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Highly Oxygenated Guaianolides and Eudesman-12-oic Acids from *Balsamorhiza sagittata* and *Balsamorhiza macrophylla*

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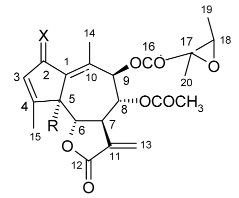
Investigation of lipophilic exudates from the aerial parts of *Balsamorhiza sagittata* and *B. macrophylla* afforded three new highly oxygenated guaianolides (1—3), in addition to known guaianolides, germacranolide and eudesmane acids. Their chemical structures were elucidated by spectroscopic methods and the data for the compounds are reported in Tables 1 and 2 and in Experimental.

Key words *Balsamorhiza sagittata*; *Balsamorhiza macrophylla*; Asteraceae; highly oxygenated guaianolide; eudesmanic acid

The genus *Balsamorhiza* has been placed in different subtribes of the large tribe Heliantheae within the Astercease.[1—3)] *Balsamorhiza sagittata* [PURSCH] NUTTALL is commonly known as arrowleaf balsamroot. Flavonoids,[4)] guaianolides, heliangolides, diterpenes, cycloartenol derivatives[5)] and antibacterial thiophene[6)] have been reported from this species. Six known methylated flavonols were isolated from the leaf of cut leaf balsamroot, *B. macrophylla.*[7)] Further fractionation of the extract of aerial parts of *Balsamorhiza sagittata* and *Balsamorhiza macrophylla* resulted in the isolation of three new guaianolide type sesquiterpenes, in addition to several known compounds. Here we report their structural elucidation.

Separation of the terpenoid portion of the resinous exudate of *B. sagittata* [PURSCH] NUTT. on a silica gel open column yielded three new guaianolides, 2-deoxo-5-deoxy-8-*O*-acetyl-17,18 epoxy pumilin (**1**), 2-deoxo-8-*O*-acetyl pumilin (**2**) and methyl-9β-(epoxyangeloyloxy)-5α,6α-dihydroxy-2-oxo-3,4-dehydro-δ-guaien-12-oate (**3**), in addition to the known compounds 17,18-epoxy-8-*O*-acetyl pumilin (**4**),[5)] 8-*O*-acetyl pumilin (**5**),[8)] and 9β-acetoxy-3-epi-nobiliun (**6**).[5)] Investigation of the exudate terpenoids of *B. macrophylla* afforded three known eudesmanic acids, 3-oxo-eremophila-9,11(13)dien-12-carboxylic (**7**),[9)] 3-oxo eremophila-4,11(13) dien-12-oic (**8**)[10)] and 10-hydroxy-3-oxoeremophila-1,11(13) dien-12-oic acids (**9**).[9)]

ESI-ICR mass spectrum of compound **1** exhibited a molecular ion peak $[M+Na]^+$ at *m*/*z* 425 and exact mass at *m*/*z* 425.1567, establishing the elemental composition as $[C_{22}H_{26}O_7Na]^+$. Its IR spectrum showed an absorption band at $1752\,cm^{-1}$ (γ-lactone). The ^1H-NMR spectrum of compound **1** revealed a signal at δ 3.63 (t, $J=10.5$ Hz, H-6), correlated in ^1H–^1H COSY with two signals at δ_H 3.46 (br d, $J=10.5$ Hz, H-5) and 3.33 (t, $J=10.5$ Hz, H-7), suggesting the presence of a C_5H–$C_6H(O)$–C_7H moiety. Additionally, the signal at δ_H 5.24 (t, $J=10.5$ Hz, H-8) correlated with two signals at δ_H 3.33 (t, $J=10.5$ Hz, H-7) and 5.53 (br d, $J=10.5$ Hz, H-9), indicating the presence of a C_7H–$C_8H(O)$–$C_9H(O)$ moiety. Accordingly, compound **1** contained a C_5H–$C_6H(O)$–C_7H–$C_8H(O)$–$C_9H(O)$ moiety. Furthermore, the ^1H-NMR displayed signals for an epoxy angelate moiety as a doublet at δ 1.40 ($J=5.5$ Hz, H-19), quartet at δ 3.09 ($J=5.5$ Hz, H-18) and singlet at δ 1.52 (H-20). The ^{13}C-NMR spectrum exhibited 22 carbon signals which were classified by a DEPT experiment as follows: three quaternary carbonyl carbons at δ 169.0, 169.9 and 169.6 for C-12, C-16 and the carbonyl carbon of acetate, five methyl carbons at δ 15.4, 17.9, 14.3, 19.9 and 21.2 for C-14, C-15, C-19, C-20 and the methyl carbon of acetate, and five oxygenated carbons at δ 82.1, 70.3, 74.6, 59.6 and 61.2 for C-6, C-8, C-9, C-17 and C-18, respectively. The connectivity of the partial moieties and the positions of acyl groups, epoxyangelate and acetate, and the $C_{6,12}$-lactonization were



