_2Cl_2 (7 l). The combined extracts were evapd under red. pres. to yield a gummy material. The material was dissolved in Me_2CO and stored in a refrigerator overnight. After filtering, the Me_2CO soln was evapd to yield 31.5 g of crude material. This crude concentrate was first separated by silica gel CC eluting with hexane containing increasing amounts of EtOAc (0–100%). Fractions of *ca* 500 ml were collected and monitored by TLC.

Those fractions exhibiting similar spots on TLC were combined and concentrated. Compound **3** (100 mg) was obtained by crystallization (EtOAc–hexane) of the material from fraction 82 from the silica gel column. Compound **9** (248 mg) was purified over a Sephadex LH-20 column eluted with cyclohexane–CH_2Cl_2–MeOH (7:4:1). Compounds **10** (300 mg) and **11** (134 mg) were purified by crystallization (EtOAc–hexane) of the material from fraction 61 and 41 from the silica gel column, respectively. Compounds **1** (22 mg), **2** (7 mg), **4** (9 mg), **5** (3 mg), **6** (23 mg), leptocarpin (**7**) (316 mg) and tirotundifolin A (**8**) (3 mg) were obtained by prep. HPLC (silica gel column, 10 mm × 25 cm, RI detector, solvents: hexane–EtOAc using different ratios for different compounds) of the material from the silica gel CC.

Lacinolide A (**1**). The X-ray data were collected on a Nicolet R 3m/V diffractometer equipped with a graphite monochromator utilizing MoKα radiation ($\lambda = 0.71073$ Å). The crystal was orthorhombic, space group $P\ 2_12_12_1$, $a = 11.920$ (3), $b = 12.023$ (2), $c = 17.997$ (4) Å, $V = 2579$ (1) Å^3, $Z = 4$, D_c(g/cm^3, 293 K) $= 1.243$, chemical formula $C_{27}H_{30}O_8$, $= 482.5$ g and $F(000) = 1024$ electrons; 6499 reflections (two equivalent sets) were measured using ω-scan; scan range of 1° symmetrically around K$\alpha_{1,2}$ maximum; scan rate 3.0 to 6.0 deg/min dependent upon intensity; 2θ range 4.0° to 55.0°. 30 reflections with $20.49° < 2\theta < 25.64°$ were used to refine the unit cell parameters. Four reflections (400, 302, 004 and 130) were remeasured every 96 reflections to monitor instrument and crystal stability. After merging the equivalent sets ($R_{int} = 0.034$), a total of 1257 reflections of intensity larger than $3\sigma(I)$ were used in refining 316 variables. The structure was solved by direct methods [26] from which the locations of all non-hydrogens were obtained. The refinement was carried out by weighted full-matrix least squares. The hydrogen atoms bonded to C-4′, C-13, C-15 as well as the aromatic hydrogen atoms were not found in the difference Fourier map and their positions were calculated. All non-hydrogen atoms were treated anisotropically; hydrogen atoms isotropically. The refinement converged to $R = 0.052$ and $wR = 0.054$ for 1257 reflections [$F_o > 6\sigma(F_o)$; $R = 0.16$ and $wR = 0.088$ for all data]; goodness-of-fit 1.61 and a maximum shift/e.s.d. 0.428, minimum and maximum residual peaks in the final difference Fourier map were -0.19 and 0.19 e/Å^3, respectively. The bond length and angles, anisotropic thermal parameters, positional parameters for the hydrogen atoms and the structure factor tables are all available upon request to S.H.S.

EIMS of **1**, (probe) 70 eV, *m/z* (rel. int.): 383 $[M - C_5H_7O_2]^+$ ($C_{27}H_{30}O_8 = 482$) (7.7), 261 $[383 - \text{benzoic acid}]^+$ (7.0), 244 $[M - \text{epoxyangelic acid} - \text{benzoic acid}]^+$ (15.1), 122 $[\text{benzoic acid}]^+$ (13.4), 105 (100), 43 (16.3). Direct CIMS methane (0.4 torr), *m/z* (rel. int.): 483 $[M + H]^+$ (100), 449 $[M - Me - H_2O]^+$ (12.0), 367 $[483 - \text{epoxyangelic acid}]^+$ (8.5), 361 $[483 - \text{benzoic acid}]^+$ (20.0), 245 $[483 - \text{epoxyangelic acid} - \text{benzoic acid}]^+$ (54.9), 227 $[245 - H_2O]^+$ (20), 123 $[\text{benzoic acid} + H]^+$ (20). FABMS, *m/z* (rel. int.): 483 $[M + H]^+$ (100), 465 $[M - H_2O]^+$ (8), 361 $[483 - \text{benzoic acid}]^+$ (9), 245 $[483 - \text{epoxyangelic acid} - \text{benzoic acid}]^+$ (33.3).

