Novel Sesquiterpenoids from *Siegesbeckia orientalis*

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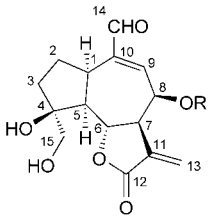
Five new sesquiterpenoids, namely, 8β-(angeloyloxy)-4β,6α,15-trihydroxy-14-oxoguaia-9,11(13)-dien-12-oic acid 12,6-lactone (**1**), 4β,6α,15-trihydroxy-8β-(isobutyryloxy)-14-oxoguaia-9,11(13)-dien-12-oic acid 12,6-lactone (**2**), 11,12,13-trinorguai-6-ene-4β,10β-diol (**3**), (1(10)*E*,4*E*,8*Z*)-8-(angeloyloxy)-6α,15-dihydroxy-14-oxogermacra-(1(10),4,8,11(13)-tetraen-12-oic acid 12,6-lactone (**9**), and (1(10)*E*,4β)-8β-(angeloyloxy)-6α,14,15-trihydroxygermacra-1(10),11(13)-dien-12-oic acid 12,6-lactone (**11**), and three new artifacts, (1(10)*E*,4*Z*)-8β-(angeloyloxy)-9α-ethoxy-6α,15-dihydroxy-14-oxogermacra-1(10),4,11(13)-trien-12-oic acid 12,6-lactone (**6**), (1(10)*E*,4*Z*)-8β-(angeloyloxy)-9α,13-diethoxy-6α,15-dihydroxy-14-oxogermacra-1(10),4-dien-12-oic acid 12,6-lactone (**7**), and (1(10)*E*,4*Z*)-8β-(angeloyloxy)-9α-ethoxy-6α,15-dihydroxy-13-methoxy-14-oxogermacra-1(10),4-dien-12-oic acid 12,6-lactone (**8**), together with the three known sesquiterpenoids **4**, **5**, and **10**, were isolated from the aerial parts of *Siegesbeckia orientalis* L. Their structures were established by spectral methods, especially 1D- and 2D-NMR spectral methods.

1. Introduction. – The plants of the genus *Siegesbeckia* belonging to the family Compositae are annual herbs widely distributed in tropical, subtropical, and temperate parts of the world. Three species of this genus grow in China, and the aerial parts have been used as a traditional Chinese medicine 'Xi-Xian' to treat rheumatic arthritis, hypertension, malaria, neurasthenia, and snakebite [1]. The extracts and some chemical constituents of *Siegebeckia* plants exhibited antioxidative [2], antiallergic [3], infertile [4], and other bioactivities. A series of *ent*-kaurane [1][5], and *ent*-pimarane [1] [5–10] diterpenes and sesquiterpenes [11][12] from *Siegebeckia* species have been reported. Quite recently, we have reported the isolation of fifteen *ent*-pimarane diterpenoids including eight new ones from the EtOH extracts of the aerial parts of *Siegesbeckia orientalis* [13]. A further investigation led to the isolation of eleven sesquiterpenoids, of which eight represent new compounds (**1**–**3**, **6**–**9**, and **11**). The new compounds **6**–**8** are likely artifacts produced during extraction and purification, which involved EtOH and MeOH as the solvents. This report deals with the isolation and structure elucidation of these compounds.

2. Results and Discussion. – Compound **1** was obtained as a white amorphous powder. Its IR spectrum revealed the presence of OH groups (3444 cm^{-1}), a γ-lactone (1761 cm^{-1}), unsaturated ester (1720 cm^{-1}), and unsaturated aldehyde moiety (1695 cm^{-1}), and C=C bonds (1647 cm^{-1}). The molecular formula was deduced as $C_{20}H_{24}O_7$ from the HR-EI-MS (*m*/*z* 376.1542 M^+; calc. 376.1522). The NMR data (*Tables 1* and *2*) established the guaiane-type sesquiterpenoid structure and unambig-



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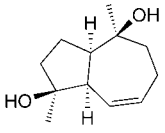

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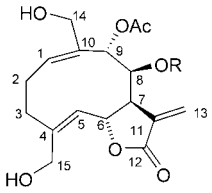

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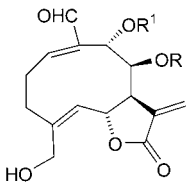

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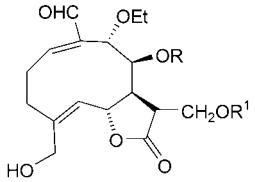

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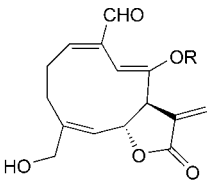

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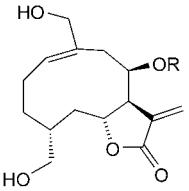
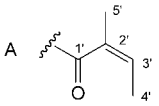
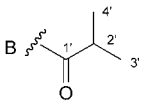


10 R = B
11 R = A





uously defined the relative configuration of **1**. In the few cases where the absolute configuration of guaiane sesquiterpenes was firmly established [14–16], H–C(5) invariably is α-oriented, and H–C(7) is α-oriented in all guaiane sesquiterpenes [17]. Therefore, we tentatively propose the absolute configuration of compound **1** as shown. Thus, the structure of **1** was deduced as 8β-(angeloyloxy)-4β,6α,15-trihydroxy-14-oxo-guaia-9,11(13)-dien-12-oic acid 12,6-lactone.

The NMR spectrum of **1** suggested a guaiane-type sesquiterpenoid structure and showed the signals for an angelate moiety (δ(H) 1.83 (*dq*, *J* = 1.3, 1.2 Hz, Me), 1.96 (*dq*, *J* = 7.1, 1.3 Hz, Me), and 6.16 (*qq*, *J* = 7.1, 1.2 Hz, 1 H); δ(C) 20.5 and 16.0), an α,β-unsaturated aldehyde moiety (δ(H) 9.38 (*s*, 1 H); δ(C) 194.9), and an α-methylene-γ-lactone moiety (δ(H) 5.67 (*d*, *J* = 2.8 Hz, 1 H) and 6.38 (*d*, *J* = 3.3 Hz, 1 H). It also exhibited the existence of an oxygenated methylene (δ(H) 3.57 and 3.65 (each *d*, *J* = 11.1 Hz, 1 H); δ(C) 70.0) and an oxygenated quaternary C-atom at δ(C) 83.5. The connectivity of the ^{1}H- and ^{13}C-NMR signals was determined by the HMQC spectrum, and the constitutional formula of **1** was established by the HMBC spectrum (*Fig. 1*), in which the correlations of H–C(14) (δ 9.38) to C(1) (δ 39.1), C(9) (δ 142.6), and C(10) (δ 146.8) indicated that the aldehyde group was linked to C(10); the correlations of CH_2(15) (δ 3.57 and 3.65) with C(3) (δ 36.2) and C(5) (δ 51.7), and correlations of C(4) (δ 83.5) with CH_2(3) (δ 1.76 and 1.90) suggested that the oxygenated methylene group was CH_2(15) bearing an OH group and being located at C(4), which was also substituted by another OH group. The γ-lactone unit with an α-exocyclic C=C bond was attached at C(6) and C(7), as judged from the severely downfield-shifted H–C(6) signal (δ 4.99, (*dd*, *J* = 11.0, 9.6 Hz, 1 H)), which was confirmed by the HMBC correlations (*Fig. 1*). The angelate moiety, located at C(8) accounted for the deshielding of H–C(8) (δ 6.08, (*dd*, *J* = 6.6, 1.6 Hz)). This conclusion was supported by the HMBC correlation between H–C(8) and

