Polyol Monoterpenes and Sesquiterpene Lactones from the Pacific Northwest Plant *Artemisia suksdorfii*

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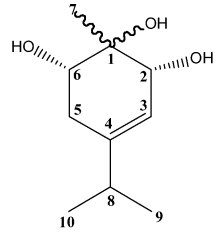
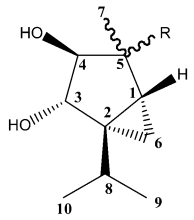
Five new polyol monoterpenes (**1**−**5**) and seven new sesquiterpene lactones (**6**−**12**), along with five previously identified compounds, were isolated from the aerial parts of *Artemisia suksdorfii*. The structures of the new compounds were established by high-field NMR techniques (^{1}H, ^{13}C, ^{1}H−^{1}H DEPT, COSY, HMQC, and HMBC) and in case of **6** confirmed by X-ray analysis.

Plants of the genus *Artemisia* (family Asteraceae, tribe Anthemideae) have been used in folk medicine by many cultures since ancient times. Herbal teas from those species have been used as analgesic, antibacterial, antipasmodic, and hemostatic agents. Historically, *Artemisia* has been a productive genus in the search for new biologically active compounds. Phytochemical investigations have proven that this genus is rich in sesquiterpenes and monoterpenes.[1−4] The guaianolide structural type is the main sesquiterpene class of this genus. Compounds with this fused 5,7,5-ring system have been reported to possess cytotoxic, root-growth stimultory, germination inhibitory, and immunomodulatory activity.[5−9] Artemisinin, an endoperoxide sesquiterpene lactone, is a constituent of the annual herb *Artemisia annua*.[10] Artemisinin and its derivatives are promising new antimalarial drugs.[11,12] The importance of this genus has led us to investigate *Artemisia suksdorfii* Piper, a native perennial of the coastal Pacific Northwest area of the United States.

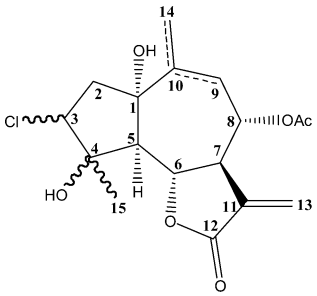
Organic solvent extraction of the aerial part of *A. suksdorfii* followed by fractionation on silica gel, Sephadex LH-20, preparative TLC, and reversed-phase HPLC has yielded five new polyol monoterpenes (**1**−**5**) and seven new sesquiterpenes (**6**−**12**), in addition to five known compounds.



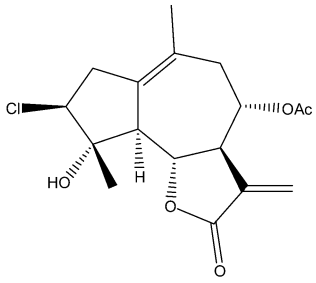
1 α OH, β CH_3
2 β OH, α CH_3



3 R=α OH, β CH_3
4 R=α OCH_3, β CH_3
5 R=β OH, α CH_3



6 α OH, β CH_3, β Cl, Δ^9
7 β OH, α CH_3,α Cl, Δ^9
8 α OH, β CH_3, β Cl, $\Delta^{10,14}$



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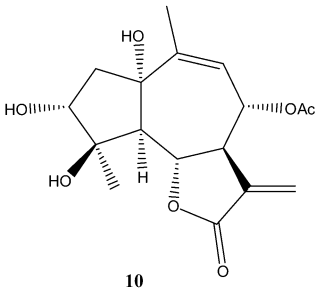

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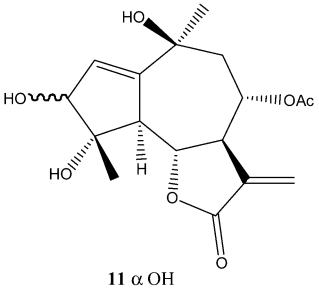

11 α OH
12 β OH

Results and Discussion

The molecular formula of **1** was established as $C_{10}H_{18}O_3$ on the basis of HRCIMS and ^{13}C and DEPT NMR analysis. The CIMS exhibited an ion peak $[M - H]^+$ at *m*/*z* 185 ($C_{10}H_{18}O_3$), followed by a fragment at *m*/*z* 169 $[M - H_2O]^+$. The HRCIMS showed a $[M - H]^+$ ion at *m*/*z* 185.1178. The ^{1}H NMR spectrum of **1** exhibited one olefinic proton as a narrow doublet at δ 5.73 (J = 2.5 Hz, H-3) that correlated in the ^{1}H−^{1}H COSY spectrum with a second narrow doublet at δ 4.77 (J = 2.5 Hz, H-2). Also, the signal at δ 4.27 (1H, dd, J = 10, 6, H-6) showed correlations with two signals at δ 2.63 (1H, dd, J = 17, 6 Hz, H-5β) and 2.40 (1H, dddd, J = 17, 10, 2.5, 2.5 Hz, H-5$_\alpha$). The large coupling constant of H-6 was consistent with H-6ax. The isopropyl group was determined from two methyl doublets at δ 1.00 (d, J = 7 Hz, H-9) and 0.99 (d, J = 7, H-10), and the signal at δ 2.02 was assigned to H-8 (sept., J = 7, 7 Hz). The ^{1}H

