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SESQUITERPENE LACTONES FROM *GAILLARDIA PULCHELLA*

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Key Word Index—*Gaillardia pulchella*; Compositae; Heliantheae; sesquiterpene lactones; pseudoguaianolides; seco-pseudoguaianolides; guaianolide; X-ray.

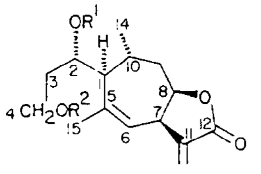
Abstract—The isolation of one guaianolide and eleven pseudoguaianolides as well as two seco-pseudoguaianolides including five new sesquiterpene lactones from above-ground parts of *Gaillardia pulchella* are described. The five new lactones are 4-*O*-acetyl-4,5-seco-neopulchell-5-ene, 6β-acetoxypulchellin-4-*O*-angelate, 6α-hydroxypulchellin, 6α-hydroxypulchellin-4-*O*-angelate, 2α,4α-dihydroxy-1α,10βH-guaia-5,11(13)-diene-8α, 12-olide. The structures were elucidated by spectroscopic methods and the stereochemistry of one compound, 6α-hydroxyneopulchellin-4-*O*-angelate, was established by X-ray analysis.

INTRODUCTION

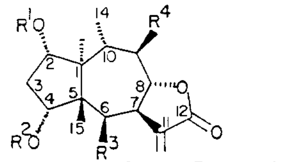
Several populations of *Gaillardia pulchella* Foug have been studied chemically. The main sesquiterpene lactones found in the aerial parts of *G. pulchella* from Florida, North Carolina and cultivated material from the Botanical Garden in Berlin are the pseudoguaianolides [1, 2]. However, extractions of *G. pulchella* collected in eastern New Mexico and Arizona furnished eudesmanolides as major sesquiterpene lactone constituents [3]. We have now chemically examined the aerial parts of *G. pulchella* from Austin, Texas and the main sesquiterpene lactones are pseudoguaianolides. The present chemical results indicate a close relationship of the *G. pulchella* in Austin to those populations of this species found in the southeastern USA.

RESULTS AND DISCUSSION

The dichloromethane extract of aerial parts of *G. pulchella* yielded, after column chromatography over silica gel, Sephadex LH-20 and HPLC (silica gel), 14 sesquiterpene lactones, namely, 4,5-seco-neopulchell-5-ene-2-*O*-acetate (**1**) [2], 4-*O*-acetyl-4,5-seco-neopulchell-5-ene (**2**), pulchellin (**3**) [1], 6β,9β-dihydroxypulchellin-2-*O*-isovalerate (**4**) [2], 4-*O*-acetyl-6β, 9β-dihydroxypulchellin-2-*O*-angelate (**5**) [2], 6β, 9β-diacetylpulchellin (**6**) [2], 6β-acetoxypulchellin-4-*O*-angelate (**7**), 6α-angeloyloxypulchellin-4-*O*-isovalerate (**8**) [2], 6α-ageloyloxypulchellin (**9**) [2], 6α-hydroxypulchellin-4-*O*-angelate (**10**), 6α-hydroxypulchellin (**11**), neopulchellin (**12**) [4], 6α-hydroxyneopulchellin (**13**) [2] and 2α,4α-dihydroxy-1α,10βH-guaia-5,11(13)-diene-8α,12-olide (**14**); of these **2**, **7**, **10**, **11** and **14** are new.



1 R¹ = Ac R² = H
2 R¹ = H R² = Ac



	R^1	R^2	R^3	R^4
3	H	H	H	H
4	iVal	H	OH	CH
5	Ang	Ac	OH	OH
6	H	H	OAc	OAc
7	H	Ang	OAc	H

Similar structures for lactones **1** and **2** were deduced from their almost identical mass spectra (see Experimental). The ^{13}C NMR and PDFA (one-pulse, decoupler off during acquisition) spectra of **1** and **2** showed in addition to two carbons for an acetoxyl group 15 carbons resonances for the skeletal moiety including three double bonds and two rings (Table 1); fragments $[M-HOAc]^+$ at m/z 248 (25.0% for **1** and 9.4% for **2**) also supported these deductions. From the ^{1}H NMR spectrum and 2D-COSY of **1**, the structure 4,5-seco-neopulchell-5-ene-2-*O*-acetate could be assigned; this compound was previously reported from cultivated material of *G. pulchella* from the Botanical Garden in Berlin. The ^{1}H NMR spectrum of **2** (Table 2) was very similar to