Table 1. *^{1}H-NMR Data* (400 MHz, in $CDCl_3$) *of* **1**–**3**, *and* **6**. δ in ppm, J in Hz. Trivial numbering.

	1	**2**	**3**	**6**
H–C(1)	3.27 (*ddd*, J = 8.4, 7.5, 6.1)	3.24 (*ddd*, J = 8.3, 7.6, 6.5)	2.04 (*dd*, J = 11.6, 1.7)	6.76 (*dd*, J = 10.0, 7.5)
CH_2(2)	1.59 (*dd*, J = 12.1, 7.5), 2.07 (*dd*, J = 12.1, 6.1)	1.59 (*dd*, J = 12.3, 7.6), 2.06 (*dd*, J = 12.3, 6.5)	1.69 (*dd*, J = 11.3, 7.6), 1.78 (*dd*, J = 11.3, 6.5)	2.59 (*dd*, J = 14.4, 12.5), 2.65 (*ddd*, J = 14.4, 10.0, 2.3)
CH_2(3)	1.76 (*dd*, J = 13.5, 7.0), 1.90 (*dd*, J = 13.5, 6.5)	1.76 (*dd*, J = 13.3, 7.1), 1.91 (*dd*, J = 1 3.3, 5.9)	1.66 (*dd*, J = 7.6, 6.5)	2.01 (*dd*, J = 12.9, 12.5), 2.84 (*ddd*, J = 12.9, 5.9, 2.3)
H–C(5)	2.45 (*dd*, J = 11.0, 8.4)	2.45 (*dd*, J = 11.0, 8.3)	2.23 (*ddd*, J = 11.6, 2.2, 2.1)	5.02 (*d*, J = 10.7)
H–C(6)	4.99 (*dd*, J = 11.0, 9.6)	4.99 (*dd*, J = 11.0, 9.7)	5.74 (br. *d*, J = 11.0)	5.19 (*dd*, *v* 10.7, 10.2)
H–C(7)	3.20 (*dddd*, J = 9.6, 3.3, 2.8, 1.6)	3.16 (*ddd*, J = 9.7, 3.3, 2.9)	5.80 (*ddd*, J = 11.0, 5.4, 2.8)	2.72 (*ddd*, J = 10.2, 3.4, 3.0)
H–C(8) or CH_2(8)	6.08 (*dd*, J = 6.6, 1.6)	5.98 (*d*, J = 6.7)	2.01 (*dd*, J = 18.0, 9.4), 2.31 (*m*)	6.62 (*dd*, J = 8.5, 1.4)
H–C(9) or CH_2(9)	6.79 (*d*, J = 6.6)	6.73 (*d*, J = 6.7)	1.61 (*ddd*, J = 14.0, 9.4, 1.7), 1.83 (*ddd*, J = 14.0, 9.5, 1.9)	3.93 (*dd*, J = 8.5, 1.8)
CH_2(13)	5.67 (*d*, J = 2.8), 6.38 (*d*, J = 3.3)	5.62 (d, J = 2.9), 6.36 (*d*, J = 3.3)		5.90 (*dd*, J = 3.0, 1.3), 6.28 (*dd*, J = 3.4, 1.5)
H–C(14) or Me(14)	9.38 (*s*)	9.38 (*s*)	1.27 (*s*)	9.50 (*d*, J = 1.8)
CH_2(15) or Me(15)	3.57 (*d*, J = 11.1), 3.65 (*d*, J = 11.1)	3.56 (*d*, J = 11.0), 3.65 (*d*, J = 11.0)	1.19 (*s*)	4.47 (*d*, J = 12.5), 4.35 (*d*, J = 12.5)
H–C(2′)		2.55 (*qq*, J = 7.1, 7.0)		
H–C(3′) or Me(3′)	6.16 (*qq*, J = 7.1, 1.2)	1.11 (*d*, J = 7.0)		6.04 (*qq*, J = 7.1, 1.5)
Me(4′)	1.96 (*dq*, J = 7.1, 1.3)	1.13 (*d*, J = 7.1)		1.96 (*dq*, J = 7.1, 1.5)
Me(5′)	1.83 (*dq*, J = 1.3, 1.2)			1.87 (*q*, J = 1.5)
MeCH_2O–C(9)				3.37 (*dq*, J = 9.0, 7.0), 3.09 (*dq*, J = 9.0, 7.0)
MeCH_2O–C(9)				1.05 (*t*, J = 7.0)

C(1′). The C(9)=C(10) bond and the aldehyde group at C(10) were assigned from the HMBC correlations of H–C(9) to C(8), C(10), C(1), and C(14), and the HMBC correlations of H–C(14) to C(1), C(10), and C(9).

The relative configuration of **1** was deduced from its NOESY data (*Fig. 2*). The correlations H–C(5)/H–C(1), H–C(7), and CH_2(15) showed that they are all situated on the same face of **1**. The same holds for H–C(8), which was correlated with H–C(1) and H–C(7). The two protons of the CH_2(2) and CH_2(3), groups that are also positioned on this side of the compound were assigned *via* their correlations with H–C(1). The other two diastereoisomeric protons of CH_2(2) and CH_2(3) correlating with H–C(6) established that the C(6)–O bond is on the same side as H–C(1) and H–C(5).

