New Eremophilenolides from *Senecio dianthus*

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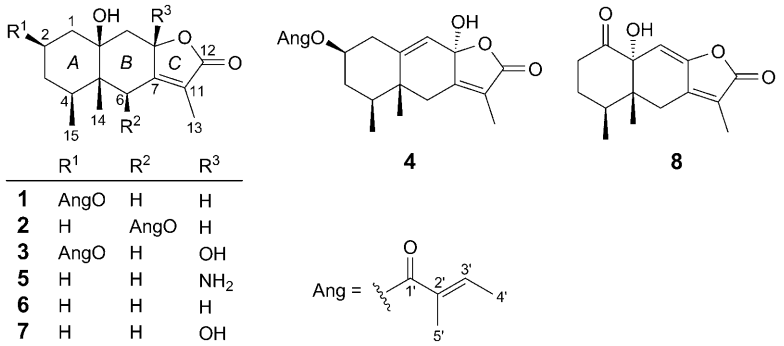
From the aerial parts of *Senecio dianthus*, four new eremophilenolides (**1**–**4**, resp.) and one new eremophilenolide alkaloid (**5**), of the relatively uncommon eremophilenoid-type sesquiterpenoid lactones, were isolated together with three known sesquiterpenoid lactones, 10β-hydroxyeremophil-7(11)-en-12,8α-olide (**6**), 8β,10β-dihydroxyeremophil-7(11)-en-12,8α-olide (**7**), and 10α-hydroxy-1-oxoeremophila-7(11),8(9)-dien-12,8-olide (**8**). On the basis of IR, MS, and NMR data, particularly 2D-NMR analyses, the structures of the new compounds were established as: 2β-(angeloyloxy)-10β-hydroxyeremophil-7(11)-en-12,8α-olide (**1**), 6β-(angeloyloxy)-10β-hydroxyeremophil-7(11)-en-12,8α-olide (**2**), 2β-(angeloyloxy)-8β,10β-dihydroxyeremophil-7(11)-en-12,8α-olide (**3**), 2β-(angeloyloxy)-8α-hydroxyeremophila-7(11),9(10)-dien-12,8β-olide (**4**), and 8β-amino-10β-hydroxyeremophil-7(11)-en-12,8α-olide (**5**). In addition, the relative configuration of **1** was corroborated by X-ray diffraction analysis.

Introduction. – As part of our continuing research on the identification of novel bioactive natural products from Traditional Chinese Medicine (TCM), we have investigated the chemical constituents of *Senecio dianthus* FRANCH, which is mostly distributed in Tibet and reputed for reducing fever and detoxification in Tibetan herbal medicine [1]. Previous investigations on the genus *Senecio* indicated that pyrolizidine alkaloids and furo-eremophilanes are the typical compounds isolated from this genus, but nothing is known about the chemical constituents of *Senecio dianthus*. In this present study, five new eremophilenolides (sesquiterpenoid lactones of eremophilane type), a relatively uncommon group of sesquiterpenoid lactone family with only a few dozen of members identified so far, were isolated from the EtOH extract of the aerial parts. Here, we report the isolation and structure elucidation of these new compounds.

Results and Discussion. – 1. *Structure Elucidation.* The AcOEt fraction of the EtOH extract from the aerial parts of the plant was separated by SiO_2 column chromatography (CC), and seven eremophilenolides, **1**–**6** and **8** (*Fig. 1*), were isolated. The BuOH fraction of the EtOH extract was separated by SiO_2 CC, and another eremophilenolide alkaloid, **5**, was isolated. The structures of two known compounds **6** and **7** were readily assigned to 10β-hydroxyeremophil-7(11)-en-12,8α-olide and 8β,10β-dihydroxyeremophil-7(11)-en-12,8α-olide, respectively, by comparing the physical and NMR spectral data with those reported in the literature [2]. Both were isolated first



	R^1	R^2	R^3
1	AngO	H	H
2	H	AngO	H
3	AngO	H	OH
5	H	H	NH_2
6	H	H	H
7	H	H	OH

Fig. 1. *Structures of compounds* **1**–**8**

from *Hertia cheirifolia*, and their absolute configurations were determined by chemical transformation [3] and X-ray diffraction analysis [4].