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Table 1. ^{1}H NMR Data of Compounds **1**−**5** ($CDCl_3$, 500 MHz, δ values)

position	**1**	**2**	**2**[a]	**3**	**4**[b]	**5**
H-1β				1.20 dd (8.5, 3.5)	1.18	1.29
H-2β	4.77 d (2.5)	3.90 m	4.12 br s			
H-3	5.73 d	5.56 d	3.81 br s			
H-3β	(2.5)	(3.0)		3.91 d (6.5)	3.96	4.20
H-4α				3.42 d (6.5)	3.44	3.18
H-5α	2.40 dddd (17, 10, 2.5, 2.5)	1.98 ddd (14.5, 10, 2)	1.99			
H-5β	2.63 dd (17, 6)	2.44 dd (14.5, 5.5)	2.40			
H-6α				0.93 dd (6.5, 3.5)	0.41	0.62
H-6β	4.27 dd (10, 6.0)	3.89 m	3.71 dd (10, 6.0)	0.44 dd (8.5, 6.5)	0.47	0.53
H-7	1.70 s	1.11	1.10	1.22	1.20	1.27
H-8	2.02 sept.	2.26	2.22	1.46	1.44	1.51
H-9	1.00 d (7.0)	1.04	1.02	0.93	0.93	0.99
H-10	0.99 d (7.0)	1.04	1.05	0.99	0.99	1.00

[a] In CD_3OD. [b] OCH_3: δ_H 3.31.

Table 2. ^{13}C NMR Data of Compounds **1**−**5** ($CDCl_3$, 500 MHz, δ values)[a]

position	**1**[b]	**2**	**3**	**4**[c]	**5**
1	75.6 s	73.6	30.5 d	18.7	30.9
2	73.0 d	72.3	33.1 s	33.3	34.8
3	123.1 d	118.5	76.4 d	76.6	79.7
4	142.0 s	147.5	82.6 d	81.8	82.1
5	34.6 t	33.1	75.8 s	80.5	75.6
6	76.3 d	69.6	10.3 t	10.6	11.6
7	14.8 q	16.9	23.1 q	27.1	23.4
8	34.6 d	34.5	31.1 d	31.4	31.2
9	21.5 q	21.5	20.2 q	20.0	20.3
10	21.2 q	20.9	19.4 q	19.2	19.7

[a] All assignments were based on 1D and 2D NMR measurements (HMBC, HMQC, DEPT, COSY). [b] In pyridine-d_5. [c] OCH_3: δ 50.6.

NMR signal of H-8 was observed downfield at δ 2.02, indicating the presence of a Δ^3 double bond, which was supported by the HMBC spectrum: H-3/C-8 and H-3/C-5 correlated with each other. A NOE experiment was used to establish the stereochemistry of **1**, in which H-6β showed a correlation with H-5β and H-2β showed a correlation with H-7. Therefore, **1** was identified as (+)-(1*S**,2*R**,6*S**)-trihydroxy-*p*-menth-3-ene, a newly reported natural product.

NMR and HRCIMS data revealed that **2** is an epimer of **1**. The NMR data for **2** (Tables 1 and 2) were very similar to those of **1** except for the chemical shift differences associated mostly with the epimerization at C-1. Overlapping of ^{1}H NMR signals for H-2 and H-6 at δ 3.90 in $CDCl_3$ was solved by switiching to CD_3OD as the solvent, which showed H-6 as a double doublet at δ 3.71 (J = 10, 6 Hz) and H-2 at δ 4.12 (brs). The other proton and carbon signals were determined by ^{1}H−^{1}H COSY, HMQC, and HMBC experiments (Tables 1 and 2). In a NOE experiments, H-2β/H-5β and H-5β/H-6β correlated with each other. Therefore, **2** was identified as (+)-(1*R**,2*R**,6*S**)-trihydroxy-*p*-menth-3-ene, a newly reported natural product.

The NMR spectra of **3** were markedly different than those of **1** and **2** as a result of the presence of two upfield protons at δ 0.44 (J = 8.5 and 6.5 Hz) and 0.99 (dd, J = 6.5 and 3.5 Hz). These correlated with a carbon signal at δ 10.3 in the HMQC spectrum. Additionally, the ^{13}C NMR and DEPT spectra were different as a result of the presence of a nonoxygenated methine proton at δ 30.5 and nonoxygenated quaternary carbon at δ 33.1. These data, together with the CIMS peak of $[M + H]^+$ at *m*/*z* 187, proved that **3** was a bicyclic monoterpene. The chemical shifts of the protons at δ 0.44, 0.99, and 1.20 were typical for a monoterpene having a chiral cyclopropane moiety.[14] The other proton signals were assigned as an isopropyl group at δ 1.46 (1H, sept., J = 7.0 Hz, H-8) and 0.93 (6H, d, J = 7.0 Hz, H-9,10) and secondary alcoholic protons at δ 3.42 (d, J = 6.5 Hz) and 3.91 (d, J = 6.5 Hz). The C-3 and C-4 signals were assigned on the basis of a HMBC experiment, and H-6/C-3 and H-7/C-4 correlated with each other. In a NOE experiment, H-3β/H-7, H-9/H-3β and H-10/H-3β, H-6β/H-1β, and H-6β/H-9 correlated with each other, suggesting the β-orientation of these protons. Therefore, **3** was identified as (+)-(3*S**,4*R**,5*R**)-trihydroxysabinane, a newly reported natural product.