Compound **2** was obtained as a pale gum. The IR spectrum showed the absorption bands of OH groups (3431 cm^{-1}), a γ-lactone (1767 cm^{-1}), saturated ester (1738 cm^{-1}), and α,β-unsaturated aldehyde moiety (1697 cm^{-1}), and C=C bonds (1648 cm^{-1}). The HR-EI-MS showed the molecular-ion peak at m/z 364.1507 establishing the molecular formula as $C_{19}H_{24}O_7$ (calc. 364.1522). The ^{1}H- and ^{13}C-NMR spectra of **2** and **1** were very similar except for the signals of the ester group at C(8). The peaks at m/z 276

Table 2. *^{13}C-NMR Data* (100 MHz, $CDCl_3$) *of* **1**–**3**, *and* **5**–**11**. δ in ppm. Trivial numbering.

	1	**2**	**3**	**5**	**6**	**7**	**8**	**9**	**10**	**11**
C(1)	39.1	39.0	50.6	155.3	155.8	154.8	155.2	156.6	131.5	131.5
C(2)	31.6	31.8	21.7	27.3	27.7	27.4	27.4	30.1	26.4	26.5
C(3)	36.2	36.2	40.3	32.4	32.8	32.5	32.4	32.5	30.2	30.4
C(4)	83.5	83.6	80.1	144.2	141.7	138.6	138.5	143.6	42.0	42.3
C(5)	51.7	51.6	51.2	128.7	129.5	129.9	129.3	124.0	40.3	40.5
C(6)	76.9	76.7	130.1	73.8	74.0	73.6	73.5	77.3	79.1	79.3
C(7)	47.9	47.7	131.6	51.4	51.2	47.0	46.8	52.7	42.0	47.8
C(8)	64.3	64.2	23.6	71.1	69.3	70.6	70.4	144.5	76.0	76.3
C(9)	142.6	142.4	42.7	70.3	76.4	76.2	75.9	113.9	30.7	31.0
C(10)	146.8	146.7	75.0	140.4	139.9	141.5	141.0	140.3	133.1	133.5
C(11)	133.5	133.5		134.2	134.1	44.0	43.9	131.9	136.7	136.9
C(12)	167.8	168.0		169.2	169.7	175.7	175.2	168.1	170.0	170.0
C(13)	122.5	122.4		121.9	122.9	64.0	64.3	121.9	123.8	123.8
C(14)	194.9	195.0	21.8	195.5	194.6	193.4	193.5	190.9	67.5	67.7
C(15)	70.0	70.0	22.9	60.5	61.0	60.6	60.3	60.7	67.7	67.9
C(1′)	166.6	176.3		167.6	166.6	167.1	166.7	165.0	176.5	167.1
C(2′)	126.5	33.8		126.8	127.6	127.3	126.9	125.1	34.1	127.3
C(3′)	140.6	18.8		140.1	138.3	139.2	139.0	142.7	18.6	139.9
C(4′)	16.0	19.2		15.9	15.9	15.8	15.9	15.2	18.9	15.8
C(5′)	20.5			20.5	20.7	20.7	20.7	19.4		20.3
Me*C*H$_2$O–C(9)					64.6	64.4	66.2			
*Me*CH$_2$O–C(9)					15.2	15.1	15.1			
Me*C*H$_2$O–C(13) or MeO–C(13)						66.9	59.2			
*Me*CH$_2$O–C(13)						14.9				

($[M-88]^+$) and 71 ($[COCHMe_2]^+$) in the EI-MS and the NMR data (see *Tables 1* and *2*) clearly indicated the existence of an isobutyryl moiety. Thus the structure of **2** was elucidated as 4β,6α,15-trihydroxy-8β-(isobutyryloxy)-14-oxoguaia-9,11(13)-dien-12-oic acid 12,6-lactone.

Compound **3** was a white amorphous powder. The IR spectrum displayed the absorption bands of OH groups (3377 cm^{-1}) and a C=C bond (1641 cm^{-1}). The EI-MS gave fragment-ion peaks at *m*/*z* 178 ($[M-H_2O]^+$), 163 ($[M-H_2O-Me]^+$), 160 ($[M-2\,H_2O]^+$), and 145 ($[M-2\,H_2O-Me]^+$). The HR-EI-MS (see *Exper. Part*) combined with the ^{13}C-NMR spectrum (with DEPT) revealed a molecular formula $C_{12}H_{20}O_2$. The NMR data (*Tables 1* and *2*) suggested that compound **3** is a norguaiane sesquiterpene, and its structure was elucidated as 11,12,13-trinorguai-6-ene-4β,19β-diol.

The ^{1}H-NMR spectrum of **3** showed the presence of two Me groups (δ 1.19 and 1.27, each *s*) and two olefinic protons (δ 5.74 (br. *d*, *J* = 11.0 Hz, 1 H) and 5.80 (*ddd*, *J* = 11.0, 5.4, 2.8 Hz, 1 H)). The ^{13}C-NMR spectrum showed the expected twelve C-signals, which were assignable to the presence of two Me, four CH_2, four CH (two olefinic CH at δ 130.1 and 131.6), and two oxygenated quaternary C-atoms (δ 75.0 and 80.1). All the protons were assigned to the corresponding C-atoms by a HMQC experiment. The constitution of **3** was suggested by its HMBC spectrum (*Fig. 1*), in which Me(14) (δ 1.27, *s*) showed correlations with C(1) (δ 50.6), C(10) (δ 75.0), C(9) (δ 42.7), C(8) (δ 23.6), and the Me(15) (δ 1.19, *s*) correlated with C(4) (δ 80.1), C(5) (δ 51.2), and C(3) (δ 40.3), thus locating the two Me groups at C(4) and C(10), and also indicating that the two OH groups were attached to C(4) and C(10). The HMBC correlations also indicated the presence of a C(6)=C(7) bond.