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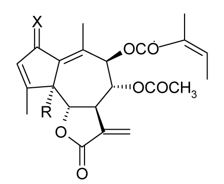

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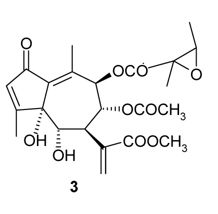

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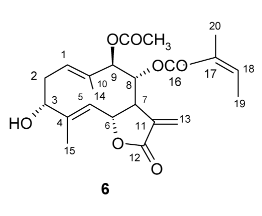

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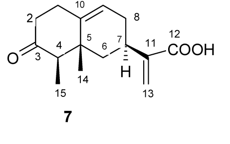

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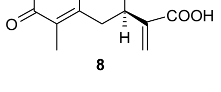

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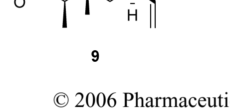

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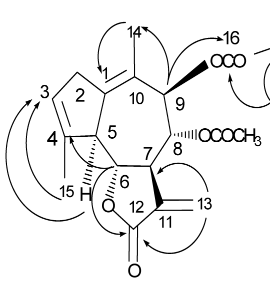

Fig. 1. Selected HMBC Correlations of **1**

established by the HMBC spectrum of **1**. In this spectrum C–H, correlations were found between the protons of the exomethylene group (H-13a and H-13b) and C-7 (δ_C 53.8) and C-12 (δ_C 169.0); between H-5 and C-3 (δ_C 126.6), C-4 (δ_C 139.9), C-6 (δ_C 82.1) and C-7 (δ_C 53.8); and between H-2 and C-3 (δ_C 126.6). The correlation between H-6 and C-4 (δ_C 139.9) and C-12 (δ_C 169.0) supported the $C_{6,12}$-lactonization. Additionally, HMBC experiments (Fig. 1) showed correlations between H-15 and C-3 (δ_C 126.6), C-4 (δ_C 139.9) and C-5 (δ_C 54.7); between H-14 and C-1 (δ_C 126.3), C-9 (δ_C 74.6) and C-10 (δ_C 140.1); between H-19 and C-18 (δ_C 61.2); between H-20 and C-16 (δ_C 169.9) and C-18 (δ_C 61.2); and between H-9 and C-16 (δ_C 169.9) which supported the location of the epoxyangelate group at C-9. Furthermore, all proton and carbon signals were determined by ^{1}H–^{1}H COSY, HMQC and HMBC (Tables 1, 2). The stereochemistry of **1** was determined from the observed coupling constants and NOE. The relative stereochemistry at C-5, C-6, C-7, C-8 and C-9 were derived from the coupling constants ($J_{5,6}=J_{6,7}=J_{7,8}=J_{8,9}=10.5$ Hz), which were in agreement with the *anti*-diaxial disposition of the protons at C-5 (α), C-6 (β), C-7 (α), C-8 (β) and C-9 (α). Clear NOE were observed between H-6 and H-8 indicating the β-orientation of these protons. Irradiation of the signal at δ 3.46 (H-5) enhanced signals at δ 3.33 (H-7) and H-9 at δ 5.53, which suggested the α-orientation of H-5, H-7 and H-9. Therefore, compound (**1**) was identified as 2-deoxo-5-deoxy-8-*O*-acetyl-17,18 epoxy pumilin.