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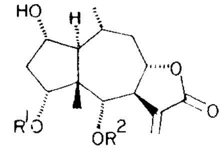
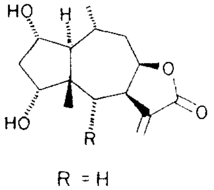
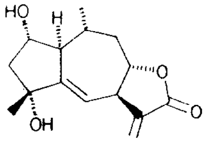


	R^1	R^2
8	iVal	Ang
9	H	Ang
10	Ang	H
11	H	H



12 R = H
13 R = OH



14

Table 1. ^{13}C NMR data for sesquiterpene lactones **1**, **2** and **14** (90 MHz, $CDCl_3$, δ-scale in ppm)

C	**1**	**2**	**14**
1	53.2 *d*	56.1 *d*	48.1
2	71.0 *d*	69.0 *d*	73.9
3	35.9 *t*	34.9 *t*	47.0
4	58.5 *t*	62.2 *t*	77.2
5	138.6 *s*	138.9 *s*	157.6
6	122.0 *d*	121.6 *d*	119.5
7	44.7 *d*	45.0 *d*	57.9
8	80.2 *d*	80.8 *d*	80.4
9	36.9 *t*	36.6 *t*	44.9
10	28.0 *d*	27.6 *d*	34.1
11	138.2 *s*	138.6 *s*	138.6
12	170.9 *s*	171.3 *s*	169.8
13	118.9 *t*	118.6 *t*	118.9
14	23.1 *q*	23.4 *q*	20.8
15	25.8 *q*	26.4 *q*	28.0
OAc	20.8 *q* 169.7 *s*	20.7 *q* 170.2 *s*	

that of **1** [2] except for the signals of H-1, 2 and 4: δ 2.42 *br dd* (H-1), 5.49 *ddd* (H-2), 3.67 *ddd* and 3.50 *ddd* (H-4 and 4') for **1** and 2.21 *br dd* (H-1), 3.90 *ddd* (H-2), 4.36 *ddd* and 4.17 *ddd* (H-4 and 4') for **2**. The presence of a 4-acetoxyl group in **2** was deduced from the highfield shift of the H-2 signal and the downfield shift of H-4 signals compared with those for **1**. The ^{13}C NMR signal for C-4 (δ 62.2 *t*) supported the conclusion that the primary hydroxyl (4-OH) was esterified. That **1** and **2** had the same stereochemistry followed from both exhibiting the same coupling constants. Therefore, **2** was established as 4-*O*-acetyl-4,5-seco-neopulchell-5-ene.

The ^1H and ^{13}C NMR spectra of **3**–**11** (Tables 1–4) showed that **3** is pulchellin [1] and that **4**–**11** are pulchellin derivatives. 2D-COSY allowed the assignment of all signals for **3**–**11**. Compounds **4**–**6**, **8** and **9** have been previously reported [2]. The coupling constants between H-6 and 7 indicated that **4**–**7** are 6β-oxygenated pulchellin derivatives ($J_{6,7} = 3$ Hz), and **8**–**11** are 6α-oxygenated pulchellin derivatives ($J_{6,7} = 10$ Hz) [2]. The typical signals in ^1H NMR spectrum of the new compound **7** indicated the presence of angeloyloxyl and acetoxy groups (Table 2). The identical chemical shifts of H-4 (δ 4.80), H-6 (δ 5.82) and singlet for the acetate methyl group appearing at relatively higher field (δ 1.96) in the ^1H NMR spectrum of **7** (Table 2) compared with these signals for the two known compounds 4-*O*-acetyl-6β-acetoxy-9β-hydroxypulchellin-2-*O*-angelate and neopulchellin-4-*O*-angelate [2] showed the relative position of the ester residues. Thus, we assigned **7** as 6β-acetoxypulchellin-4-*O*-angelate.