Lacinolide B (**2**). Direct CIMS (methane, 0.4 torr), *m/z* (rel. int.): 415 $[M + H]^+$ ($C_{20}H_{27}O_7Cl = 414$) (30.2), 417 (10.6), 379 $[M - Cl]^+$ (6.9), 263 $[M - \text{dihydroxyangelate} - H_2O]^+$ (92.6), 245 $[263 - H_2O]^+$ (62.1), 95 (100).

1β,10α-*Epoxy*-3β-*hydroxy*-8β-(2′R,3′R)-*epoxyangeloyloxyheliangolide* (**3**). EIMS (probe) 70 eV, *m/z* (rel. int.): 360 $[M - H_2O]^+$ ($C_{20}H_{26}O_7 = 378$) (1), 262 $[M - \text{Epang}]^+$ (2), 244 $[M - \text{Epang} - H_2O]^+$ (13), 95 (55), 43 (100). Direct CIMS (methane, 0.4 torr), *m/z* (rel. int.): 379 $[M + H]^+$ (34), 361 $[M + H - H_2O]^+$ (4), 279 $[M - C_5H_7O_2]^+$ (19), 263 $[M + H - \text{Epang}]^+$ (100), 245 $[263 - H_2O]^+$ (60).

1β,10α-*Epoxy*-3β-*hydroxy*-8β-(2′S,3′S)-*epoxyangeloyloxyheliangolide* (**4**). EIMS (probe) 70 eV, *m/z* (rel. int.): 360 $[M - H_2O]^+$ ($C_{20}H_{26}O_7 = 378$) (1), 262 $[M - \text{Epang}]^+$ (4), 244 $[M - \text{Epang} - H_2O]$ (17), 95 (85), 43 (100). Direct CIMS (methane, 0.45 torr), *m/z* (rel. int.): 379 $[M + H]^+$ (18), 361 $[M + H - H_2O]^+$ (15), 263 $[M + H - \text{Epang}]^+$ (35), 245 $[263 - H_2O]^+$ (35), 95 (100).

1β,10α-*Epoxy*-3β-*acetoxy*-8β-(2′S,3′S)-*epoxyangeloyloxyheliangolide* (**5**). EIMS (probe) 70 eV, *m/z* (rel. int.): 261 $[M - OAc - \text{Epang}]^+$ (10), 43 (100). Direct CIMS (methane, 0.4 torr), *m/z* (rel. int.): 421 $[M + H]^+$ ($C_{22}H_{28}O_8 = 420$) (76), 403 $[M + H - H_2O]^+$ (10), 361 $[421 - HOAc]^+$ (26), 245 $[361 - C_5H_8O_3]^+$ (100), 227 $(245 - H_2O]^+$ (36).

1β-10α-*Epoxy*-3β-*acetoxy*-8β-(2′R,3′R)-*epoxyangeloyloxyheliangolide* (**6**). EIMS, probe 70 eV, *m/z* (rel. int.): 360 $[M - HOAc]^+$ (2), 345 $[360 - Me]^+$ (2), 321 $[M - C_5H_7O_2]^+$ (5), 261 $[321 - HOAc]^+$ (32), 244 $[M - HOAc - \text{Epang}]^+$ (55), 95 (70), 43 (100). Direct CIMS (methane, 0.45 torr), *m/z* (rel. int.): 421 $[M + H]^+$ (94), 403 $[M + H - H_2O]^+$ (34), 361 $[M + H - HOAc]^+$ (63), 245 $[M + H - HOAc - \text{Epang}]^+$ (100), 227 $[245 - H_2O]^+$ (67).

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