The molecular formula of **1** was established as $C_{20}H_{28}O_5$ by HR-ESI-MS (*m*/*z* 371.1840 ($[M+Na]^+$, $C_{20}H_{28}NaO_5^+$; calc. 371.1834). The IR showed broad absorption bands at 3424, 1729, 1699, 1685, and 1640 cm^{-1} suggesting the presence of functional groups of α,β-unsaturated-γ-lactone and unsaturated ester, characteristic of unsaturated sesquiterpenoid lactones such as **6** and **7**. The ^{13}C-NMR (*Table*) spectrum of **1** showed 20 C-atom signals which were assigned by DEPT experiments to eight quaternary C-atoms, and three CH, four CH_2, and five Me groups which could be accounted for a sesquiterpenoid lactone nucleus (15 C-atoms) with an additional angeloyl substitutent (five C-atoms). The ^{13}C-NMR signals (*Table*) of **1** due to the sesquiterpenoid lactone portion were very similar to those of **6**, except for the signals of C(1), C(2), and C(3), presumably due to the introduction of a substituent at C(2), the resonance of which was shifted to low-field. In the ^{1}H-NMR spectrum (*Table*), besides the typical signals attributed to the sesquiterpenoid moiety as for a tertiary Me group (δ(H) 1.07 (*s*)), a secondary Me group (δ(H) 0.91 (*d*, $J=6.7$)), and an olefinic Me group (δ(H) 1.83 (*d*, $J=1.3$)), an additional group of signals (δ(H) 6.05 (*qq*, $J=7.2, 1.3$, 1 H); 1.97 (*s*, 3 H); 1.85 (*d*, $J=1.3$, 3 H); 4.78–4.84 (*m*, 1 H)), which could be assigned to an angeloyloxy (AngO) group, were also observed. This suggested that **1** was an analog of **6** with an additional (AngO) group. This assignment was confirmed by ^{1}H-detected 2D-NMR spectroscopy which provides the direct through-bond connectivity of one bond (HSQC) and multiple-bond (two or three) bonds (HMBC), together with determination of the relative configuration based on the coupling constants and spatial proximity information from COSY and NOESY (*Fig. 2*). In the HMBC, a strong ^{1}H,^{13}C long-range correlation was observed of H–C(2) (δ(H) 4.81) to CO C-atom C(1′) (δ(C) 167.3), providing exclusive evidence for the linkage of the AngO group to C(2). The NOESY correlation between H_α–C(4) and H–C(2) allows the assignment of the AngO group as β-oriented. The pair of non-equivalent CH_2 H-atoms (from HSQC) at C(9) could be differentiated to H_α–C(9) (δ(H) 1.85–1.86 (*m*)) and H_β–C(9) (δ(H) 2.36 (*dd*, $J=13.2, 6.7$)) by NOESY correlations H–C(4)/H_α–C(9) and H_β–C(9)/H_β–C(6). Thus, the β-configuration of H–C(8) was deduced based on the NOE effect between H_β–C(9) and H–C(8). The relative configuration of **1** was confirmed undoubtedly by

Table. *The ^{13}C- and ^{1}H-NMR Spectroscopic Data of Compounds* **1**–**5**. Recorded at 150 and 600 MHz, respectively; δ in ppm, J in Hz.