On the basis of ^1H NMR spectra and 2D-COSY the structure of the new compound **10** is similar to those of the known compounds **8** and **9** [2]. Its ^1H NMR spectrum indicated the presence of an angelate moiety. The corresponding signals in ^{13}C NMR spectra of **8** and **10** differ only slightly (Table 4), and the positioning of the ester group at C-4, not at C-6, in **10** was deduced from the highfield shift of the H-6 signal in the ^1H NMR spectrum compared with that signal in the spectrum of **8** [2]. All data (^1H and ^{13}C NMR, 2D-COSY, IR and mass spectrometry) indicated that the structure of **10** is 6α-hydroxypulchellin-4-*O*-angelate. However, the ^1H NMR spectrum of **10** exhibited unusual pairs of double doublets for H-13 and 13' and a downfield shift of H-13' when compared with signals observed for the known compounds **8** and **9** [2]. Furthermore, the chemical shifts for C-8 (δ 76.8–79.7 ppm) in ^{13}C NMR spectra of 6α-oxygenated pulchellin **8**–**11** are very different from those (δ 64.0–67.4 ppm) of 6β-oxygenated pulchellin **4**–**7** (Tables 3 and 4). Nevertheless, X-ray analysis of **10** confirmed the structure. Compound **10** crystallizes in the orthorhombic system, space group $P\ 2_1\,2_1\,2_1$, $a = 15.079(9)$ Å, $b = 13.761(7)$ Å, $c = 9.342(4)$ Å, $V = 1938.7(7)$ Å^3, $Z = 4$; 4139 reflections greater than $3\sigma(I)$ were refined to $R = 0.042$ and $R_w = 0.056$. An ORTEP drawing of **10** with the atom labelling scheme is shown in Fig. 1 and the anisotropic thermal parameters in Table 5. The atomic positional parameters with their equivalent isotropic thermal parameters, all bond lengths and angles, the torsion angles and hydrogen bonding distances are available upon request, from the fourth author. Figure 1 provides the relative configuration of all ring substituents. Atoms 02, 04, 06, 08, C14, H1 and H7 can be seen occupying the same side of the ring (below the ring) and therefore are labelled α-substituents. C11 and C15 occupy positions above the rings and, therefore, are labelled β-substituents. The molecules are linked together through hydrogen bonding with a water molecule and through 02, 04, 06 and 012. The two five-membered rings adopt the twist conformation ($^3T_4$) where atoms (C3) and (C4) lie on opposite sides of the plane defined by atoms (C1), (C2) and (C5).

The ^1H and ^{13}C NMR spectra of **11** (Tables 2 and 4) showed that this lactone was closely related to **8**–**10** and that hydroxyl groups are at C-2, 4 and 6: this conclusion was supported by ions $[M-H_2O]^+$ (5.6%), $[M-2H_2O]^+$ (18.1%) and $[M-3H_2O]^+$ (6.0%) in the

Table 2. ^{1}H NMR data for sesquiterpene lactones **2, 4, 7, 10, 11** and **14** (360 MHz, **2, 7, 11** and **14** in $CDCl_3$, **4** and **10** in acetone $-d_6$, δ-scale in ppm)

H	2	4	7	10	11	14
1	2.21 *br dd*	2.36 *dd*	2.05 *	2.34 *dd*	2.14 *dd*	2.42 *m*
2	3.90 *ddd*	5.02 *ddd*	4.18 *m*	4.21 *ddd*	4.05 *m*	4.18 *ddd*
3	1.86 *m*	1.53 *dd*	1.73 *dd*	1.47 *dd*	1.54 *dd*	2.03 *dd*
3		2.57 *ddd*	2.53 *ddd*	2.56 *ddd*	2.28 *ddd*	1.85 *dd*
4	4.36 *ddd*	3.84 *t*	4.80 *d*	5.01 *d*	4.06 *d*	
4′	4.17 *ddd*					
6	5.69 *br s*	4.98 *dd*	5.82 *d*	3.73 *d*	3.78 *d*	5.99 *dd*
7	3.40 *m*	3.08 *dddd*	3.13 *dddd*	3.36 *dddd*	2.98 *dddd*	3.42 *dddd*
8	4.51 *ddd*	4.58 *t*	4.55 *ddd*	4.09 *ddd*	4.13 *ddd*	3.78 *ddd*
9	2.61 *ddd*	3.30 *ddd*	1.43 *ddd*	1.47 *ddd*	1.43 *ddd*	1.69 *ddd*
9	1.61 *ddd*		2.39 *ddd*	2.18 *ddd*	2.33 *ddd*	2.44 *ddd*
10	2.36 *m*	1.86 *m*	2.06 *	1.86 *m*	1.78 *m*	1.46 *m*
13	6.19 *d*	6.22 *d*	6.19 *d*	6.14 *d*	6.18 *d*	6.21 *d*
13′	5.56 *d*	5.63 *d*	5.36 *d*	6.06 *dd*	6.16 *d*	5.66 *d*
14	1.15 *d*	1.16 *d*	1.22 *d*	1.20 *d*	1.18 *d*	1.16 *d*
15	1.86 *br s*	0.94 *s*	0.80 *s*	1.02 *s*	0.82 *s*	1.29 *s*
OAc	2.05 *s*		1.96 *s*			
2′		2.16 *d*				
3′		2.06 *m*	6.08 *qq*	5.98 *qq*		
4′		0.95 *d*	2.01 *dq*	1.93 *dq*		
5′		0.95 *d*	1.88 *dq*	1.86 *dq*		