The ESI-ICR-MS of **2** gave a molecular ion peak $[M+Na]^+$ at *m/z* 425 and exact mass determination at *m/z* 425.1560, which established the elemental composition as $C_{22}H_{26}O_7Na^+$. The IR spectrum showed absorption bands at 3446 (OH), and 1777 cm^{-1} (γ-lactone). The NMR spectral data of compound **2** were quite similar to those of compound **1**. Differences indicated the presence of an angelate group in **2**, instead of epoxy angelate in **1**, from the typical angelate signals at δ 6.22 (q, H-18), 2.02 (dq, H-19) and 1.87 (q, H-20). The ^{13}C-NMR and DEPT experiments exhibited 22 carbon signals. Among them, four oxygenated methine carbon signals appeared at δ 81.8, 83.4, 69.7 and 72.7 assigned for C-5, C-6, C-8 and C-9, respectively, two methylene carbon signals at 35.8 and 120.5 for C-2 and C-13, five methyl carbon signals at 15.7, 13.9, 20.5, 16.0 and 20.5 assigned for C-14, C-15, C-19, C-20 and methyl of acetate, respectively, and three quaternary carbon signals at δ 168.8, 166.5 and 169.9 assigned for C-12, C-16 and the carbonyl carbon of acetate, respectively. Again, the connectivity of these partial moieties, the positions of acyl groups, angelate and acetate, and the $C_{6,12}$-lactonization were determined by the HMBC spectrum of **2**. The HMBC spectrum showed important correlations between H-2 and C-1 (δ_C 129.9) and C-10 (δ_C 138.8); between H-3 and C-2 (δ_C 38.5), C-4 (δ_C 142.4) and C-5 (δ_C 81.8); and between the exomethylene protons and C-7 (δ_C 45.7), C-11 (δ_C 137.0), and C-12 (δ_C 168.8). The correlation between H-6 and C-5 (δ_C 81.8), C-7 (δ_C 45.7) and C-12 (δ_C 168.8), supported the $C_{6,12}$-lactonization. Also, the HMBC spectrum showed correlations between H-9 and C-8 (δ_C 69.7), C-14 (δ_C 15.7) and C-16 (δ_C 166.5) which supported the location of the angelate at C-9. Moreover, it displayed correlations between H-15 and C-3 (δ_C 127.4), C-4 (δ_C 142.4) and C-5 (δ_C 81.8); and between H-14 and C-1 (δ_C 129.9), C-9 (δ_C 72.7) and C-10 (δ_C 138.8). All proton and carbon signals were determined by ^{1}H–^{1}H COSY, HMQC and HMBC (Tables 1, 2). The stereochemistry was proved by the coupling constants. The α-orientation of the hydroxyl group at C-5 was suggested from the downfield shift of H-7α and H-9α, compared with the signals of H-7 and H-9 in compound **1**.[5,11] Therefore, compound **2** was identified as 2-deoxo-8-*O*-acetyl pumilin.