Position	**1**		**2**		**3**		**4**		**5**	
	δ(C)	δ(H)	δ(C)	δ(H)	δ(C)	δ(H)	δ(C)	δ(H)	δ(C)	δ(H)
1	41.3 (*t*)	1.95 (*dd*, J = 7.3, 1.4, H_α), 1.88–1.89 (*m*, H_β)	35.1 (*t*)	1.71 (*td*, J = 13.4, 4.6, H_α), 1.50 (br. *d*, J = 13.2, H_β)	39.6 (*t*)	1.87 (*d*, J = 9.5)	37.6 (*t*)	2.27 (*d*, J = 7.0, H_α), 2.52 (*dd*, J = 13.1, 2.8, H_β)	34.1 (*t*)	1.74–1.79 (*m*, H_α), 1.38–1.43 (*m*, H_β)
2	68.4 (*d*)	4.78–4.84 (*m*, H_β)	21.9 (*t*)	1.59–1.63 (*m*, H_α), 1.32–1.41 (*m*, H_β)	68.5 (*d*)	4.77–4.83 (*m*, H_α)	71.3 (*d*)	4.80–4.85 (*m*, H_α)	21.7 (*t*)	1.56–1.58 (*m*, H_α), 1.38–1.43 (*m*, H_β)
3	35.3 (*t*)	1.88–1.89 (*m*, H_α), 1.37–1.43 (*m*, H_β)	29.7 (*t*)	1.42–1.47 (*m*, H_α), 1.32–1.41 (*m*, H_β)	35.1 (*t*)	1.85–1.89 (*m*, H_α), 1.39 (*dd*, J = 23.8, 12.3, H_β)	35.8 (*t*)	1.53 (*dd*, J = 24.5, 12.4, H_α), 1.94 (*d*, J = 14.5, H_β)	29.5 (*t*)	1.38–1.43 (*m*, H_α), 1.28–1.36 (*m*, H_β)
4	31.6 (*d*)	1.51–1.57 (*m*, H_α)	33.5 (*d*)	1.42–1.47 (*m*, H_α)	31.4 (*d*)	1.45–1.49 (*m*, H_α)	40.5 (*d*)	1.74–1.78 (*m*, H_α)	33.1 (*d*)	1.38–1.43 (*m*, H_α)
5	44.3 (*s*)		46.2 (*s*)		45.6 (*s*)		44.7 (*s*)		45.6 (*s*)	
6	31.4 (*t*)	2.48 (*d*, J = 14.0, H_α), 2.70 (*d*, J = 14.0, H_β)	72.0 (*d*)	5.96 (br. *s*, H_α)	30.1 (*t*)	2.51 (*dd*, J = 14.2, 1.3, H_α), 2.63 (*d*, J = 14.2, H_β)	36.0 (*t*)	2.43 (*d*, $J = J$ = 12.7, H_α), 2.75 (*d*, J = 7.0, H_β)	29.1 (*t*)	2.39 (*dd*, J = 14.0, 1.5, H_α), 2.60 (*d*, J = 14.1, H_β)
7	160.3 (*s*)		155.4 (*s*)		157.9 (*s*)		157.8 (*s*)		153.8 (*s*)	
8	78.0 (*d*)	4.99–5.02 (*m*, H_β)	76.2 (*d*)	5.15 (*ddd*, J = 11.1, 6.9, 1.8, H_β)	102.4 (*s*)		99.8 (*s*)		85.3 (*s*)	
9	42.0 (*t*)	1.85–1.86 (*m*, H_α), 2.36 (*dd*, J = 13.2, 6.7, H_β)	41.3 (*t*)	1.99–2.01 (*m*, H_α), 2.33 (*dd*, J = 13.0, 6.8, H_β)	43.6 (*t*)	2.22 (*d*, J = 14.5, H_α), 2.29 (*d*, J = 14.1, H_β)	121.2 (*d*)	5.81 (*s*)	42.9 (*t*)	1.95 (*d*, J = 14.3, H_α), 2.22 (*d*, J = 14.3, H_β)
10	74.9 (*s*)		75.4 (*s*)		74.1 (*s*)		148.0 (*s*)		73.6 (*s*)	
11	121.1 (*s*)		126.0 (*s*)		123.0 (*s*)		122.8 (*s*)		125.1 (*s*)	
12	174.9 (*s*)		174.0 (*s*)		172.0 (*s*)		171.6 (*s*)		173.8 (*s*)	
13	8.3 (*q*)	1.83 (*d*, J = 1.3)	8.9 (*q*)	2.00 (*d*, J = 1.6)	8.3 (*q*)	1.82 (*d*, J = 1.3)	8.2 (*q*)	1.87 (*s*)	6.7 (*q*)	1.76 (*d*, J = 1.5)
14	14.9 (*q*)	1.07 (*s*)	10.6 (*q*)	1.11 (*s*)	14.9 (*q*)	1.09 (*s*)	17.4 (*q*)	0.94 (*s*)	13.9 (*q*)	1.03 (*s*)
15	15.7 (*q*)	0.91 (*d*, J = 6.7)	16.4 (*q*)	0.93 (*d*, J = 6.4)	16.0 (*q*)	0.93 (*d*, J = 6.6)	15.1 (*q*)	1.02 (*d*, J = 6.8)	15.4 (*q*)	0.87 (*d*, J = 6.5)
1′	167.3 (*s*)		165.7 (*s*)		167.5 (*s*)		167.4 (*s*)			
2′	127.9 (*s*)		125.6 (*s*)		127.9 (*s*)		127.9 (*s*)			
3′	137.7 (*s*)	6.05 (*ddd*, J = 14.4, 7.2, 1.3)	141.8 (*d*)	6.21 (*ddd*, J = 14.6, 7.3, 1.5)	137.6 (*s*)	6.04 (*dd*, J = 16.6, 7.2)	137.9 (*d*)	6.07 (*dd*, J = 13.9, 7.2)		
4′	15.8 (*q*)	1.97 (*s*)	15.9 (*q*)	2.03 (*dd*, J = 7.3, 1.4)	15.7 (*q*)	1.93 (*d*, J = 7.3)	15.8 (*q*)	1.98 (*d*, J = 7.1)		
5′	20.5 (*q*)	1.85 (*d*, J = 1.3)	20.6 (*q*)	1.91 (*t*, J = 1.3)	20.5 (*q*)	1.85 (*s*)	20.5 (*q*)	1.89 (*s*)		
HO–C(10)				3.03 (*s*)						