Compound **4** was assigned a molecular formula of $C_{11}H_{18}O_2$ by HRCIMS, which gave an ion peak at *m*/*z* 201.1493 $[M + H]^+$. The ^{1}H NMR spectrum was identical with **3** except for the presence of an additional methyl signal at δ 3.31, which correlated with a carbon signal at δ 50.6, in the HMQC spectrum. The placement of a methyl group at C-5 was determined by HMBC; the important correlations were observed between C-5 and the methoxyl group (δ_H 3.31), H-7, H-4, and H-1$_\beta$. The stereochemistry of **4** was the same as **3**. Therefore, **4** was identified as (+)-(3*S**,4*R**)-dihydroxy-(5*R**)-methoxysabinane, a newly reported natural product.

The ^{1}H and ^{13}C NMR data of **5** were again quite similar to those of **3**. Differences in the chemical shifts between **3** and **5** indicated that the two compounds are epimeric at C-5. Most notable was H-6$_\alpha$, which appeared at δ 0.62 in **5** and 0.99 in **3**, as well as H-6$_\beta$, appearing at δ 0.53 in **5** and 0.44 in **3**. The stereochemistry of **5** was deduced from a NOE experiment: H-6α/H-7 and H-6α/H-4α correlated with each other, indicating the α-orientation of H-7. The HRCIMS of **5** gave a molecular ion peak at *m*/*z* 187.1336 ($C_{10}H_{18}O_3$). Therefore, **5** was identified as (+)-(3*S**,4*R**,5*S**)-trihydroxysabinane, a newly reported natural product.

Compound **6** was obtained as colorless crystals, mp 225−227 °C, $[\alpha]^{20}_D$ +54.0° (*c* 0.33, $CHCl_3$). The presence of a

Table 3. ^{1}H NMR Data of Compounds **6**−**12** ($CDCl_3$, 500 MHz, δ values)

position	6	7	8	9	10	11	12
H-2α	2.39 dd (13, 7.5)	2.98 dd (15, 5)	2.44 dd (14, 13)	2.96 dd (15, 8)	2.50 dd (14.5, 4.5)	5.84 dd (2.5, 2.5)	5.66
H-2*β*	2.22 dd (13, 13)	1.93 d (15)	2.10 dd (14, 7)	2.48 dd (15, 11.5)	2.15 br s (14.5)		
H-3	4.43 dd (13, 7.5)	4.11 d (5)	4.49 dd (13, 7)	4.22 dd (11.5, 8)	3.77 br s	4.04 d (2.5)	4.48
H-5α	2.60 d (11)	2.88 d (10)	2.34 d (11.5)	2.86 br d (10.5)	2.51 d (10.5)	3.26 br d (10)	3.06
H-6*β*	4.21 dd (11, 9)	4.42 dd (10, 10)	4.12 dd (11.5, 8.5)	4.06 dd (10.5, 10.5)	4.34 dd (10.5, 9)	4.04 dd (10, 9.5)	4.12
H-7α	3.80 m	3.95	3.37	3.16	3.74	3.07	4.39
H-8*β*	5.27 br dd (10.5, 4)	5.21 br dd (9, 3)	4.85 ddd (11, 11, 5)	5.01 ddd (11, 10.5, 4)	5.22 dd (10.5, 3)	5.08 ddd (6, 6, 2)	5.06
H-9α	5.60 d (4)	5.60	2.92 dd (11, 11)	2.45 dd (15, 4)	5.51 br d (3)	1.87 dd (17, 6)	1.92
H-9*β*			2.65 dd (11, 5)	2.53 (15, 10.5)		2.08 (17, 2)	2.04
H-13a	5.77 d (3)	5.74	5.82	5.88	5.72	5.56	5.51
H-13b	6.34 d (3)	6.31	6.29	6.39	6.30	6.19	6.13
H-14	1.93 br s	1.93	5.23 br s 5.27 br s	1.79	1.93	1.44	1.39
H-15	1.26 s	1.82	1.30	1.46	1.53	1.35	1.25
OAc	2.17 s	2.14	2.16	2.23	2.13	2.14	2.09

Table 4. ^{13}C NMR Data of Compounds **6**−**12** ($CDCl_3$, 500 MHz, δ values)[a]

position	6	7	8	9	10	11	12
1	75.3 s	81.2	76.7	128.0	81.8	151.3	145.4
2	46.6 t	45.8	44.3	39.2	45.4	127.1	128.8
3	63.0 d	79.4	63.7	63.5	79.4	79.5	81.4
4	79.5 s	79.9	80.4	80.9	82.1	78.6	84.9
5	64.4 d	63.6	62.9	55.8	64.2	57.8	59.0
6	76.2 d	76.7	77.8	79.5	75.6	77.0	77.7
7	43.2 d	42.2	47.8	51.8	44.0	46.7	46.8
8	72.9 d	73.0	74.6	70.5	73.2	72.2	72.3
9	123.7 d	123.1	36.3 t	41.9	122.9	43.1	43.6
10	140.2 s	141.2	143.5	127.2	140.1	78.6	70.0
11	136.2 s	136.8	135.3	135.4	136.7	137.5	137.4
12	169.6 s	169.7	169.6	168.7	169.2	169.8	169.9
13	123.9 t	123.2	124.5	123.8	123.7	122.1	121.9
14	24.3 q	25.1	117.1 t	23.7 q	24.7	30.4	30.2
15	17.3 q	24.9	16.8	17.4	24.3	22.0	17.1
OAc	170.5 s	170.6	170.2	169.7	170.4	170.7	170.7
	20.9 q	21.0	20.8	21.1	21.2	21.3	21.1