The EI-MS of compound **3** exhibited a molecular ion peak $[M]^+$ at *m/z* 464 and exact mass at *m/z* 464.1683, which established the elemental composition as $C_{23}H_{28}O_{10}$. Compound **3** had NMR spectral data similar to compound **4** (Tables 1, 2). However, the ^{1}H-NMR spectrum revealed the presence of two broad singlet signals at δ 5.80 and 6.40. The absence of a correlation between these two signals and H-7 in ^{1}H–^{1}H COSY suggested that compound **3** had an ester function instead of the lactone moiety (C=O, IR: $\nu=1720$ cm^{-1}). Additionally, the ^{1}H-NMR spectrum indicated the presence of an epoxy angelate at δ 3.03 (q, H-18), 1.30 (d, H-19) and 1.45 (s, H-20), a methyl ester at δ 3.76 (s), and an acetyl group at δ 2.10 (s) (C=O, IR: $\nu=1758$ cm^{-1}). The two methyls of the sesquiterpene were found at δ 2.28 (H-14, s) and 2.27 (H-15, d). One of the methyls for H-15 that showed correlation in ^{1}H–^{1}H COSY with the quartet signal at δ 6.19 could be assigned for H-3 (allylic coupling). The ^{13}C-NMR spectrum and DEPT experiments displayed 23 carbons signals; 7 oxygen bearing carbons at 81.8 (s), 77.2 (d), 70.6 (d), 71.3 (d), 52.4 (q), 59.5 (s), 60.2 (d), 4 carbonyl carbons at δ 193.0, 168.5, 170.0, 173.9 (s); and 6 olefinic carbons at δ 135.3 (d), 133.3 (s), 146.8 (s), 143.9 (s), 128.3 (t), 138.5 (s). The HMBC spectrum displayed several important correlations between H-3 and C-1 (δ_C 133.3) and C-2 (δ_C 193.0) and C-5 (δ_C 81.8); between OMe, H-13 and C-12 (δ_C 168.5); between H-6 and C-4 (δ_C 143.9) and C-11 (δ_C 138.5); and between H-9 and C-1 (δ_C 133.3), C-10 (δ_C 146.8) and C-16 (δ_C 173.9), which supported the location of the epoxy angelate at C-9. Moreover, it displayed correlations between H-15 and C-3 (δ_C 135.3); and between H-14 and C-1 (δ_C 133.3), C-9 (δ_C 71.3) and C-10 (δ_C 146.8). All signals were determined by ^{1}H–^{1}H COSY, HMQC. The stereochemistry of compound **3** was proved by coupling constants and NOESY spectrum. The *anti*-orientation of H-6 and H-7 was deduced from the coupling constant ($J=11.0$ Hz). The NOESY spectrum indicated clear effects between H-7 with H-9 and H-6 with H-8. Moreover, the α-orientation of the hydroxyl group at C-5 was deduced from the downfield shift of the signals H-7α and H-9α.[5,11] Therefore, compound **3** was established to be methyl-9β-(epoxyangeloyloxy)-5α,6α-dihydroxy-2-

Table 1. ^{1}H-NMR Spectral Data of Compounds **1**—**3** and **9** (400 MHz, $CDCl_3$, δ-Values)

Proton	**1**	**2**	**3**$^{b)}$	**9**
1				6.49, d, J=10.5
2	3.00, br d, J=22.0	2.97, br d, J=22.0		5.78, d, J=10.5
3	5.53, br s	5.65, br s	6.19, q, J=1.5	
4				2.84, q, J=6.5
5	3.46, br d, J=10.5			
6	3.63, t, J=10.5	4.04, d, J=11.0	3.64, br d, J=11.0	1.34, br t, J=11.5 1.55, m
7	3.33, t, J=10.5	4.08, tt, J=11, 3	3.73, m	2.56, t, J=11.5
8	5.24, t, J=10.5	5.34, t, J=11.0	5.23, t, J=11.0	1.55, m 1.61, m
9	5.53, br d, J=10.5	6.22,$^{a)}$ d, J=11.0	6.38, d, J=11.0	1.78, br d, J=14.0 1.92, dd, J=14.0, 3.5
13a	5.49, d, J=3.0	5.41, d, J=3.0	5.80, br s	5.33, br s
13b	6.11, d, J=3.0	6.11, d, J=3.0	6.40, br s	5.94, br s
14	1.59, s	1.62, s	2.28, s	0.72, s
15	1.91, s	1.90, s	2.27, d, J=1.5	0.98, d, J=6.5
18	3.09, q, J=5.5	6.22,$^{a)}$ qq, J=5.5, 1.5	3.03, q, J=5.5	
19	1.40, d, J=5.5	2.02, dq, J=5.5, 1.5	1.30, d, J=5.5	
20	1.52, s	1.87, dq, J=1.5, 1.5	1.45, s	
AcO	2.10, s	2.00, s	2.10, s	
MeO			3.76, s	

a) Overlapping signals. *b*) In Varian Unity 600 MHz NMR spectrometry.