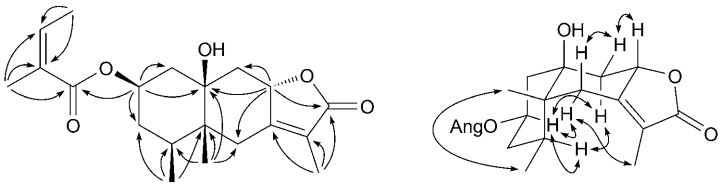


Fig. 2. *Selected HMBC* (→) *and NOESY* (↔) *correlations of compound* **1**

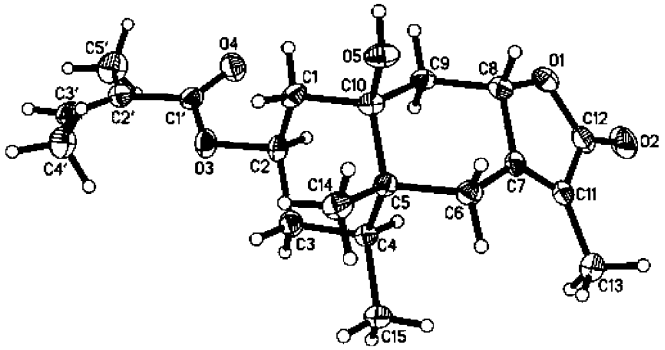


Fig. 3. *ORTEP Drawing of compound* **1**

X-ray diffraction analysis (*Fig. 3*). Therefore, the structure of **1** was determined as 2β-(angeloyloxy)-10β-hydroxyeremophil-7(11)-en-12,8α-olide.

The molecular formula of **2** was established as $C_{20}H_{28}O_5$ by HR-ESI-MS (*m*/*z* 371.1834 ($[M+Na]^+$, $C_{20}H_{28}NaO_5^+$; calc. 371.1834). Similar to that of **1**, the IR spectrum of **2** exhibited typical absorptions of an α,β-unsaturated-γ-lactone (1739 cm^{-1}), an α,β-unsaturated ester (1650 cm^{-1}), and a C=C bond (1640 cm^{-1}). In addition, **2** gave ^{1}H- and ^{13}C-NMR spectral profiles (*Table*) very similar to those of **1**, suggesting **2** as an AngO-substituted eremophilenolide with a structure close to that of **1**. A closer inspection of the 2D-NMR spectra revealed that the AngO group should be at C(6) in **2** rather than at C(2) in **1**. This is confirmed by the HMBC correlations of H–C(6) to C(1′), C(5), and C(7), as well as of H–C(14) to C(6). The β-orientation of AngO was evident from NOESY correlation between H–C(6) and H–C(4). Moreover, the HMBC correlation of HO–C(10) (δ(H) 3.03) to C(1) and C(10), and of H–C(1) to H–C(9), provided further evidence for the skeleton connectivity. In NOESY spectrum, correlations were observed between HO–C(10) and H–C(8), supporting the α-configuration of the γ-lactone. Thus, the structure of **2** was determined as 6β-(angeloyloxy)-10β-hydroxyeremophil-7(11)-en-12,8α-olide.