J (Hz): **2**: 1,2 = 1, 10 = 5; 2,3 = 4; 2,3′ = 8.5; 3,4 = 3,4′ = 3′,4 = 5.6; 3′, 4′ = 10.5; 4, 4′ = 13.8; 7,8 = 10.5; 7,13 = 7,13′ = 3.2; 8,9 = 6.3; 8,9 = 11.2; 9, 9 = 13.9; 9, 10 = 7.1; 9, 10 = 2.2; 10, 14 = 7.4; **4**: 1,2 = 7; 1,10 = 10; 2,3 = 1.5; 2,3 = 8.5; 3,3 = 15; 3,4 = 4.5; 4,OH = 3.2; 6,OH = 6; 6,7 = 3; 7,8 = 9; 7,13 = 3.2; 7,13′ = 3; 8,9 = 9; 9,OH = 7; 9,10 = 10; 10,14 = 7; 3′, 4′ = 3′,5′ = 6.5; **7**: 2,3 = 2.2; 2,3 = 9.2; 3,3 = 16.2; 3,4 = 5; 6,7 = 3.5; 7,8 = 8.9; 7,13 = 3.5; 7,13′ = 3; 8,9 = 12; 8,9 = 3; 9 ,9 = 13; 9, 10 = 10; 9, 10 = 3; 10, 14 = 7; 3′, 4′ = 7; 3′,5′ = 4′, 5′ = 1.5; **10**: 1,2 = 8.9; 1,10 = 9.1; 2,3 = 3.3; 2,3 = 8.7; 3, 3 = 15.7; 3, 4 = 5.1; 6,7 = 10.2; 7.8 = 10; 7,13 = 7,13′ = 3.2; 8.9 = 12; 8,9′ = 3.2; 9,9 = 12.4; 9, 10 = 10; 9, 10 = 3.2; 10,14 = 6.9; 13,13′ = 1.9; 3′,4′ = 7; 3′,5′ = 4′,5′ = 1.5; **11**: 1,2 = 6.5; 1,10 = 9; 2,3 = 1.5; 2,3 = 9; 3,3 = 15; 3, 4 = 5; 6,7 = 10; 7,8 = 9, 7,13 = 3; 7,13′ = 2.5; 8,9 = 11; 8,9 = 3; 9, 9 = 14; 9, 10 = 10; 9, 10 = 3.5; 10, 14 = 7; **14**: 1,2 = 2.4; 1,6 = 2.8; 2,3 = 6.1; 2,3 = 2.4; 3,3 = 13; 6,7 = 4; 7,8 = 9; 7,13 = 3.7; 7,13′ = 3.2; 8,9 = 12; 8,9 = 2.5; 9,9 = 13; 10,14 = 7.

* Signal overlapping.

mass spectrum of **11** (see Experimental). Thus the structure of **11** is 6α-hydroxypulchellin.

The ^{1}H NMR spectrum of the new lactone **14** differed characteristically from those of **3**–**13** (Table 2) by a singlet at δ 1.29 for H-15 (Me) which, together with the 2D-COSY, suggested **14** to be a guaianolide. Moreover, the ^{1}H NMR spectrum of **14** was similar to that of the known compound 4α-hydroxy-2α-isovaleryloxy-1α,10βH-guaia-5,11(13)-diene-8α,12-olide isolated from *Loxothysanus sinuatus* [5]. Since no signals were observed for a side chain and the signal of H-2 was shifted upfield in the ^{1}H NMR spectrum of **14**, it appeared that the 2-isovaleryloxy group in 4α-hydroxy-2α-isovaleryloxy-1α,10β H-guaia-5,11(13)-diene-8α,12-olide was replaced by a hydroxyl group in **14**. Thus, **14** is assigned as 2α,4α-dihydroxy-1α,10β H-guaia-5,11(13)-diene-8α,12-olide.