[a] All assignments were based on 1D and 2D NMR measurements (HMBC, HMQC, DEPT, COSY).

chlorine atom in the molecule was deduced from the HRCIMS, which gave a molecular ion peak at *m*/*z* 357.1096 (calcd 357.1105, $C_{17}H_{21}O_6Cl$). Other fragments are reported in the Experimental Section. ^{13}C NMR and DEPT experiments (Table 4) of compound **6** revealed the presence of 17 carbon signals, including three methyls, two methylenes, six methines, and six quaternary carbons. The ^{1}H NMR spectrum (Table 3) exhibited signals at δ 6.34 (1H, d, J = 3 Hz, H-13b) and 5.77 (1H, d, J = 3 Hz, H-13a), typical of exomethylene lactone protons. An additional signal was observed at δ 5.60 (1H, d, J = 4 Hz, H-9) that showed a correlation with an olefinic carbon at δ 123.7 (d) in the HMQC spectrum. Three functional double doublets were observed at δ 5.27 (δ_C 72.9, 1H, J = 10.5, 4 Hz, H-8), 4.43 (δ_C 63.0, 1H, J = 13, 7.5 Hz, H-3), and 4.21 (δ_C 76.2, 1H, J = 11, 9 Hz, H-6). The other protons were determined from the ^{1}H−^{1}H COSY and HMQC NMR spectra.

Although the sterechemistry of the chiral centers in **6** at C-3, C-5, C-6, and C-7 could be established from the coupling constants, a NOE experiment supported the proposed structure. The protons H-3/H-5 and H-7/H-5 showed correlations with each other, suggesting an α-orientation of the three protons. Finally, the relative stereochemistry of **6** was confirmed by X-ray analysis, as shown in Figure 1, supporting the structure and sterochemistry as 1α,4α-dihydroxy-3*β*-chloro-8α-acetoxyguai-9,11(13)-dien-6α,12-olide, a newly reported natural product.

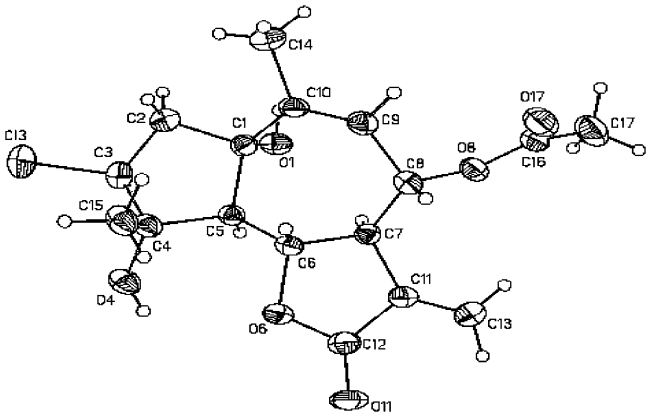

Figure 1. ORTEP drawing of **6**.

The ^{1}H and ^{13}C NMR spectra of **7** were similar to those of **6**. The presence of 17 carbon signals, together with the molecular ion peak at *m*/*z* 357 in the CIMS, supported the same molecular formula $C_{17}H_{21}O_6Cl$. In fact, their NMR spectra were almost identical except for a coupling constant change for H-3 of 5 Hz (δ_H 4.11) in **7** compared to 13 and 7.5 Hz (δ_H 4.43) in **6**. Additionally, H-15 appeared at δ 1.82 (s), in contrast to δ 1.26 (s) in **6**. The ^{13}C NMR spectrum showed pronounced differences in the chemical shifts of C-1 to C-4 (Table 4), suggesting the *β*-orientation of H-3 and the α-orientation of H-15. This was supported by the observation of NOE correlations between H-5/H-7, H-5/H-15, and H-15/H-5. The chemical shift of H-5 at δ 2.88, compared to 2.60 in **6**, suggested the same α-orientation of the hydroxyl group at C-1.[15,16] The other proton and carbon signals were determined from the ^{1}H−^{1}H COSY, HMQC, and HMBC spectra. Therefore, compound **7** was identified as 1α,4*β*-dihydroxy-3α-chloro-8α-acetoxyguai-9,11(13)-dien-6α,12-olide, a newly reported natural product.

Comparison of the ^{1}H and ^{13}C NMR spectral data of **8** with those of **6** indicated these compounds to be isomers.

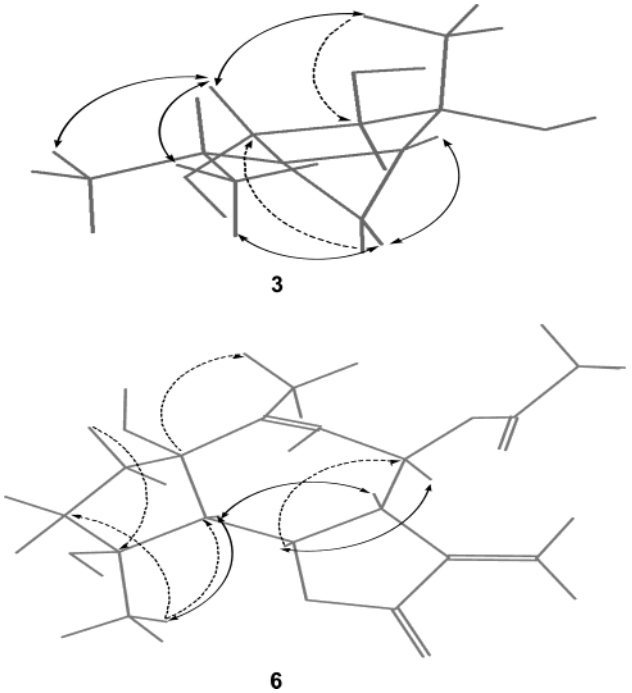

Figure 2. Selected key NMR correlations for **3** and **6** (↔ NOE, → HMBC).