The molecular formula of **3** was established as $C_{20}H_{28}O_6$ by HR-ESI-MS (*m*/*z* 387.1789 ($[M+Na]^+$, $C_{20}H_{28}NaO_6^+$; calc. 387.1784). The ^{1}H- and ^{13}C-NMR data (*Table*) were very similar to those of **1**. The most noticeable difference between them was due to the presence of a quaternary C-atom signal at δ(C) 102.4 in **3** instead of a signal of a CH group at δ(C) 78.0 in **1**, indicating a tertiary OH group at C(8) in **3**. The orientation of HO–C(8) was determined as β on the basis of ^{1}H-NMR data. It was reported that

the relative order of ^{1}H chemical shifts of Me(15) and Me(14) is diagnostic for the configuration at C(8) [5], *i.e.*, Me(15) resonates at lower field than Me(14) in the 8α-MeO derivatives, while the order reversed in their 8β-counterparts. Thus, HO at C(8) should be β-oriented, as Me(15) resonated at higher field than Me(14). However, more direct evidence for the β-orientation of HO at C(8) was obtained from a NOESY experiment whereby an indicative NOE correlation was observed between Me(15) and H–C(6), which would not have been observed if HO at C(8) would be α-oriented, on the basis of a *Dreiding* model of this skeleton [6]. Therefore, the structure of **3** was determined as 2β-(angeloyloxy)-8β,10β-dihydroxyeremophil-7(11)-en-12,8α-olide.

Compound **4** was shown to have the molecular formula $C_{20}H_{26}O_5$ as deduced from HR-ESI-MS (*m/z* 369.1684 ($[M+Na]^+$, $C_{20}H_{26}NaO_5^+$; calc. 369.1678)), indicating eight degrees of unsaturation. It showed a ^{13}C-NMR spectrum similar to that of **3**. However, a close inspection revealed considerable differences. Two C-atom signals corresponding to additional C=C bond were observed at δ(C) 121.2 and 148.0 in **4**, while the O-bearing quaternary C-atom signal at δ(C) 74.1 in **3** disappeared. This indicated the presence of a C(9)=C(10) bond. Further confirmation was provided by the HMBC correlation of Me(14) to C(10) (δ(C) 148.0). According to the empirical '8-configuration diagnostic principle' [5] based on the order of the chemical shifts of Me(15) (δ(H) 1.02 (*d*, $J=6.8$)) and Me(14) (δ(H) 0.94 (*s*)), and in contrast to **3**, the orientation of OH at C(8) of **4** was elucidated as α, as Me(15) resonated at lower field than Me(14). Thus, the structure of **4** was established as 2β-(angeloyloxy)-8α-hydroxyeremophil-7(11),9(10)-dien-12,8β-olide.

Compound **5** was shown to have a molecular formula $C_{15}H_{23}NO_3$ as established by HR-ESI-MS (positive-ion mode; *m/z* 288.1573 ($[M+Na]^+$, $C_{15}H_{23}NNaO_3^+$; calc. 288.1576). The NMR data (*Table*) were very similar to those of 8β,10β-dihydroxyeremophilenolide (**7**) except for an additional NH_2 group at C(8). In the ^{1}H,^{1}H-COSY spectrum, a long-range spin coupling ($J=1.5$) between the olefinic Me (Me(13)) and H_β–C(6) was observed. This can only be accounted for with a β-orientation of NH_2 at C(8) which is in line with a dihedral angle of *ca.* 30° in a *Dreiding* model [6]. This feature was shared by all the compounds of this family as observed in **1**, **2**, and **3**, but not in **4**, which exhibits an α-orientation for HO at C(8). Therefore, the structure of **5** was determined as 8β-amino-10β-hydroxyeremophil-7(11)-en-12,8α-olide. This is the first report of an amino group attached to an eremophilane-type sesquiterpenoid.

Experimental Part

General. Optical rotation: *Perkin-Elmer 341* polarimeter at 589 nm. IR Spectra: *Perkin-Elmer* FT-IR spectrometer. NMR Spectra: *Bruker Avance 600* spectrometer; chemical shifts in δ [ppm] with TMS as an internal standard. ESI-MS: *Finnigan LCQ^{DECA}* spectrometer. HR-ESI-MS: *Bruker BioTOF Q* spectrometer. X-Ray crystallography: *Siemens P4* four-circle diffractometer.