The structures of **1, 3–6, 8, 9, 12** and **13** were confirmed by comparison of their spectral properties with reported data [2, 6]. The previously unreported ^{13}C NMR data of these known compounds are presented in Tables 1, 3, 4.

EXPERIMENTAL

Plant material. G. pulchella Foug was collected by Sarah Cox on 26 June, 1986, just off Hwy 29 on Loop 332, 8.3 miles NW of Leander, Texas. A voucher speciman (S. Cox, S. N.) is deposited in the Plant Resources Center at the University of Texas at Austin, Texas.

Isolation of sesquiterpene lactones. Unground plant material (1 kg) was extd with CH_2Cl_2 for 1 hr. The extract was concd to a syrup at low temp. (~40°), then redissolved in MeOH. The resulting soln was kept in a refrigerator overnight. After filtering to remove the ppt., the filtrate was concd to a syrup at low temp. (~40°). The syrup was dried completely under a high vacuum system. The extract (12.4 g) was first chromatographed over a silica gel column packed in hexane–EtOAc (19:1). The column was eluted with a hexane–EtOAc gradient, with increasing amounts of EtOAc. Further purification was achieved by a combination of Sephadex LH-20 chromatography (cyclohexane–CH_2Cl_2–MeOH 7:4:1) and HPLC [semi-prep silica gel column (10 mm × 25 cm); RI detector; hexane–EtOAc

Table 3. ^{13}C NMR data for sesquiterpene lactones **3–7** (90 MHz, $CDCl_3$, δ-scale ppm)

C	**3**	**4**	**5**	**6**	**7**
1	48.1	47.1 *d*	46.4	45.7	50.0 *d*
2	75.5	81.0 *d*	80.0	74.6	74.7 *d*
3	45.9	43.9 *t*	38.0	42.4	44.3 *t*
4	80.9	80.0 *d*	82.3	80.0	82.3 *d*
5	44.3	52.9 *s*	51.3	52.6	51.3 *s*
6	42.1	79.0 *d*	79.7	78.7	76.8 *d*
7	56.3	49.1 *d*	49.8	52.3	58.0 *d*
8	82.3	64.4 *d*	64.1	68.3	67.4 *d*
9	33.8	78.9 *d*	79.0	79.4	40.3 *t*
10	28.6	37.7 *d*	36.4	35.0	28.7 *d*
11	140.8	137.9 *s*	135.7	136.6	136.0 *s*
12	170.4	172.4 *s*	170.5	170.6	170.2 *s*
13	119.5	120.7 *t*	122.2	120.5	120.7 *t*
14	21.2	22.4 *q*	17.6	19.8	20.5 *q*
15	25.9	22.3 *q*	21.1	20.4	20.1 *q*
OAc			17.1	17.4	17.9 *q*
			169.0	168.3	169.1 *q*
				16.5	
				169.8	
1′		169.7 *s*	167.3		166.7 *q*
2′		40.9 *t*	127.4		127.7 *s*
3′		25.9 *d*	138.0		138.3 *d*
4′		17.9 *q*	15.6		15.7 *q*
5′		17.5 *q*	20.3		20.9 *q*

Table 4. ^{13}C NMR data for sesquiterpene lactones **8–13** (90 MHz, **8, 9, 11, 12** and **13** in $CDCl_3$, **10** in acetone-d_6 δ-scale in ppm)