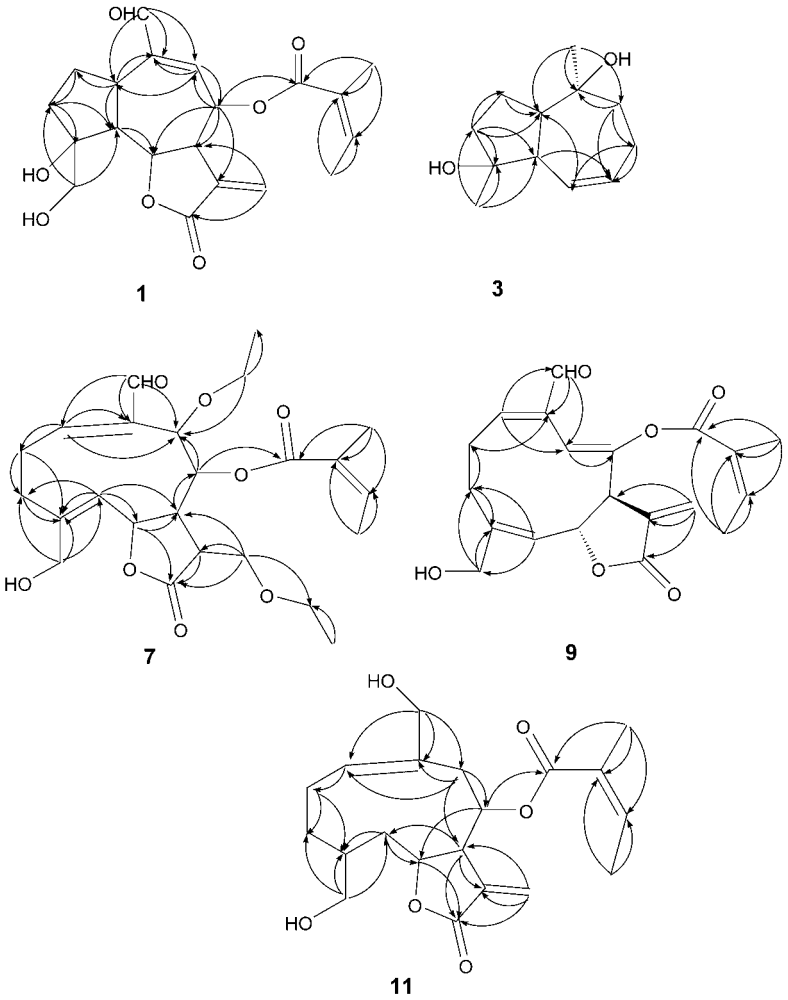


Fig. 1. *Selected HMBC correlations* (H → C) *of* **1**, **3**, **7**, **9**, *and* **11**

The relative configuration of **3** was assigned by NOESY data (*Fig. 2*), in which the correlation between H–C(1) and H–C(5) indicated that the five-membered ring and the seven-membered ring were *cis*-fused; the correlations between H–C(1) and Me(15) , and between H–C(5) and Me(14) suggested that both Me(15) and Me(14) were on the in α-side.

Compound **6** was obtained as a waxy solid. The IR spectrum displayed the absorption bands of OH groups (3477 cm^{-1}), a γ-lactone (1767 cm^{-1}), unsaturated ester (1722 cm^{-1}), and α,β-unsaturated aldehyde moiety (1687 cm^{-1}), and C=C bonds (1626 cm^{-1}). The positive-mode ESI-MS gave a quasimolecular ion at *m*/*z* 427 ($[M + Na]^+$), and the molecular formula was determined as $C_{22}H_{28}O_7$ from the HR-ESI-MS (see *Exper. Part*). The ^{1}H-NMR spectrum (*Table 1*) of **6** was almost identical with that of the known compound **5**, except for the presence of an EtO group as judged from the

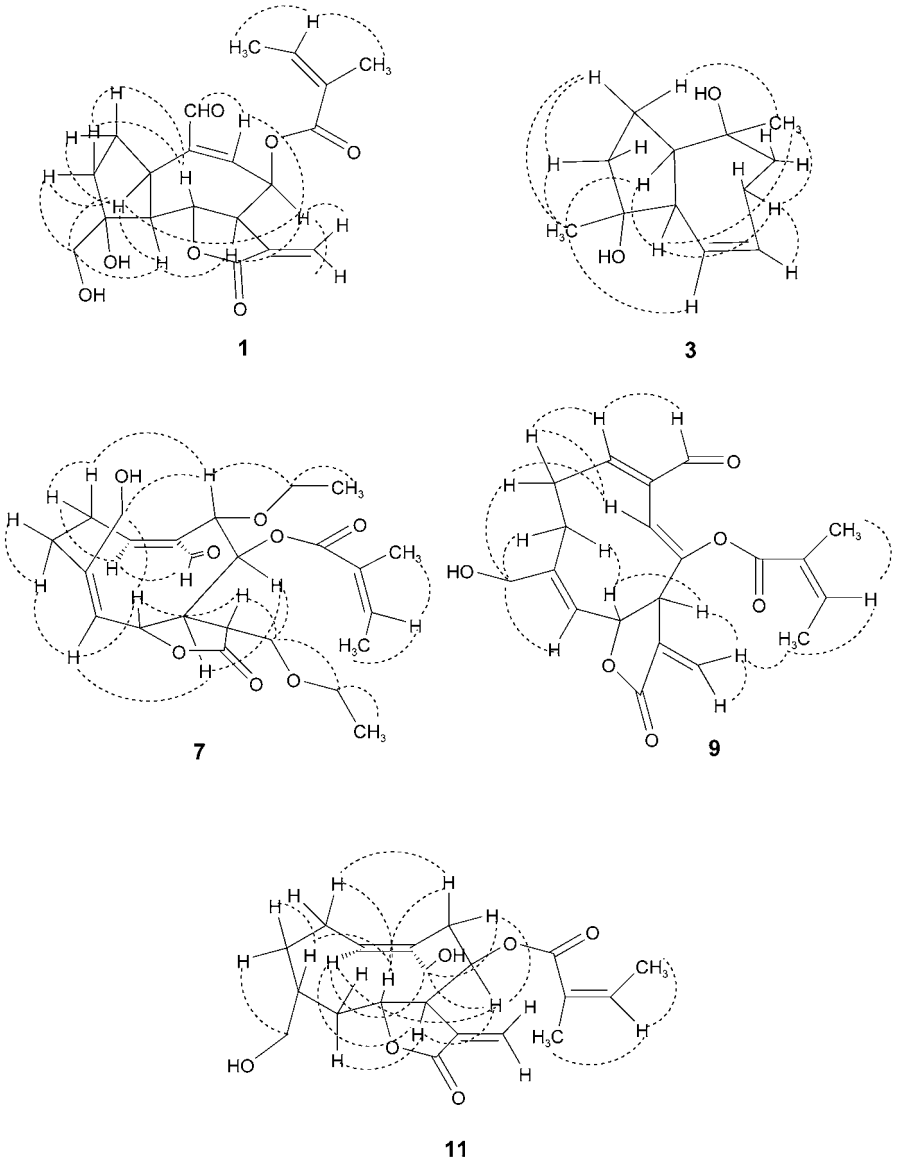


Fig. 2. *Key NOESY correlations* (dashed) *of* **1**, **3**, **7**, **9**, *and* **11**

NMR data (see *Tables 1* and *2*), which was placed at C(9) (slight downfield shift of C(9) signal (δ 76.4)). Thus, the structure of **6** was elucidated as (1(10)*E*,4*Z*)-8β-(angeloyloxy)-9α-ethoxy-6α,15-dihydroxy-14-oxogermacra-1(10),4,11(13)-trien-12-oic acid 12,6-lactone.