Plant Material. The aerial parts of *S. dianthus* were collected in Lhasa, Tibet, China, in May 2005. Prof. *G. Suolang* identified the plant, and a voucher specimen (No. 009860) was deposited with Tibet Autonomous Region Institute for Food and Drug Control, P. R. China.

Extraction and Isolation. The air-dried and powdered roots (4.7 kg) of *S. dianthus* were extracted three times with 90% EtOH, each for 7 d at r.t. After filtration and removal of the solvent, the deep green residue of 660 g was dissolved in H_2O and extracted with AcOEt and then BuOH. The AcOEt extract (180 g) was subjected to column chromatography (CC; SiO_2 (1.5 kg); petroleum ether (PE)/acetone

20 : 1, 15 : 1, 10 : 1, 8 : 1, 6 : 1, 4 : 1, 2 : 1, and 1 : 1) to yield 14 fractions. *Fr. 5* (8 g) was subjected to CC (SiO_2 (200 g); PE/acetone 10 : 1) to yield compound **4** (12 mg). *Fr. 6* (11 g) was purified by CC (*ODS* SiO_2 (200 g); MeOH/H_2O from 40 to 100%) to give five subfractions, and compound **6** (120 mg) was obtained from the *Subfr. 4* (2.8 g) by recrystallization from MeOH. Compound **7** (25 mg) was obtained from *Fr. 7* (14 g) by CC (*ODS* SiO_2 (200 g); MeOH/H_2O from 40 to 100%). Compound **3** (2.8 g) was obtained from *Fr. 8* (10 g) by CC (SiO_2 (300 g); PE/acetone 5 : 1). Compound **8** (4.5 g) was obtained from *Fr. 9* (19 g) by recrystallization from MeOH and the mother liquid was further purified by CC (*ODS* SiO_2; with MeOH/H_2O 60%) to give compound **1** (340 mg). Compound **2** (6.8 mg) was obtained from *Fr. 11* (9.4 g) by CC (SiO_2 (300 g); PE/acetone 5 : 1).

The BuOH extract (80 g) was subjected to CC (SiO_2 (1.0 kg, 160–200 mesh); $CHCl_3$/MeOH 30 : 1, 20 : 1, 15 : 1, 10 : 1, 8 : 1, 6 : 1, and 4 : 1, each 4 l) to yield five fractions. *Fr. 2* (4 g) was further purified by CC *ODS* SiO_2 (65 g); MeOH/H_2O 50%) to give compound **5** (40 mg).

2β-(Angeloyloxy)-10β-hydroxyeremophil-7(11)-en-12,8α-olide (= rel-*(4a*R,*5*S,*7*R,*8a*S,*9a*S*)-2,4,4a,5,6,7,8,8a,9,9a-Decahydro-8a-hydroxy-3,4a,5-trimethyl-2-oxonaphtho[2,3-*b*]furan-7-yl (2*E*)-2-Methylbut-2-enoate*; **1**). Colorless prisms (MeOH). M.p. 170–171°. $[\alpha]_D^{20} = +87$ ($c = 0.2$, $CHCl_3$). IR (KBr): 3423, 1729, 1699, 1685, 1640. ^{1}H- and ^{13}C-NMR: see the *Table*. ESI-MS (pos.): 371 ($[M+Na]^+$), 719 ($[2M+Na]^+$). HR-ESI-MS (pos.): 371.1840 ($[M+Na]^+$, $C_{20}H_{28}NaO_5^+$; calc. 371.1834).

6β-(Angeloyloxy)-10β-hydroxyeremophil-7(11)-en-12,8α-olide (= rel-*(4*R,*4a*S,*5*S,*8a*S,*9a*S*)-2,4,4a,5,6,7,8,8a,9,9a-Decahydro-8a-hydroxy-3,4a,5-trimethyl-2-oxonaphtho[2,3-*b*]furan-4-yl (2*E*)-2-Methylbut-2-enoate*; **2**). Colorless prism (acetone). M.p. 212–214°. $[\alpha]_D^{20} = +126$ ($c = 0.155$, $CHCl_3$). IR (KBr): 3457, 1745, 1739, 1651, 1640. ^{1}H- and ^{13}C-NMR: see the *Table*. ESI-MS (pos.): 387 ($[M+Na]^+$), 719 ($[2M+Na]^+$). HR-ESI-MS (pos.): 371.1834 ($[M+Na]^+$, $C_{20}H_{28}NaO_5^+$; calc. 371.1834).