The general features of the NMR data of **8** closely resembled those of **6**, except for the position of the double bond at C-10. The replacement of the olefinic methyl at δ 1.93 (H-14) in **6** by two olefinic protons at δ 5.23 and 5.27 in **8** suggested a $\Delta^{10,14}$ double bond in this compound, instead of the Δ^{9} double bond in **6**. This was indicated by the observation of H-8 at δ 4.85 as a ddd due to the presence of two protons at C-9. Also, the chemical shifts and coupling constants of H-3, H-5, and H-6 were in agreement with the *trans*-diaxial disposition of the protons at H-5 (α), H-6 (*β*), and H-7 (α). In a NOE experiment, H-6/H-15 and H-3/H-5 showed correlations with each other. The presence of a $\Delta^{10,14}$ double bond was supported by the HMBC spectrum, H-2, H-10, and H-14 correlating with C-1, while H-13 correlated with C-12. Therefore, compound **8** was identified as 1α,4α-dihydroxy-3*β*-chloro-8α-acetoxyguai-10(14),11(13)-dien-6α,12-olide, a new natural product.

Compound **9** gave a molecular formula of $C_{17}H_{21}O_5Cl$, as established by HRCIMS at *m/z* 341.1165. A loss of 16 amu compared to compounds **6**−**8** indicated the loss of an oxygen atom. A second difference of **9** compared to structures **6**−**8** was the presence of two disubstituted olefinic carbons observed at δ 128.0 and 127.2 and the presence of exomethylene lactone carbons at δ 135.4 (s) and 123.8 (d) in a DEPT NMR experiment. The DEPT as well as HRCIMS spectral data indicated a $\Delta^{1,10}$ double bond in the molecule. This was supported by the HMBC experiment (Figure 2), in which H-14/C-1 and H-9/C-10 correlated with each other. The stereochemistry of **9** was deduced from comparison of its coupling constants and chemical shifts with those of **5**−**8**. Therefore, compound **9** was assigned as the new compound 4α-hydroxy-3*β*-chloro-8α-acetoxyguai-1(10),11(13)-dien-6α,12-olide.

HRCIMS of compound **10** revealed the absence of a chlorine atom in the molecule from the molecular ion peak $[M + H - H_2O]^+$ at *m/z* 321.1345, $C_{17}H_{22}O_7$. However, the ^{1}H and ^{13}C NMR spectral data were very close to those of **6** and **7**. The exomethylene protons were observed in the ^{1}H NMR spectrum at δ 6.30 (d, J = 3 Hz, H-13b) and 5.72 (d, J = 3 Hz, H-13a) and correlated with a carbon signal at δ 123.7 in the HMQC spectrum. Additionally, four proton signals occurred downfield at δ 5.51 (brd, J = 3 Hz, H-9), 5.22 (dd, J = 10.5, 3 Hz, H-8), 4.34 (dd, J = 10.5, 9 Hz, H-6), and 3.77 (brs, H-3). Three singlets, integrating for three protons each, at δ 2.13, 1.93, and 1.53, were assigned from the HMQC and HMBC spectral data to the acetyl groups at C-8, H-14, and H-15, respectively. The stereochemistry of compound **10** was established by a NOE experiment, in which H-5/H-15 and H-5/H-7 exhibited correlations with each other. The presence of H-5 downfield at δ 2.51 supported the α-orientation of the hydroxyl group at C-1. Therefore, the new compound **10** was established structurally as 1α,3α,4*β*-trihydroxy-8α-acetoxyguai-9,11(13)-dien-6α,12-olide.

A ^{1}H NMR comparison of **6** and **11** indicated the absence of an olefinic methyl at C-10 in **11** and substitution by a methyl group neighboring a hydroxyl at δ 1.44 (s). ^{13}C NMR and DEPT experiments indicated the presence of two double bonds in the molecule: the first was typical for the exomethylene lactone at δ 137.5 (s) and 122.1 (t) located between C-11 and C-13, and the second double bond was located within the five-membered ring. On the basis of the HMBC NMR data, C-1 correlated with H-3, H-5, and H-14, indicating that the second double bond was located between C-1 and C-2. The CIMS exhibited a molecular ion peak at *m/z* 339 followed by successive losses of water to give ion peaks at *m/z* 321 and 303. The HRCIMS gave an ion peak at *m/z* 339.1453 ($C_{17}H_{22}O_7$). Finally, the stereochemistry was established by a NOE experiment, in which H-6/H-15 and H-3/H-15 correlated with each other. This established a *β*-orientation for the protons at C-3, C-6, and C-15. Additionally, H-5/H-14 showed an NOE correlation confirming the α-orientation of the protons at C-5 and C-14. From these data, **11** was identified as 3α,4α,10*β*-trihydroxy-8α-acetoxyguai-1,11(13)-dien-6α,12-olide, a newly reported natural product. The 11,13-dihydro derivative of **11** was reported from *Artemisia siversiana*.[3]