Compound **7** was obtained as an amorphous powder. The IR spectrum showed the absorption bands due to the presence of an OH group (3496 cm^{-1}), a γ-lactone

(1782 cm^{-1}), unsaturated ester (1718 cm^{-1}), and unsaturated aldehyde moiety (1689 cm^{-1}), and C=C bonds (1624 cm^{-1}). The molecular formula was deduced as $C_{24}H_{34}O_8$ with eight degrees of unsaturation from the HR-EI-MS (*m/z* 450.2242 (M^+, calc. 450.2254)). The ^{1}H- and ^{13}C-NMR data of **7** (*Tables 3* and *2*) showed high similarity with those of **5** (*Tables 1* and *2*), except for the absence of the typical exocyclic C=C bond. Instead, the presence of a supplementary CH_2O and an additional EtO group suggested that the exocyclic C=C bond had undergone a 1,4-addition of EtOH. The constitution and relative configuration of **7** were finally established from the analysis of 2D-NMR data, especially the HMBC (*Fig. 1*) and NOESY (*Fig. 2*) data, and the structure was thus determined as (1(10)*E*,4*Z*)-8β-(angeloyloxy)-9α,13-diethoxy-6α,15-dihydroxy-14-oxogermacra-1(10),4-dien-12-oic acid 12,6-lactone.

The ^{1}H-NMR spectrum of **7** showed the signals of an angelate moiety at δ(H) 6.12 (*qq*, *J* = 7.2, 1.4 Hz, 1 H), 2.08 (*dq*, *J* = 7.2, 1.5 Hz, Me), and 1.92 (*qd*, *J* = 1.5, 1.4 Hz, Me), which could be confirmed by the EI-MS fragment ions at *m/z* 83 and 55. The presence of an α,β-unsaturated aldehyde was indicated by the signal of H–C(14) (δ 9.48 (*d*, *J* = 2.1 Hz)), and the signal of C(14) (δ 193.4). Two signals of CH_2(15) at δ 4.29 and 4.45 (each *d*, *J* = 12.6 Hz) and the signal of C(15) δ 60.6 indicated that a CH_2(15) OH group was present. The ^{13}C-NMR spectrum showed the signals of three C=C bonds, two ester C=O, three OCH, and four OCH_2.

The configuration of the C(10)=C(1) bond was assigned on the basis of the NOESY correlation H–C(14)/H–C(1) and the (*Z*) configuration of the C(4)=C(5) bond by the NOESY correlations H–CH_2(15)/H–C(6) and H–C(5)/H_α–C(3). The relative configuration at C(6) to C(9) was identical with that of the known compound **5**, as established by comparing their δ(C), and δ(H), and coupling constants of relevant protons, and was confirmed by a NOESY experiment (*Fig. 2*).

Compound **8** was obtained as white amorphous powder. The IR spectrum showed the absorption bands due to an OH group (3489 cm^{-1}), a γ-lactone (1782 cm^{-1}), unsaturated ester (1718 cm^{-1}), and unsaturated aldehyde moiety (1689 cm^{-1}), and C=C bonds (1624 cm^{-1}). The molecular formula was determined as $C_{23}H_{32}O_8$ from the HR-EI-MS at (*m/z* 436.2103 (M^+; calc. 436.2097)). The ^{1}H- and ^{13}C-NMR spectra of **7** and **8** revealed that both compounds are very similar, the only difference being the presence of a MeO group in **8**, in place of the EtO group at C(13) in **7** (see *Tables 2* and *3*). The structure of **8** was, therefore, elucidated as (1(10)*E*,4*Z*)-8β-(angeloyloxy)-9α-ethoxy-6α,15-dihydroxy-13-methoxy-14-oxogermacra-1(10),4-dien-12-oic acid 12,6-lactone.

Compounds **6**–**8** were considered to be most likely artifacts produced in the courses of extraction and chromatography by using EtOH and MeOH as the solvents.

Compound **9** was obtained as pale gum. The IR spectrum revealed the presence of an OH group (3435 cm^{-1}), a γ-lactone (1768 cm^{-1}), ester (1736 cm^{-1}), and unsaturated aldehyde moiety (1686 cm^{-1}), and C=C bonds (1612 cm^{-1}). The molecular formula $C_{20}H_{22}O_6$ with ten degrees of unsaturation was deduced from the HR-ESI-MS (*m/z* 381.1336 ($[M + Na]^+$; calc. 381.1314)). The NMR data (*Tables 2* and *3*) and comparison with similar compounds [18] allowed us to establish the structure of (1(10)*E*,4*E*,8*Z*)-8-(angeloyloxy)-6α,15-dihydroxy-14-oxogermarca-1(10),4,8,11(13)-tetraen-12-oic acid 12,6-lactone for **9**.

The ^{1}H-NMR spectrum of **9** displayed the signals of an angelate moiety, an aldehyde group at δ(H) 9.43 (*s*, 1 H), a CH_2OH group at δ(H) 4.05 and 4.28 (each (*d*, *J* = 13.6 Hz), and a γ-lactone with an α-exocyclic C=C bond (see *Table 3*). The ^{13}C-NMR spectrum with DEPT experiments resolved 20 C-signals including two Me, four CH_2 (one olefinic at δ 121.9 and one oxygenated at δ 60.7), seven CH (one aldehydic at δ 190.9, four olefinic

at δ 156.6, 142.7, 124.0, and 113.9, and one oxygenated at δ 77.3), and seven quaternary C-atoms (two C=O at δ 168.1 and 165.0, and five olefinic at δ 144.5, 143.6, 140.3, 131.9, and 125.1). These data suggested that compound **9** is a germacranolide-type sesquiterpenoid. Compared with **5**, the molecular mass of **9** was 18 units less, and as one more C=C bond is present in **9**, it is likely derived from **5** by loss of one H_2O. The additional C=C bond was tentatively located between C(8) and C(9). The constitution of **9** was deduced *via* analysis of the 2D-NMR, especially of the HMBC spectrum (*Fig. 1*).

Table 3. *^{1}H-NMR Data* (400 MHz, in $CDCl_3$) *of Compounds* **7**–**9**, *and* **11**. δ in ppm. Trivial numbering.