Table 2. ^{13}C-NMR Data of Compounds **1**—**3**, **7** and **9** (100 MHz, $CDCl_3$, δ-Values)

No.	**1**	**2**	**3**	**7**	**9**
1	126.3 s	129.9	133.3	30.9 t	154.1 d
2	38.0 t	35.8	193.0 s	43.1 t	126.6 d
3	126.6 d	127.4	135.3	212.0 s	202.9
4	139.9 s	142.4	143.9	52.7 d	46.6
5	54.7 d	81.8 s	81.8 s	41.7 s	45.7
6	82.1 d	83.4	77.2	40.2 t	37.3
7	53.8 d	45.7	52.4	31.5 d	33.5
8	70.3 d	69.7	70.6	31.4 t	25.7
9	74.6 d	72.7	71.3	120.6 d	33.5 t
10	140.1 s	138.8	146.8	142.2 s	73.0
11	137.1 s	137.0	138.5	144.0 s	128.3
12	169.0 s	168.8	168.5	172.3 s	172.0
13	120.6 t	120.5	128.3	125.5 t	120.3
14	15.4 q	15.7	11.7	22.2 q	16.7
15	17.9 q	13.9	16.5	7.5 q	6.9
16	169.9 s	166.5	173.9		
17	59.6 s	126.8	59.5		
18	61.2 d	141.5 d	60.2 d		
19	14.3 q	20.5	13.7		
20	19.9 q	16.0	19.3		
AcO	169.6; 21.2 q	169.9; 20.5	170.0; 20.8		
MeO			52.4 q		

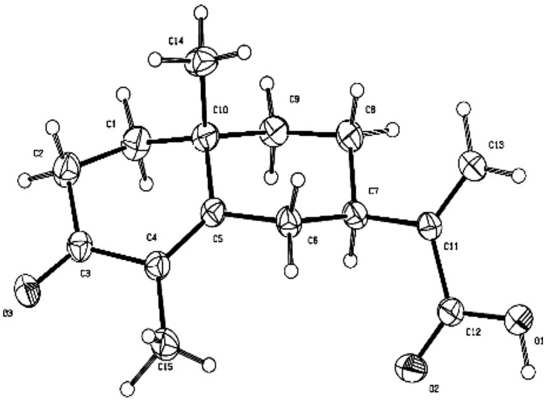

Fig. 2. ORTEP Diagram of the Crystal Structure of **8**

oxo-3,4-dehydro-δ-guaien-12-oate.

Repeated chromatography of the terpenoid portion of the leaf resin of *Balsamorhiza macrophylla* on silica gel afforded three known eudesmanic acids **7**,[9] **8**[10] and **9**.[9] The relative stereochemistry of compound **8** was determined by X-ray crystallographic analysis (Fig. 2). The methyl ester of compound **9** was reported by Zdero *et al.* to be a methyl ester derivative[9] and this is the first report of **9** being a as free acid from natural source. The EI-MS spectrum of compound **9** exhibited a molecular ion peak $[M-H_2O]^+$ at *m/z* 246, which indicated the molecular formula $C_{15}H_{20}O_4$ for **9**. The ^{1}H-NMR spectrum (Table 1) revealed a quartet signal at δ 2.84 (J=6.5 Hz, H-4), which showed correlation in ^{1}H–^{1}H COSY with a doublet at δ 0.98 (J=6.5 Hz, H-15). It also showed a triplet signal at δ 2.56 (J=11.5 Hz, H-7), indicating correlation in ^{1}H–^{1}H COSY with H-6, and appeared as a broad triplet at δ 1.34 (J=11.5 Hz, H-6a) and a multiple signal at δ 1.55 (m, H-6b). Furthermore, it showed two doublets at δ 6.49 (J=10.5 Hz, H-1) and 5.78 (J=10.5 Hz, H-2). The ^{13}C-NMR spectrum (Table 2) displayed 15 carbon signals and was classified by DEPT experiments as follows: 2 carbonyl carbon signals at δ 202.9 and 172.0 assigned for C-3 and C-12; 2 methyl carbon signals at δ 16.7 and 6.9, assigned for C-14 and C-15; 4 methylene carbon signals at δ 37.3, 25.7, 33.5, 120.3, assigned for C-6, C-8, C-9 and H-13; four methine carbon signals at δ 154.1, 126.6, 46.6, and 33.5, a signed for C-1, C-2, C-4 and C-7, respectively, and 3 quaternary carbon signals at δ 45.7, 73.0, and 128.3, assigned for C-5, C-10 and C-11, respectively. HMBC indicated several correlations: H-1 with C-3 and C-5, H-2 with C-4 and C-10, H-4 with C-3, C-14 and C-15, H-13 with C-7 and C-12, and H-14 with C-6 and C-10. The presence of H-14 upfield at 0.72 supported the α-orientation of the hydroxyl group at C-10.