2β-(Angeloyloxy)-8β,10β-dihydroxyeremophil-7(11)-en-12,8α-olide (= rel-*(4a*R,*5*S,*7*R,*8a*S,*9a*S*)-2,4,4a,5,6,7,8,8a,9,9a-Decahydro-8a,9a-dihydroxy-3,4a,5-trimethyl-2-oxonaphtho[2,3-*b*]furan-7-yl (2*E*)-2-Methylbut-2-enoate*; **3**). Glassy gum. $[\alpha]_D^{20} = +47$ ($c = 0.2$, $CHCl_3$). ^{1}H- and ^{13}C-NMR: see the *Table*. ESI-MS (pos.): 387 ($[M+Na]^+$), 751 ($[2M+Na]^+$). HR-ESI-MS (pos.): 387.1789 ($[M+Na]^+$, $C_{20}H_{28}NaO_6^+$; calc. 387.1784).

2β-(Angeloyloxy)-8α-hydroxyeremophila-7(11),9(10)-dien-12,8β-olide (= rel-*(4a*R,*5*S,*7*R,*9a*R*)-2,4,4a,5,6,7,8,9a-Octahydro-9a-hydroxy-3,4a,5-trimethyl-2-oxonaphtho[2,3-*b*]furan-7-yl (2*E*)-2-Methylbut-2-enoate*; **4**). Colorless needle (acetone). M.p. 172–174°. $[\alpha]_D^{20} = -18$ ($c = 0.17$, $CHCl_3$). IR (KBr): 3435, 1751, 1703, 1643. ^{1}H- and ^{13}C-NMR: see the *Table*. ESI-MS (pos.): 369 ($[M+Na]^+$), 715 ($[2M+Na]^+$). HR-ESI-MS (pos.): 369.1684 ($[M+Na]^+$, $C_{20}H_{26}NaO_5^+$; calc. 369.1672).

*8β-Amino-10β-hydroxyeremophil-7(11)-en-12,8α-olide (= rel-(4a*R,*5*S,*8a*S,*9a*S*)-9a-Amino-4a,5,6,7,8,8a,9,9a-octahydro-8a-hydroxy-3,4a,5-trimethylnaphtho[2,3-*b*]furan-2(4*H*)-one*; **5**). Colorless needles. M.p. 210–212°. $[\alpha]_D^{20} = +175$ ($c = 0.3$, MeOH). IR (KBr): 3442, 1702, 1643, 1135, 1100. ^{1}H- and ^{13}C-NMR: see the *Table*. ESI-MS (pos.): 288 ($[M+Na]^+$), 553 ($[2M+Na]^+$). HR-ESI-MS (pos.): 288.1573 ($[M+Na]^+$, $C_{15}H_{23}NNaO_3^+$; calc. 288.1576).

X-Ray Diffraction of **1**. The X-ray crystallographic data collection and refinement of **1** ($0.68 \times 0.48 \times 0.36$ mm) were conducted on a crystal at 295 K. $C_{20}H_{28}O_5$, orthorhombic, space group $P2_12_12_1$, $a = 7.326$ (1) Å, $b = 14.099$ (3) Å, $c = 18.348$ (3) Å, $\alpha = \beta = \gamma = 90$, $V = 1895.13$ (46) Å^3, $Z = 4$, $d = 1.221$ Mg/m^3, $\mu = 0.087$ mm^{-1}, F (000) = 752. Intensity data were collected with a *Siemens P4* four-circle diffractometer with a graphite monochromator, MoK_α ($\lambda = 0.71073$ Å) radiation. A total of 2763 unique reflections were collected, of which 2496 were observed. The structure was solved by direct methods using SHELXS-97 and refined by full-matrix least-squares calculations. The final R indices ($I > 2\sigma(I)$) were $R_1 = 0.0768$, $wR_2 = 0.0737$. The crystallographic data have been deposited in the *Cambridge Crystallographic Data Centre* with deposition No. CCDC-289136. Copies of data can be obtained on application to the CCDC, 12 Union Road, Cambridge CB2 1EZ, UK (fax: +44 (1223) 336 033, or e-mail: deposit@ccdc.cam.ac.uk).

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