C	**8**	**9**	**10**	**11**	**12**	**13**
1	46.4 *d*	48.0	49.8	52.3	46.8	46.8
2	73.2 *d*	75.2	73.9	75.4	77.1	76.7
3	43.7 *t*	43.9	45.1	43.9	44.5	42.2
4	80.4 *d*	79.5	82.2	79.7	81.3	76.7
5	51.3 *s*	55.3	55.4	54.5	40.8	52.9
6	81.9 *s*	80.1	81.6	81.4	39.8	79.9
7	55.2 *d*	53.5	53.3	52.5	54.9	51.8
8	76.8 *d*	79.5	79.3	78.5	77.4	76.7
9	40.4 *t*	40.7	41.4	41.2	35.9	35.8
10	27.0 *d*	28.0	28.3	28.6	29.0	28.6
11	136.5 *s*	137.1	137.1	138.5	140.4	136.9
12	169.4 *s*	169.1	170.4	170.5	170.1	170.3
13	123.4 *t*	123.3	123.7	123.7	122.3	126.0
14	20.0 *q*	20.8	20.8	21.1	20.7	19.8
15	21.5 *q*	23.7	23.0	24.4	22.2	20.3
1′	171.9 *s*	165.9	167.3			
2′	29.6 *t*	125.9	129.7			
3′	25.5 *d*	142.3	139.5			
4′	22.5 *q*	15.9	15.9			
5′	22.5 *q*	20.3	20.8			
1″	166.9 *s*					
2″	126.7 *s*					
3″	140.8 *d*					
4″	15.7 *q*					
5″	20.2 *q*					

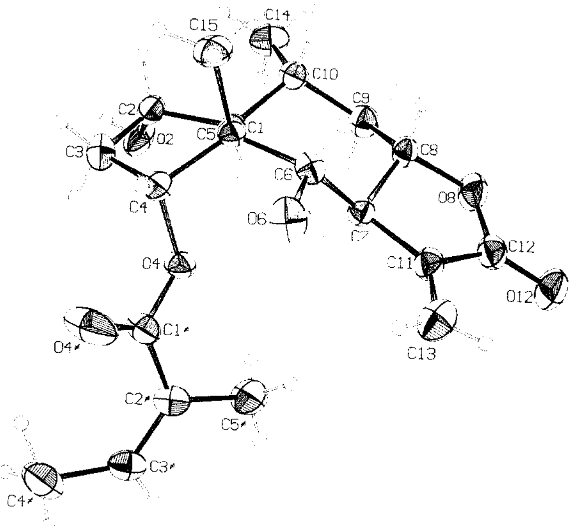


Fig. 1. ORTEP drawing of 6α-hydroxypulchellin-4-*O*-angelate (**10**).

(4:1, 7:3, 1:1, 3:7) as elutants; flow rate 2.2 ml/min]. Compound **1** (32 mg), **2** (16 mg), **3** (24 mg), **4** (2671 mg), **5** (693 mg), **6** (29 mg), **7** (94 mg), **8** (984 mg), **9** (13 mg), **10** (79 mg), **11** (24 mg) **12** (27 mg), **13** (79 mg) and **14** (9 mg) were obtained.

X-ray. Data were collected on a Syntex P 2_1 diffractometer with a graphite monochromator utilizing Mo-K_α radiation ($\lambda = 0.71069$Å) and equipped with a Syntex LT 1 low temp delivery system (163 K). The crystal was orthorhombic, $a = 15.079$ (9), $b = 13.761$ (6), $c = 9.342$ (4)Å, $V = 1938.7$ (8)Å^3, space group p $2_12_12_1$, $z = 4$, Dc (g/cc, 163*k*) = 1.310, chemical formula, $C_{20}H_{28}O_6 \cdot H_2O$, FW = 382.45 g, and $F(000) = 824$ electrons; 8071 reflections were measured using ω-scan and symmetrically over 1° about $K_{\alpha 1,2}$ maximum and an offset of +1° in ω from $K_{\alpha 1,2}$ maximum at a scan rate of 3°/min (min) and 6°/min (max) and a 2θ range of 4.0 to 65.0°. 45 well centered reflections with $14.5° < 2\theta < 21.5°$ were used to refine the unit cell parameters. Four reflections (130, 600, 022, 102) were remeasured every 196 reflections to monitor instrument and crystal stability. A total of 4139 unique reflections with intensity greater than 30 were used in refining 340 variables. The refinement converged to a goodness of fit of 1.016 and a maximum shift/e.s.d. of 0.49, minimum and maximum peaks in ΔF map (eÅ^{-3}) were −0.22 and 0.36 respectively. The structure was solved using Direct Methods (SHELX-86) from which the locations of all non-hydrogen atoms were obtained. The oxygen of the water molecule of crystallization was observed in the first difference Fourier map. The structure was refined using weighted full-matrix least squares. The hydrogen atoms of C1, C2, C3. C4, C7, C9 and the

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Unit cell parameters were obtained by least-squares refinement of the setting angles of 45 reflections with $14.5° < 2\theta < 21.5$. Crystal density measured in a $ZnCl_2$ soln.