The unpublished ^{13}C-NMR of compounds **7** and **9** are listed in Table 2.

In conclusion, the chemical investigation of the surface resin of the terpenoids of *B. sagittata* afforded guaianolides and heliangolides as its main constituents, while, *B. macrophylla* gave eudesmanes. The terpenoid constituents of both species appear to be consistent with the differences in the flavonoid constituents (unpublished data, Wollenweber), therefore, further species have to be investigated.

Experimental

General Experimental Procedures NMR spectra were measured with a Bruker AMX-400 (^{1}H-NMR: 400 MHz, ^{13}C-NMR: 100 MHz) spectrometer and a Varian Unity 600 MHz NMR spectrometer (^{1}H-NMR: 600 MHz), with TMS as an internal standard. ESI-mass spectra were acquired by means of APEX II-FIICR-MS [4.7 T, Bruker-Daltonik, Bremen, Germany]. The IR spectra [oily film, $CHCl_3$] were taken on a Perkin Elmer FT-IR spectrometer. Optical rotations were measured with a Perkin–Elmer 241 Polarimeter operating at sodium D line. TLC: Precoated silica gel $60F_{254}$ plates (Merck); Prep. TLC: silica gel PF_{254} (Merck, 200×200×0.25 mm); CC: silica gel type 60 (Merck).

Plant Material Aerial parts of flowering *B. sagittata* (PURSH) NUTT. and *B. macrophylla* NUTT. were collected in the spring of 2000 in Bogus Canyon, North Logan, Cache County, Utah and were air-dried. Further material of *B. sagittata* was collected from four populations in British Columbia (Ecological Reserve, Princeton; Anarchist Mountain, Osoyoos; Okanagan Falls; Marble Canyon area. Voucher specimens have been deposited at UBC.

Extraction and Isolation Dry aerial parts of *Balsamorhiza sagittata* and *B. macrophylla*, respectively, were briefly rinsed with acetone to dissolve the resinous exudated material. The exudates of the four *B. sagittata* collections from British Columbia were combined since they exhibited identical terpenoid and flavonoid patterns. The solutions were evaporated to dryness, redissolved in a small volume of hot MeOH, cooled to −10 °C, and the precipitating material was eliminated by centrifugation. The defatted solutions were passed over Sephadex LH-20 (Pharmacia) and eluted with MeOH to separate the flavonoids from the more aboundant terpenoids.

The terpenoid portion of *B. sagittata* and *B. macrophylla* was fractionated by flash column chromatography [5×55 cm] over silica gel [1 kg] eluting with hexane with an increasing amount of CH_2Cl_2. The first fraction (100%, hexane 1 l) of both species contained hydrocarbons and waxes. *B. sagittata*, the second fraction (hexane–CH_2Cl_2, 3 : 1, 2 l) gave a crude material which was purified by Sephadex LH-20 (3×35 cm, hexane–CH_2Cl_2–MeOH 7 : 4 : 0.5, 300 ml) to give compounds **1** (7 mg) and **5** (1.5 mg). The third fraction (CH_2Cl_2, 100%) was further purified by Sephadex LH-20 (3×35 cm, hexane–CH_2Cl_2–MeOH 7 : 4 : 1, 500 ml) to afford the compounds **2** (5.3 mg), **3** (2.2 mg), **4** (6.5 mg) and **6** (14.5 mg). *B. macrophylla*, the second fraction (hexane–CH_2Cl_2, 3 : 1, 2 l) was purified by a Sephadex column to give compounds **7** (35 mg), **8** (47 mg), **9** (7 mg).

2-Deoxo-5-deoxy-8-*O*-acetyl-17,18 Epoxy Pumilin (**1**): Yellow oil; IR $\nu_{\max}^{\mathrm{CHCl_3}}$ cm^{-1}: 2931, 1752 (broad), 1539, 1508.0, 1450, 1375, 1228, 1142, 1036, 736; ^{1}H- and ^{13}C-NMR (400, 100 MHz, $CDCl_3$): Tables 1 and 2; HR-ESI-MS *m/z*: 425.1571 $(M+Na)^+$ (Calcd for $C_{22}H_{26}O_7+Na$, 425.1567; $[\alpha]_D^{22}$ +0.03° ($c=3.88$, CH_2Cl_2).