	7	**8**	**9**	**11**
H–C(1)	6.73 (*dd*, *J* = 10.1, 7.5)	6.74 (*dd*, *J* = 10.2, 7.5)	6.70 (*dd*, *J* = 7.9, 7.8)	5.68 (br. *d*, *J* = 9.2)
CH_2(2)	2.54 (*ddd*, *J* = 12.6, 10.1, 2.3), 2.67 (*m*)	2.52 (*ddd*, *J* = 12.4, 10.2, 1.7), 2.65 (*m*)	2.57 (*m*)	2.29 (*m*)
CH_2(3)	1.95 (*m*), 2.81 (*ddd*, *J* = 12.1, 5.6, 2.3)	1.96 (*m*), 2.80 (br. *d*, *J* = 12.4)	2.02 (*m*), 2.78 (*ddd*, *J* = 9.3, 4.2, 3.8)	1.15, 2.00 (2 *m*)
H–C(4)				1.87 (*s*)
H–C(5) or CH_2(5)	4.98 (*d*, *J* = 10.5)	4.93 (*dd*, *J* = 10.4, 2.7)	4.93 (br. *s*)	1.56, 1.97 (2 *m*)
H–C(6)	5.08 (*dd*, *J* = 10.5, 5.6)	5.08 (*dd*, *J* = 10.4, 10.0)	4.93 (*d*, *J* = 7.5)	4.89 (br. *s*)
H–C(7)	2.38 (br. *d*, *J* = 5.6)	2.36 (*dd*, *J* = 10.2, 10.0, 1.7)	3.07 (*m*)	3.17 (*s*)
H–C(8)	6.19 (*d*, *J* = 8.5)	6.17 (br. *d*, *J* = 10.2)		5.40 (*m*)
H–C(9) or CH_2(9)	3.93 (*dd*, *J* = 8.5, 2.1)	3.90 (*d*, *J* = 8.4)	5.78 (*s*)	2.60, 2.69 (2 *m*)
H–C(11)	2.39 (*d*, *J* = 2.1)	2.37 (*dd*, *J* = 10.7, 1.7)		
CH_2(13)	3.67 (*dd*, *J* = 9.8, 1.9), 3.86 (*dd*, *J* = 9.8, 0.9)	3.62 (*dd*, *J* = 9.8, 1.7), 3.82 (*dd*, *J* = 9.8, 1.7)	5.77 (*d*, *J* = 3.0), 6.27 (*d*, *J* = 3.4)	5.68, 6.27 (2 br. *s*)
H–C(14) or CH_2(14)	9.48 (*d*, *J* = 2.1)	9.47 (*s*)	9.43 (*s*)	4.14 (*s*)
CH_2(15)	4.29 (*d*, *J* = 12.6), 4.45 (*d*, *J* = 12.6)	4.25 (*dd*, *J* = 12.5, 2.7), 4.43 (br. *d*, *J* = 12.5)	4.05 (*d*, *J* = 13.6), 4.28 (*d*, *J* = 13.6)	3.42 (*d*, *J* = 14.4), 3.44 (*d*, *J* = 14.4)
H–C(3′)	6.12 (*qq*, *J* = 7.2, 1.4)	6.11 (*qq*, *J* = 7.3, 1.4)	6.24 (*qq*, *J* = 7.3, 1.2)	6.08 (*q*, *J* = 7.0)
Me(4′)	2.08 (*dq*, *J* = 7.2, 1.5)	1.99 (*dq*, *J* = 7.3, 1.5)	1.97 (*dq*, *J* = 7.3, 1.3)	1.96 (*d*, *J* = 7.0)
Me(5′)	1.92 (*dq*, *J* = 1.5, 1.4)	1.91 (*dq*, *J* = 1.5, 1.4)	1.84 (br. *s*)	1.80 (*s*)
MeCH_2O–C(9)		3.10 (*dd*, *J* = 9.1, 7.0), 3.34 (*dd*, *J* = 9.1, 7.0)	3.08 (*dd*, *J* = 7.0, 1.8), 3.33 (*dd*, *J* = 7.0, 2.3)	
MeCH_2O–C(9)		1.03 (*t*, *J* = 7.0)	1.02 (*td*, *J* = 7.0, 2.3)	
MeCH_2O–C(13) or MeO–(13)		3.54 (*qd*, *J* = 7.0, 1.5)	3.35 (*s*)	
MeCH_2O–C(13)		1.15 (*t*, *J* = 7.0)		

The (*E*)-configuration of the C(10)=C(1) double bond was assigned from the typical chemical shift of H–C(14) and H–C(1), and the (*E*)-configuration of the C(4)=C(5) bond was also assigned by NOESY correlations (*Fig. 2*); these assignments were confirmed by comparison with known compounds with the same configuration [18]. The (*Z*)-configuration of the C(8)=C(9) bond was established by the NOESY data (*Fig. 2*), in which the correlation H–C(9)/CH_2(2) suggested that H–C(9) pointed towards the inside of the ring; the correlation of Me(4′)/H–C(13) indicated that the ester side chain pointed outside.

Compound **11** was obtained as waxy solid. The IR spectrum displayed the absorption bands of OH groups (3419 cm^{-1}), a γ-lactone (1760 cm^{-1}) and unsaturated-ester moiety (1716 cm^{-1}), and C=C bonds (1647 cm^{-1}). The molecular formula was established as $C_{20}H_{28}O_6$ from the HR-EI-MS (*m*/*z* 364.1885 (M^+; calc. 364.1886)). The presence of an angelate moiety was evident from the ^{1}H- and ^{13}C-NMR data (*Tables 3*

and *2*) and EI-MS fragment ions at *m/z* 281 ($[M-83]^+$), 264 ($[M-100]^+$), 83, and 55. The structure of **11** was elucidated as (1(10)*E*,4β)-8β-(angeloyloxy)-6α,14,15-trihydroxygermacra-1(10),11(13)-diene-12-oic acid 12,6-lactone.