Syntex $P2_1$ diffractometer, graphite monochromator and Syntex LT-1 low temperature delivery system. Data reduction carried out as described in ref. [7]. Crystal and instrument stability monitored by remeasurement of 4 check reflections after every 196 reflections. These data were analysed as detailed in ref. [8]. Relevant expressions are as follows: Function minimized: $\sum w(|F_o| - |F_c|)^2$, where $w = 1/[\sigma(F_o)]^2$

$R = \sum|(|F_o| - |F_c|)/\sum|F_o||$

$R_w = [\sum w(|F_o| - |F_c|)^2/\sum w|F_o|^2]^{1/2}$

$S = [\sum w(|F_o| - |F_c|)^2/(m-n)]^{1/2}$

Table 5. Anisotropic thermal parameters* for non-hydrogen atoms of compound **10**.

Atom	U_{11}	U_{22}	U_{33}	U_{12}	U_{13}	D_{23}
O4	0.0145(6)	0.0150(6)	0.0208(7)	0.0005(5)	−0.0037(6)	−0.0036(5)
O8	0.0271(8)	0.0131(6)	0.0269(8)	0.0026(6)	−0.0004(7)	0.0002(6)
O12	0.0364(9)	0.0165(7)	0.0369(9)	−0.0059(7)	−0.0060(8)	0.0052(7)
O6	0.0274(8)	0.0228(7)	0.0184(7)	0.0067(6)	0.0068(7)	−0.0005(6)
O4′	0.0216(8)	0.0333(9)	0.0618(14)	0.0096(7)	−0.0124(9)	−0.0293(10)
O2	0.0377(10)	0.0217(7)	0.0193(7)	−0.0090(7)	−0.0040(7)	0.0076(6)
C4	0.0165(8)	0.0137(7)	0.0214(9)	0.0002(7)	−0.0033(8)	−0.0030(7)
C2′	0.0161(9)	0.0213(8)	0.0162(9)	−0.0003(7)	0.0005(7)	−0.0044(7)
C7	0.0165(8)	0.0123(7)	0.0151(8)	−0.0005(7)	−0.0012(7)	0.0003(6)
C5′	0.0256(11)	0.0177(9)	0.0343(13)	−0.0021(8)	−0.0042(10)	−0.0061(9)
C1	0.0142(8)	0.0131(7)	0.0144(8)	−0.0030(6)	−0.0022(7)	0.0014(6)
C9	0.0187(9)	0.0176(8)	0.0209(9)	0.0034(7)	0.0024(8)	−0.0009(7)
C10	0.0159(8)	0.0172(8)	0.0173(8)	0.0004(7)	−0.0011(7)	−0.0005(7)
C3′	0.0172(9)	0.0276(10)	0.0175(9)	−0.0018(8)	−0.0005(8)	−0.0005(8)
C8	0.0187(9)	0.0117(7)	0.0190(9)	0.0014(7)	−0.0013(8)	0.0004(7)
C12	0.0252(10)	0.0169(8)	0.0192(9)	−0.0008(8)	−0.0062(8)	0.0017(7)
C5	0.0137(7)	0.0125(7)	0.0164(8)	0.0003(6)	−0.0030(7)	−0.0014(7)
C11	0.0207(9)	0.0159(8)	0.0161(8)	−0.0016(8)	−0.0029(8)	0.0014(7)
C3	0.0252(10)	0.0173(8)	0.0317(12)	0.0016(8)	−0.0008(10)	0.0061(8)
C2	0.0206(9)	0.0150(8)	0.0202(9)	−0.0044(7)	−0.0022(8)	0.0029(7)
C4′	0.0196(10)	0.0367(12)	0.0327(13)	0.0065(9)	−0.0032(10)	0.0041(11)
C15	0.0212(9)	0.0203(8)	0.0220(10)	−0.0030(8)	−0.0039(8)	−0.0060(8)
C6	0.0179(8)	0.0157(8)	0.0151(8)	0.0025(7)	−0.0013(7)	−0.0007(7)
C13	0.0311(12)	0.0258(11)	0.0256(11)	−0.0044(10)	0.0033(10)	0.0038(10)
C1′	0.0164(8)	0.0196(8)	0.0204(9)	0.0030(7)	−0.0038(8)	−0.0035(8)
C14	0.0188(9)	0.0313(11)	0.0245(10)	−0.0023(9)	0.0055(9)	−0.0013(9)
OS	0.0348(10)	0.0356(10)	0.0225(8)	−0.0108(9)	−0.0058(8)	0.0016(8)