2-Deoxo-8-*O*-acetyl Pumilin (**2**): Obtained as yellow oil; IR $\nu_{\max}^{\mathrm{CHCl_3}}$ cm^{-1}: 3446, 2926, 1777, 1751, 1725, 1646, 1437, 1377, 1258, 1234, 1149, 1042, 850, 738; ^{1}H- and ^{13}C-NMR (400, 100 MHz, $CDCl_3$): Tables 1 and 2; HR-ESI-MS *m/z*: 425.1571 $[M+Na]^+$ (Calcd for $C_{22}H_{26}O_7+Na$, 425.1561; $[\alpha]_D^{22}$ +0.024° ($c=2.75$, CH_2Cl_2).

Methyl-9*β*-(epoxyangeloyloxy)-5*α*,6*α*-dihydroxy-2-oxo-3,4-dehydro-*δ*-guaien-12-oate (**3**): White oil; IR $\nu_{\max}^{\mathrm{CHCl_3}}$ cm^{-1}: 3448, 1758, 1720, 1651, 1510, 1450, 1370, 1228, 1142, 1040, 736; ^{1}H- and ^{13}C-NMR (600, 100 MHz, $CDCl_3$): Tables 1 and 2; HR-EI-MS *m/z*: 464.1684 $[M]^+$, (Calcd for $C_{23}H_{28}O_{10}$, 464.1683, $[\alpha]_D^{22}$ +16.72° ($c=0.14$, $CHCl_3$).

17,18-Epoxy-8-*O*-acetyl Pumilin (**4**): Colorless powder; EI-MS *m/z*: 432 $[M]^+$, 414, 390, 372, 354, 316, 298, 274, 256, 238, 228, 161, 116, 83, 55; ^{1}H-NMR (400 MHz, $CDCl_3$): 6.28 (1H, q, $J=1.2$ Hz, H-3), 3.99 (1H, d, $J=10$ Hz, H-6), 4.14 (1H, m, H-7), 5.40 (1H, m, H-8), 6.28 (1H, d, $J=10$ Hz, H-9, overlapping), 6.25 (1H, $J=3.0$ Hz, H-13a), 5.62 (1H, $J=3.0$ Hz, H-13b), 2.31 (3H, d, $J=1.2$ Hz, H-14), 2.36 (3H, d, $J=1.2$ Hz, H-15), 3.19 (3H, q, $J=5.4$ Hz, H-18), 1.44 (3H, d, $J=5.4$ Hz, H-19), 1.48 (3H, s, H-20), 2.19 (3H, s, OAc); $[\alpha]_D^{22}$ −1.61° ($c=1.8$, $CHCl_3$).

8-*O*-Acetyl Pumilin (**5**): Yellow oil; EI-MS *m/z*: 416 $[M]^+$, 398, 375, 356, 316, 274, 257, 256, 239, 228, 161, 83, 55; ^{1}H-NMR (400 MHz, $CDCl_3$): 6.17 (1H, q, $J=1.2$ Hz, H-3), 3.90 (1H, d, $J=10$ Hz, H-6), 4.11 (1H, m, H-7), 5.35 (1H, t, $J=10$ Hz, H-8), 6.13 (1H, d, $J=10$ Hz, H-9, overlapping), 6.13 (1H, $J=2.8$ Hz, H-13a), 5.43 (1H, $J=2.8$ Hz, H-13b), 2.24 (3H, d, $J=0.7$ Hz, H-14), 2.27 (3H, d, $J=1.4$ Hz, H-15), 6.23 (3H, qq, $J=7.4$, 1.4 Hz, H-18), 2.00 (3H, dq, $J=7.4$, 1.4 Hz, H-19), 1.87 (3H, q, $J=1.4$ Hz, H-20), 2.02 (3H, s, OAc); ^{13}C-NMR (100 MHz, $CDCl_3$): 135.0 (C-1), 192.9 (C-2), 136.2 (C-3), 134.7 (C-4), 77.0 (C-5), 83.5 (C-6), 45.3 (C-7), 68.2 (C-8), 72.6 (C-9), 146.3 (C-10), 134.7 (C-11), 168.3 (C-12), 121.0 (C-13), 12.4 (C-14), 15.3 (C-15), 166.2 (C-16), 126.4 (C-17), 141.5 (C-18), 15.9 (C-19), 20.3 (C-20), 170.2, 20.3 (OAc).