The NMR spectra of **11** showed the presence of CH_2OH groups (δ(H) 4.14 (*s*, 2 H) and 3.42 and 3.44 (each *d*, *J* = 14.4 Hz, 1 H); δ(C) 67.7 and 67.9) and a γ-lactone with and α-exocyclic C=C bond (δ(H) 5.68 and 6.27 (each br. *s*, 1 H); δ(C) 136.9 and 123.8). The spectral data of **11** were very similar to those of the known **10**, the only difference consisting in the nature of the ester group at C(8), *i.e.*, an angelyloxyl group in **11** instead of the isobutyryloxy group in **10**. The structure of **11** was further confirmed by 2D-NMR experiments: the HMBC spectrum (*Fig. 1*) revealed correlations of CH_2(15) (δ 3.42 and 3.44) with C(3) (δ 30.4), C(4) (δ 42.3), and C(5) (δ 40.5), and of CH_2(5) (δ 1.56 and 1.97) with C(4) and C(6) (δ 79.3) indicating that the usual C(4)=C(5) bond is saturated in **11**. H–C(8) (δ 5.40, m) correlated with C(1′) (δ 167.1) locating the angelyloxy group at C(8).

The relative configuration of **11** was established by NOESY data (*Fig. 2*), with the correlations H–C(4)/H–C(6) and H_β–C(3), and H–C(15)/H_α–C(2) and H–C(5) indicating that the 4-(hydroxymethyl) was α-orientated; the cross-peaks H–C(8)/H–C(7), H–C(14), and H–C(1), and H–C(7)/H–C(1) and H–C(14) revealed that H–C(8) was on the α-side.

The known compounds 2-methylbut-2-enoic acid (3a*S*,4*S*,5*S*,6*Z*,10*Z*,11a*R*)-5-(acetyloxy)-2,3,3a,4,5,8,9,11a-octahydro-6,10-bis(hydroxymethyl)-3-methylene-2-oxocyclodeca[*b*]furan-4-yl ester (**4**) [19], lecocarpinolide (F) **5** [20], and (4β,10*E*)-6α,14,15-trihydroxy-8β-(isobutyryloxy)germacra-10,11(13)-diene-12-oic acid 12,6-lactone (**10**) [18] isolated from this plant were identified by comparison of their spectral data with those reported.

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Experimental Part

General. All solvents used were of anal. grade (*Shanghai Chemical Plant*). Column chromatography (CC): silica gel (200–300 mesh), silica gel *H60*, *Sephadex LH-20*, C_{18} reversed-phase silica gel (150–200 mesh; *Merck*), and *MCI GEL CHP20P* (75–150 μ); *Mitsubishi Chemical Industry Ltd.* TLC: pre-coated silica gel *GF254* plates (*Qingdao Marine Chemical Plant*). Optical rotations: *Perkin-Elmer 341* polarimeter (Na filter, λ = 589 nm). IR Spectra: *Perkin-Elmer 577* spectrometer. NMR Spectra: *Bruker AM-400* spectrometer with $SiMe_4$ as internal standard. MS: *Finnigan MAT-95* (EI and HR-EI). *Finnigan LCQ^{DECA}* (ESI) and *Micromass Q-tof Global* (HR-ESI) mass spectrometers; in *m/z* (rel. %).

Plant Material. The aerial part of *Siegesbeckia orientalis* L. was purchased from *Hua Yu Pharmaceutical Co., Ltd*, Shanghai, in May 2002, and authenticated by one of us, Dr. *Y. Xiang*. A voucher specimen (accession number Sieg-2002-1Y) was deposited in our laboratory.

Extraction and Isolation. The air-dried powder of the aerial part of *S. orientalis* (3 kg) was extracted with 95% EtOH at r.t. The crude extract was dissolved in H_2O (2 l) and the suspension extracted successively with petroleum ether, AcOEt, and BuOH. The AcOEt-soluble part was subjected to CC (silica gel, petroleum ether/AcOEt 5:1, 4:1, 3:1, and 2:1, AcOEt, and MeOH): *Fractions 1–5*. *Fr. 4* was subjected to CC (*MCI* gel, 50% MeOH/H_2O): *Fr. 4.1–4.3*. *Fr. 4.2* was subjected to CC (silica gel, $CHCl_3$/Me_2CO 5:1, 3:1, and 2:1 and Me_2CO): *Fr. 4.2.1–4.2.8*. Each of the latter was then purified by CC (C_{18}, 60% MeOH/H_2O; then *Sephadex LH-20*, EtOH): **1** (35 mg), **2** (5 mg), **4** (14 mg), **5** (240 mg), **7** (24 mg), **8** (48 mg), **10** (90 mg), and **11** (49 mg). *Fr. 4.3* was subjected to CC (silica gel, $CHCl_3$/MeOH 50:1, 30:1, 20:1, and 10:1, and MeOH), and then purified by CC (*Sephadex LH-20*, EtOH; then C_{18}, 50% MeOH/H_2O: **6** (214 mg) and **9** (7 mg). *Fr. 3* was subjected to CC (silica gel, $CHCl_3$/MeOH 50:1): one major fraction. The latter was further purified by CC (C_{18}, 55% MeOH/H_2O): **3** (2.5 mg).

*(2Z)-2-Methylbut-2-enoic Acid (3a*R*,4*R*,6a*R*,9*S*,9a*S*,9b*S*)-6-Formyl-2,3,3a,4,6a,7,8,9,9a,9b-decahydro-9-hydroxy-9-(hydroxymethyl)-3-methylene-2-oxoazuleno[4,5-*b*]furan-4-yl Ester* (**1**). Powder. $[\alpha]_D^{20} = -202$ (c = 2.25, $CHCl_3$). IR (KBr): 3444, 2928, 1761, 1720, 1695, 1647, 1456, 1383, 1229, 1146, 1040, 959, 906, 814, 733, 561.

^{1}H-NMR: *Table 1*. ^{13}C-NMR: *Table 2*. EI-MS: 376 (3, M^+), 345 (51), 277 (3), 276 (2), 245 (7), 199 (10), 83 (100), 55 (23). HR-EI-MS: 376.1542 (M^+, $C_{20}H_{24}O_7$; calc. 376.1522).

*2-Methylpropanoic Acid (3a*R*,4*R*,6a*R*,9*S*,9a*S*,9b*S*)-6-Formyl-2,3,3a,4,6a,7,8,9,9a,9b-decahydro-9-hydroxy-9-(hydroxymethyl)-3-methylene-2-oxoazuleno[4,5-*b*]furan-4-yl Ester* (**2**). Gum. $[\alpha]_D^{20} = -180$ ($c = 1.00$, $CHCl_3$). IR (KBr): 3431, 2928, 1767, 1738, 1697, 1648, 1468, 1385, 1323, 1246, 1149, 1040, 559. ^{1}H-NMR: *Table 1*. ^{13}C-NMR: *Table 2*. EI-MS: 364 (0.4, M^+), 333 (73), 276 (3), 263 (10), 245 (63), 227 (27), 217 (21), 199 (56), 173 (14), 171 (24), 149 (27), 129 (16), 71 (100). ESI-MS: 387 ($[M + Na]^+$). HR-EI-MS: 364.1507 (M^+, $C_{19}H_{24}O_7^+$; calc. 364.1522).