Comparison of the HRCIMS and ^{1}H and ^{13}C NMR data of **11** and **12** indicated that these compounds were epimeric at C-3 (Tables 3 and 4). Clear differences were observed in the chemical shifts of the protons and carbons at H-2, H-3, and H-5 (0.18, −0.44, and 0.20 ppm, respectively). In the ^{13}C NMR spectrum, marked shifts were observed at C-1, C-2, C-3, and C-4 (5.9, −1.7, −1.9, and −6.3 ppm, respectively) The sterochemistry was established from a NOE experiment that showed on irradiation of H-6 enhancements of H-8 (δ_H 5.06), H-9 (δ_H 2.04), and H-15 (δ_H 1.26), suggesting the *β*-orientation of H-8, H-9, and H-15. Also, irradiation of H-3 enhanced H-5, which proved the α-orientation of H-3 and H-5. Therefore, **12** was identified as 3*β*,4α,10*β*-trihydroxy-8α-acetoxyguai-1,11(13)-dien-6α,12-olide, a newly reported natural product.

The structure of the known compounds 8α-acetoxy-3α,4α-epoxy-1α-hydroxyguai-9,11(13)-dien-6α,12-olide,[16] arteglasin A,[17] and arteglasin B[16] were deduced from their complete ^{1}H, ^{13}C NMR, HMQC, and HMBC NMR spectra.

Experimental Section

General Experimental Procedures. Optical rotations were recorded on a JASCO-20C automatic recording spectropolarimeter. The IR spectra ($CHCl_3$) were recorded on a Perkin-Elmer FT-IR spectrometer. ^{1}H, ^{13}C NMR and 2D spectra were recorded on a Bruker AMX-400 spectrometer with TMS as internal standard. CIMS were recorded on a TSQ-70 triple stage quadrupole mass spectrometer (70 eV).

Plant Material. The aerial parts of *A. suksdorfii* were collected by one of the authors (G.S.) during the flowering stage, in September 1999, in Linn County, Corvallis, OR. A voucher specimen (192499) has been deposited at Oregon State University Herbarium, OR.

Extraction and Isolation. The air-dried aerial parts (950 g) of *A. suksdorfii* were macerated at room temperature in CH_2Cl_2−MeOH (1:1) for 24 h. The extract was concentrated under reduced pressure to give 30 g of green oily residue. The extract was fractionated on a silica gel column eluted with a CH_2Cl_2−*n*-hexane step gradient. The fractions were monitored by TLC. Fraction 2 (*n*-hexane−CH_2Cl_2, 1:1, 1.5 g) was separated by a Sephadex LH-20 column (*n*-hexane−CH_2Cl_2−MeOH, 9:1:1) to afford several fractions, of which the first fraction gave 8α-acetoxy-3α,4α-epoxy-1α-hydroxyguai-9,11(13)-dien-6α,12-olide (17 mg), arteglasin B (18 mg), and arteglasin A (15 mg). The second fraction was purified by HPLC (Eurospher, C_{18}, MeOH−H_2O, 6:4) to afford 1α,4α-dihydroxy-3β-chloro-8α-acetoxyguaian-9,11(13)-dien-12,6α-olide (**6**) (16 mg) and 1α,4β-dihydroxy-3α-chloro-8α-acetoxyguai-9,11(13)-dien-6α,12-olide (**7**) (9 mg). The third fraction (*n*-hexane−CH_2Cl_2, 25:75, 0.9 g) was separated by preparative TLC (*n*-hexane−CH_2Cl_2, 7:0.5) to give 1α,4α-dihydroxy-3β-chloro-8α-acetoxyguai-10(14),11(13)-dien-6α,12-olide (**8**) (11 mg) and 4α-hydroxy-3β-chloro-8α-acetoxyguai-1(10),11(13)-dien-6α,12-olide (**9**) (6 mg). The fourth fraction (CH_2Cl_2, 100%) was subjected to passage over a Sephadex LH-20 column (*n*-hexane−CH_2Cl_2−MeOH, 9:1:1.5) to afford two complex mixtures. The first was purified by HPLC (Eurospher, C_{18}, MeOH−H_2O, 6.5:3.5) to afford 3β,4α,10β-trihydroxy-8α-acetoxyguai-1,11(13)-dien-6α,12-olide (**11**) (5 mg), monoterpenes (+)-(1*S**)-7-dihydroxysabinane (10 mg) and (−)-(1*R**)-7-dihydroxysabinane (7 mg), and 3α,4α,10β-trihydroxy-8α-acetoxyguai-1,11(13)-dien-6α,12-olide (**12**) (3.5 mg). The second mixture was purified by preparative TLC (*n*-hexane−CH_2Cl_2−MeOH, 7:1:1.5), yielding 1α,3α,4β-trihydroxy-8α-acetoxyguai-9,11(13)-dien-6α,12-olide (**10**) (4 mg) and **8** (5 mg). The fifth fraction (CH_2Cl_2−MeOH, 85:15) was a complex mixture, which was separated using a Sephadex LH-20 column (*n*-hexane−CH_2Cl_2−MeOH, 9:1:2) to give **1** (7 mg), **2** (3 mg), **3** (2.5 mg), and **5** (6 mg).