9*β*-Acetoxy-3-epi-nobiliun (**6**): Colorless crystal; EI-MS *m/z*: 404 $[M]^+$, 344, 304, 244, 216, 179, 83, 55; ^{1}H-NMR (400 MHz, $CDCl_3$): 5.46 (1H, br t, $J=8$ Hz, H-1), 2.65 (1H, m, H-2*β*), 2.20 (1H, ddd, $J=8$, 13, 13 Hz, H-2*α*), 4.72 (1H, br dd, $J=5.4$, 11.5 Hz, H-3*β*), 5.13 (1H, br d, $J=11$ Hz, H-5), 4.78 (1H, br d, $J=11$ Hz, H-6*β*), 2.87 (1H, br d, $J=10$ Hz, H-7*α*), 5.20 (1H, t, $J=10$ Hz, H-8*β*), 5.34 (1H, d, $J=10$ Hz, H-9*α*), 6.32 (1H, d, $J=1.8$ Hz, H-13a), 5.64 (1H, d, $J=1.8$ Hz, H-13b), 1.79 (3H, d, $J=1.2$ Hz, H-14), 1.85 (3H, s, H-15), 6.10 (1H, qq, $J=7.2$, 1.8 Hz, H-18), 1.94 (3H, dq, $J=7.2$, 1.8 Hz, H-19), 1.82 (3H, q, $J=1.8$ Hz, H-20), 2.20 (3H, s, OAc); ^{13}C-NMR (100 MHz, $CDCl_3$): 126.6 (C-1), 32.5 (C-2), 67.7 (C-3), 141.0 (C-4), 123.1 (C-5), 75.0 (C-6), 48.4 (C-7), 69.8 (C-8), 80.4 (C-9), 132.6 (C-10), 133.8 (C-11), 168.0 (C-12), 127.6 (C-13), 17.3 (C-14), 12.3 (C-15), 169.6 (C-16), 126.8 (C-17), 140.2 (C-18), 15.7 (C-19), 20.2 (C-20), 166.1, 20.8 (OAc); $[\alpha]_D^{22}$ −2.96° ($c=2.8$, $CHCl_3$).

3-Oxo-10-hydroxy-eremophila-1,11(13)dien-12-oic Acid (**9**): Yellow oil; EI-MS *m/z*: 246 $[M-H_2O]^+$, 218, 185, 177, 167, 111, 97, 69, 55, 43; ^{1}H- and ^{13}C-NMR: Table 2.

Crystal Structure Determination of Compound 8 Crystal data: $C_{15}H_{20}O_3$, formula wt. 248.31 crystal size 1.40×0.20×0.10 mm, tetragonal $P4_2$, $a=6.7769(8)$ Å, $b=6.7769(8)$ Å, $c=29.963(3)$ Å, $V=1376.1(3)$ Å^3, $Z=4$, $D_c=1.199$ gm/cm^3, $F(000)=536$, GOF=1.047. The reflection data were collected on a Siemens P4 diffractometer operating in the ω scan mode, using graphite monochromated Cu$K\alpha$ radiation ($\lambda=1.54056$ Å). The structures were solved by direct methods using Bruker SHELEX-97 (Sheldrick, 1997) and refined by full matrix least squares on F^2 using Bruker SHELXL-97 (Sheldrick, 1997).[12] The final R and R_W were 0.327 and 0.879, respectively. Crystallographic data for the structural analysis have been deposited with the Cambridge Crystallographic Data Center and allocated the deposition number CCDC 182352. These data can be obtained free of charge *via* www.ccdc. Cam.ac.uk/cants/retrieving html/or from the CCDC, 12 union Road, Cambridge CB2 1 EZ, U.K.; Fax: +44-1223-336033; email: deposit@ccdc.cam.ac.uk).

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