*The U_{ij} are the mean-square amplitudes of vibration in A^2 from the general temperature factor expression: $\exp[-2\pi^2(h^2a^{*2}U_{11} + k^2b^{*2}U_{22} + l^2c^{*2}U_{33} + 2hka^*b^*U_{12} + 2hla^*c^*U_{13} + 2klb^*c^*U_{23})]$.

methyl hydrogens on C14 and C15 were not found in the difference Fourier map and their positions calculated; all other hydrogens were obtained from the difference Fourier map. All non-hydrogen atoms were treated anisotropically, hydrogen atoms isotropically. The refinement converged to $R = 0.042$ and $R_w = 0.056$ for 4139 reflections of intensity greater than $3\sigma(I)$.

4-O-Acetyl-4,5-seco-neopulchell-5-ene (**2**). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3480 (OH), 1775, 1730 (γ-lactone), 1740, 1240 (OAc); MS *m/z* (rel. int.): 248 $[M-HOAc]^+$ (9.4) ($C_{15}H_{20}O_3$), 192 $[M-COHCH_2CH_2OAc]^+$ (33.3), 174 (24.6), 159 (60.2), 147 (34.1), 131 (49.9), 117 (51.3), 107 $[C_8H_{11}]^+$ (100), 91 (62.2), 77 (42.4), 57 (62.8).

6β-Acetoxypulchellin-4-O-angelate (**7**). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3500 (OH), 1765 (γ-lactone), 1740, 1230 (OAc), 1720 (OCOR); MS *m/z* (rel. int.): 407 $[M+1]^+$ (1.6), 406 $[M]^+$ (0.7) ($C_{22}H_{30}O_7$), 347 $[M-OAc]^+$ (5.7), 346 $[M-HOAc]^+$, 307 $[M-OAng]^+$ (15.7), 289 $[M-OAng-H_2O]^+$ (10.7), 265 (14.5), 247 $[M-OAng-HOAc]^+$ (71.5), 229 $[M-OAng-HOAc-H_2O]^+$ (58.0), 107 $[C_8H_{11}]^+$ (34.3), 83 $[C_4H_7CO]^+$ (100), 55 $[C_4H_7]^+$ (73.9).

6α-Hydroxyneopulchellin-4-O-angelate (**10**). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3450 (OH), 1750 (γ-lactone); MS *m/z* (rel. int.): 346 $[M-H_2O]^+$ (2.7) (M^+: 364, $C_{20}H_{28}O_6$), 265 $[M-OCOR]^+$ (8.1), 264 $[M-HOCOR]^+$ (8.5), 247 $[M-OCOR-H_2O]^+$ (36.4), 246 $[M-HOCOR-H_2O]^+$ (43.0), 229 $[M-OCOR-2H_2O]^+$ (25.9), 192 (40.0), 107 $[C_8H_{11}]^+$ (82.7), 83 $[C_4H_7CO]^+$ (100), 55 $[C_4H_7]^+$.

6α-Hydroxypulchellin (**11**). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3400 (OH), 1750 (γ-lactone); MS *m/z* (rel. int.): 283 $[M+1]^+$ (2.4) (M^+: 282, $C_{15}H_{22}O_5$), 264 $[M-H_2O]^+$ (5.6), 246 $[M-2H_2O]^+$ (18.1), 228 $[M-3H_2O]^+$ (6.0), 218 (14.0), 202 (10.1), 192 (28.5), 121 (51.1), 107 $[C_8H_{11}]^+$ (100), 95 (69.0), 81 (33.7), 69 (64.8), 55 (43.8).

2α, 4α-Dihydroxy-1α, 10β H-guaia-5,11 (13)-diene-8α, 12-olide (**14**). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3420 (OH), 1760 (γ-lactone), 1720 (C=C); MS *m/z* (rel. int.): 262 $[M]^+$ (3.6) ($C_{15}H_{20}O_4$), 246 $[M-O]^+$ (47.1), 228 $[M-O-H_2O]^+$ (87.7), 213 (49.8), 185 (50.2), 171 (41.9), 157 (71.8), 141 (63.0), 128 (100), 115 (85.2), 105 (50.1), 91 (85.5), 77 (59.7), 43 (98.7).

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