(+)-(1*S,2*R**,6*S**)-Trihydroxy-*p*-menth-3-ene (1):** brownish oil; $[\alpha]^{25}_D$ +95.0° (*c* 0.3, $CHCl_3$); IR (KBr, film) ν_{max} 3360, 2990, 2980, 1660 cm^{-1}; ^1H and ^{13}C NMR, see Table 1 and Table 2, respectively; CIMS *m/z* 185 $[M - H]^+$ (100), 169 $[(M + H) - H_2O]^+$ (36), 151 $[(M + H) - 2\ H_2O]^+$ (42); HRCIMS *m/z* 185.1178 (calcd for $C_{10}H_{17}O_3$, 185.1178).

(+)-(1*R,2*R**,6*S**)-Trihydroxy-*p*-menth-3-ene (2):** colorless oil; $[\alpha]^{25}_D$ +56.0° (*c* 0.22, $CHCl_3$); IR, the same as **1**; ^1H and ^{13}C NMR, see Tables 1 and 2, respectively; CIMS *m/z* 185 $[M - H]^+$ (18), 169 $[(M + H) - H_2O]^+$ (80), 151 $[(M + H) - 2\ H_2O]^+$ (100); HRCIMS *m/z* 185.1180 (calcd for $C_{10}H_{15}O_3$, 185.1178).

(+)-(3*S,4*R**,5*R**)-Trihydroxysabinane (3):** yellowish powder; $[\alpha]^{25}_D$ +7.0° (*c* 0.7, $CHCl_3$); IR (KBr, film) ν_{max} 3384, 2924, 1455 cm^{-1}; ^1H and ^{13}C NMR, see Tables 1 and 2, respectively; CIMS *m/z* 187 $[M + H]^+$ (6),169 $[(M + H) - H_2O]^+$ (24), 151 $[(M + H) - 2\ H_2O]^+$ (78), 123 $[(M + H) - 3\ H_2O]^+$ (100); HRCIMS *m/z* 187.1336 (calcd for $C_{10}H_{19}O_3$, 187.1334).

(+)-(3*S,4*R**)-Dihydroxy-(5*R**)-methoxysabinane (4):** colorless oil; $[\alpha]^{25}_D$ +33.0° (*c* 0.1, $CHCl_3$); IR, the same as **3**; ^1H and ^{13}C NMR, see Tables 1 and 2, respectively; CIMS *m/z* 201 $[M + H]^+$ (28), 183 $[(M + H) - H_2O]^+$ (92), 169 $[(M + H) - CH_3OH]^+$ (38), 151 $[(M + H) - (CH_3OH + H_2O)]^+$ (83); HRCIMS *m/z* 201.1493 (calcd for $C_{11}H_{21}O_3$, 201.1491); 183.13901 (calcd for $C_{11}H_{19}O_2$, 183.1385).

(+)-(3*S,4*R**,5*S**)-Trihydroxysabinane (5):** colorless oil; $[\alpha]^{25}_D$ +19.0° (*c* 0.1, $CHCl_3$); IR, the same as **3**; ^1H and ^{13}C NMR, see Table 1 and Table 2, respectively; CIMS *m/z* 169 $[(M + H) - H_2O]^+$ (20), 151 $[(M + H) - 2\ H_2O]^+$ (76), 123 $[(M + H) - 3\ H_2O]^+$ (100); HRCIMS *m/z* 169.1228 (calcd for $C_{10}H_{17}O_2$, 169.1229).

1α,4α-Dihydroxy-3β-chloro-8α-acetoxyguai-9,11(13)-dien-6α,12-olide (6): colorless crystals, mp 225−227 °C; $[\alpha]^{25}_D$ +54.0° (*c* 0.33, $CHCl_3$); IR (KBr, film) ν_{max} 3421, 2925, 1750, 1734 cm^{-1}; ^1H and ^{13}C NMR, see Tables 3 and 4, respectively; CIMS *m/z* 357/359 $[M + H^+]$ (32), 339/341 $[(M + H) - H_2O]^+$ (75), 321 $[(M + H) - HCl]^+$ (44), 297/299 $[(M + H) - CH_3COOH]^+$ (100), 279 $[m/z\ 297 - H_2O]^+$ (35), 261 $[m/z\ 279 - H_2O]^+$ (78); HRCIMS *m/z* 357.1096 (calcd for $C_{17}H_{21}O_6Cl$, 357.1105), 339.1011 (calcd for $C_{17}H_{19}O_5Cl$, 339.0999).

1α,4β-Dihydroxy-3α-chloro-8α-acetoxyguai-9,11(13)-dien-6α,12-olide (7): colorless gummy residue; $[\alpha]^{25}_D$ +52.5° (*c* 0.17, $CHCl_3$); IR, the same as **6**; ^1H and ^{13}C NMR, see Tables 3 and 4, respectively; CIMS *m/z* 357/359 $[M + H^+]$ (6), 339/341 $[(M + H) - H_2O]^+$ (66), 321 $[(M + H) - HCl]^+$ (16), 297/299 $[(M + H) - CH_3COOH]^+$ (100), 279 $[m/z\ 297 - H_2O]^+$ (55), 261 $[m/z\ 279 - H_2O]^+$ (50); HRCIMS *m/z* 339.0998 (calcd for $C_{17}H_2O_5Cl$, 339.0999).