*(1S,3a*R*,4S,8a*R*)-1,2,3,3a,4,5,6,8a-Octahydro-1,4-dimethylazulene-1,4-diol* (**3**). White powder. $[\alpha]_D^{20} = 0$ ($c = 0.4$, $CHCl_3$). IR (KBr): 3377, 2968, 2924, 2850, 1641, 1444, 1371, 1302, 1109, 1094, 970, 916, 748, 563. ^{1}H-NMR: *Table 1*. ^{13}C-NMR: *Table 2*. EI-MS: 178 (7), 163 (17), 160 (12), 145 (31), 135 (21), 120 (100), 107 (28), 105 (77), 93 (37), 92 (39), 91 (45), 79 (58), 71 (25). HR-EI-MS: 178.1353 ($[M - H_2O]^+$, $C_{12}H_{18}O^+$; calc., 178.1358).

*(2*Z*)-2-Methylbut-2-enoic Acid (3a*S*,4*S*,5*S*,6*E*,10*Z*,11a*R*)-5-Ethoxy-6-formyl-2,3,3a,4,5,8,9,11a-octahydro-10-(hydroxymethyl)-3-methylene-2-oxocyclodeca[*b*]furan-4-yl Ester* (**6**). Oily solid. $[\alpha]_D^{20} = -4$ ($c = 0.761$, $CHCl_3$). IR (KBr): 3477, 2929, 1767, 1722, 1687, 1626, 1456, 1383, 1304, 1244, 1144, 1086, 1041, 982, 895, 816, 756, 667. ^{1}H-NMR: *Table 1*. ^{13}C-NMR: *Table 2*. EI-MS: 368 (8), 275 (7), 257 (8), 236 (14), 126 (20), 97 (19), 83 (100), 69 (38), 55 (64). ESI-MS: 427 ($[M + Na]^+$). HR-ESI-MS: 427.1765 ($[M + Na]^+$, $C_{22}H_{28}O_7Na^+$; calc. 427.1733).

*(2*Z*)-2-Methylbut-2-enoic Acid (3*S*,3a*S*,4*S*,5*S*,6*E*,10*Z*,11a*R*)-5-Ethoxy-3-(ethoxymethyl)-6-formyl-2,3,3a,4,5,8,9,11a-octahydro-10-(hydroxymethyl)-2-oxocyclodeca[*b*]furan-4-yl Ester* (**7**). Amorphous powder. $[\alpha]_D^{20} = -98$ ($c = 0.761$, $CHCl_3$). IR (KBr): 3496, 2976, 2931, 2872, 1782, 1718, 1689, 1624, 1458, 1383, 1309, 1230, 1157, 1128, 1086, 1041, 986, 874, 652 . ^{1}H-NMR: *Table 3*. ^{13}C-NMR: *Table 2*. EI-MS: 450 (7, M^+), 432 (4), 406 (9), 367 (7), 349 (9), 321 (6), 275 (6), 257 (8), 229 (9), 201 (7), 126 (13), 83 (100), 55 (47). HR-EI-MS: 450.2242 (M^+, $C_{24}H_{34}O_8^+$; calc. 450.2254).

*(2*Z*)-2-Methylbut-2-enoic Acid (3*S*,3a*S*,4*S*,5*S*,6*E*,10*Z*,11a*R*)-5-Ethoxy-6-formyl-2,3,3a,4,5,8,9,11a-octahydro-10-(hydroxymethyl)-3-(methoxyethyl)-2-oxocyclodeca[*b*]furan-4-yl Ester* (**8**). White powder. $[\alpha]_D^{20} = -84$ ($c = 2.35$, $CHCl_3$). IR (KBr): 3489, 2929, 1782, 1718, 1689, 1624, 1458, 1383, 1309, 1230, 1155, 1088, 1041, 982, 754. ^{1}H-NMR: *Table 3*. ^{13}C-NMR: *Table 2*. EI-MS: 436 (5, M^+), 418 (3), 392 (4), 353 (4), 335 (4), 307 (6), 229 (6), 126 (17), 83 (100), 55 (39). HR-EI-MS: 436.2103 (M^+, $C_{23}H_{32}O_8^+$; calc. 436.2097).

*(2*Z*)-2-Methylbut-2-enoic Acid (3a*S*,4*Z*,6*E*,10*E*,11a*R*)-6-Formyl-2,3,3a,8,9,11a-hexahydro-10-(hydroxymethyl)-3-methylene-2-oxocyclodeca[*b*]furan-4-yl Ester* (**9**). Gum. $[\alpha]_D^{20} = -35$ ($c = 0.761$, $CHCl_3$). IR (KBr): 3435, 2918, 2850, 1768, 1736, 1686, 1612, 1456, 1383, 1240, 1149, 1122, 1038, 995, 874, 581. ^{1}H-NMR: *Table 3*. ^{13}C-NMR: *Table 2*. EI-MS: 284 (4), 256 (5), 167 (13), 83 (100), 55 (35). ESI-MS: 381 ($[M + Na]^+$). HR-ESI-MS: 381.1336 ($[M + Na]^+$, $C_{20}H_{22}O_6Na^+$; calc. 381.1314).

*(2*Z*)-2-Methylbut-2-enoic Acid (3a*S*,4*R*,6*E*,10*R*,11a*R*)-2,3,3a,4,5,8,9,10,11,11a-Decahydro-6,10-bis(hydroxymethyl)-3-methylene-2-oxocyclobuta[*b*]furan-4-yl Ester* (**11**). Oily solid. $[\alpha]_D^{20} = -149$ ($c = 2.10$, $CHCl_3$). IR (KBr): 3419, 2926, 2872, 1760, 1747, 1716, 1647, 1444, 1385, 1269, 1229, 1151, 1043, 997, 820, 754, 625. ^{1}H-NMR: *Table 3*. ^{13}C-NMR: *Table 2*. EI-MS: 364 (3, M^+), 346 (4), 264 (5), 247 (6), 229 (5), 217 (4), 201 (4), 183 (5), 121 (4), 83 (100), 55 (28). ESI-MS: 387 ($[M + Na]^+$). HR-EI-MS: 364.1885 (M^+, $C_{20}H_{28}O_6^+$; calc.364.1886).

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