1α,4α-Dihydroxy-3β-chloro-8α-acetoxyguai-10(14),11(13)-dien-6α,12-olide (8): yellowish oil; $[\alpha]^{25}_D$ +52.5° (*c* 0.195, $CHCl_3$); IR, the same as **6**; ^1H and ^{13}C NMR, see Tables 3 and 4, respectively; CIMS *m/z* 357/359 $[M + H^+]$ (36), 339/341 $[(M + H) - H_2O]^+$ (66), 321 $[(M + H) - HCl]^+$ (88), 297/299 $[(M + H) - CH_3COOH]^+$ (18), 279 $[m/z\ 297 - H_2O]^+$ (60), 261 $[m/z\ 279 - H_2O]^+$ (100); HRCIMS *m/z* 357.1094 (calcd for $C_{17}H_{21}O_6Cl$, 357.1105).

4α-Hydroxy-3β-chloro-8α-acetoxyguai-1(10),11(13)-dien-6α,12-olide (9): yellowish powder; IR (KBr, film) ν_{max} 3433, 2934, 1748 cm^{-1}; ^1H and ^{13}C NMR, see Tables 3 and 4, respectively; CIMS *m/z* 341/343 $[M + H]^+$ (54), 305 $[M + H - HCl]$ (20), 281 $[(M + H) - CH_3COOH]^+$ (58), 263 $[(M + H) - (CH_3COOH - H_2O)]^+$ (24), 245 $[(M + H) - (CH_3COOH - 2\ H_2O)]^+$ (100); HRCIMS *m/z* 341.1165 (calcd for $C_{17}H_{21}O_5Cl$, 341.1156).

1α,3α,4β-Trihydroxy-8α-acetoxyguai-9,11(13)-dien-6α,12-olid (10): greenish oil; $[\alpha]^{25}_D$ +47.0° (*c* 0.01, $CHCl_3$ + MeOH); IR (KBr, film) ν_{max} 3427, 2930, 1745 cm^{-1}; ^1H and ^{13}C NMR, see Tables 3 and 4, respectively; CIMS *m/z* 321 $[M + H - H_2O]^+$ (95), 303 $[(M + H) - 2\ H_2O]^+$ (22), 279 $[(M + H) - (H_2O + CH_2CO)]^+$ (20), 261 $[(M + H) - (H_2O + CH_3COOH)]^+$ (100), 243 $[261 - H_2O]^+$ (52); HRCIMS *m/z* 321.1345 (calcd for $C_{17}H_{20}O_6$, 321.1338).

3β,4α,10β-Trihydroxy-8α-acetoxyguai-1,11(13)-dien-6α,12-olide (11): reddish oil; $[\alpha]^{25}_D$ +34.0° (*c* 0.21, $CHCl_3$); IR (KBr, film) ν_{max} 3450, 2930, 1756, 1742 cm^{-1}; ^1H and ^{13}C NMR, see Tables 3 and 4, respectively; CIMS *m/z* 339 $[M + H]^+$ (28), 321 $[M + H - H_2O]^+$ (32), 303 $[M + H - 2\ H_2O]^+$ (100), 279 $[M + H - CH_3COOH]^+$ (22), 261 $[m/z\ 279 - H_2O]^+$ (78), 243 $[m/z\ 261 - H_2O]^+$ (70); HRCIMS *m/z* 339.1453 (calcd for $C_{17}H_{22}O_7$, 339.1444).

3α,4α,10β-Trihydroxy-8α-acetoxy-guai-1,11(13)-dien-6α,12-olide (12): greenish oil; $[\alpha]^{25}_D$ −21.0° (*c* 0.15, $CHCl_3$); IR, the same as **11**; ^1H and ^{13}C NMR, see Tables 3 and 4, respectively; CIMS *m/z* 339 $[M + H]^+$ (100), 321 $[M + H - H_2O]^+$ (35), 303 $[M + H - 2\ H_2O]^+$ (15), 261 $[m/z\ 279 - H_2O]^+$ (35), 243 $[m/z\ 261 - H_2O]^+$ (15); HRCIMS *m/z* 339.1453 (calcd for $C_{17}H_{22}O_7$, 339.1444).

X-ray Analysis of 6. Crystal and intensity data for **6** were obtained using a Bruker P4 automated diffractometer, which utilized graphite-monochromated Mo Kα radiation. The structures were solved using direct methods and refined using full-matrix, least-squares procedures. Positions for all hydrogen atoms were calculated based on atomic geometry. The structures were solved, refined, and displayed using the program package SHELTXL PC.[18] Crystal data and experimental details follow: $C_{17}H_{21}ClO_6$, mol wt = 356.79, crystal size 0.4 × 0.3 × 0.18 mm, monoclinic, space group $P2_1$, a = 5.9816(7) Å, b = 16.792(2) Å, c = 8.6367(11) Å, β = 91.616(11)°, V = 867.2(2) $Å^3$, Z = 2, D_c = 1.366 g cm^{-3}, $F(000)$ = 376, μ(Mo Kα) = 0.249 mm^{-1}, independent data, 1952 (R_{int} = 0.0242), θ range 2.36 to 25.02°, R [$I > 2\sigma(I)$] = 0.0390, R_{all} = 0.0502, largest peak and hole in difference map, 0.196, −0.196 e $Å^{-3}$. Crystallographic data of **6** including atomic coordinates, bond lengths and angles, thermal parameters, and additional experimental details have been deposited in the Cambridge Crystallographic Data Center (CCDC 238129). Copies of the data can be obtained free of charge, on application to the Director, CCDC, 12 Union Road, Cambridge CB2 1EZ, UK [fax: +44-(0)1223-336033 or e-mail: deposite@ccdc.cam.ac.uk].

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Supporting Information Available: This material is available free of charge via the Internet at http://pubs.acs.org.

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