Terpenoids from *Loxocalyx urticifolius*

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Two new diterpenoids, loxocalyxin A (**1**) and 13-epiloxocalyxin A (**2**), and two new sesquiterpenoids, loxocalyxins B and C (**3** and **4**, resp.), together with three known compounds, were isolated from the MeOH extract of the whole plant of *Loxocalyx urticifolius* HEMSL. The structures of the new compounds were established by means of spectroscopic analysis including one- and two-dimensional NMR spectroscopy. All new structures were confirmed by X-ray crystallographic analysis. Their absolute configurations were established.

Introduction. – The genus *Loxocalyx* (Lamiaceae), one of the endemic genera of seed plants in China, comprises only two species distributed in Gansu, Guizhou, Hebei, Henan, Hubei, Hunan, Shanxi, Sichuan, and Yunnan Provinces [1]. The whole plant of *Loxocalyx urticifolius* HEMSL. has been long used as a traditional Chinese medicine for the treatment of rheumatism and dysentery and as an insecticide [2]. Up to now, little information about the chemical constituents of this plant is available [3]. As part of an ongoing research program to isolate and determine structures of secondary metabolites from medicinal endemic plants of southwestern China, we performed a phytochemical study on the whole plant of *L. urticifolius* collected in Chongqing, west China. As a result, two new *ent*-labdane-type diterpenes, loxocalyxin A[1]) (**1**) and 13-epiloxocalyxin A[1]) (**2**), and two new drimane-type sesquiterpenes, loxocalyxins B[1]) (**3**) and C[1]) (**4**) (*Fig. 1*), together with three known compounds, (3β)-lanosta-7,9(11)-dien-3-ol [4][5], phytol [6], and β-sitosterol, were isolated.

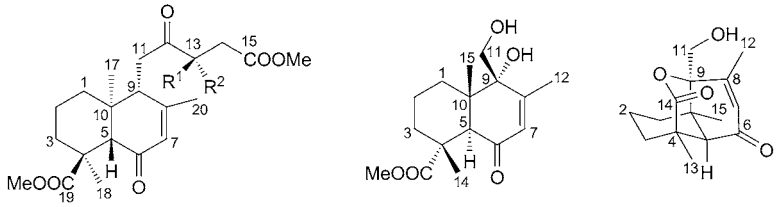

Fig. 1. *Compounds* **1**–**4**, *isolated from* Loxocalyx urticifolius

[1]) Trivial atom numbering; for systematic names, see *Exper. Part.*

Results and Discussion. – A MeOH extract of the whole plant of *L. urticifolius* was suspended in H_2O and successively extracted with petroleum ether and AcOEt. The petroleum ether and AcOEt extracts were purified by various chromatographic techniques to yield four new compounds, together with three known ones. The structures of the isolated new compounds were elucidated by extensive spectroscopic techniques and X-ray crystallographic analysis. Afterwards the absolute configurations were determined.

Compound **1** was obtained as colorless crystals, $[\alpha]_D^{20} = -159$, with the molecular formula $C_{22}H_{32}O_6$, which was deduced by HR-ESI-MS (*m/z* 415.2071 ($[M+Na]^+$). The strong absorptions at 1657, 1703, and 1729 cm^{-1} in the IR spectrum indicated the presence of several C=O groups. An α,β-unsaturated ketone moiety was suggested by an absorption maximum at 242 nm in the UV spectrum. The ^{1}H- and ^{13}C-NMR spectra (*Tables 1* and *2*) displayed resonances for two methoxycarbonyl and two C=O groups and one C=C bond. A bicyclic structure would account for the remaining unsaturation. Therefore, the structure of **1** was consistent with the skeleton of a labdane diterpene, similar to that of cativic acid (=(βS,1*S*,4a*S*,8a*S*)-1,4,4a,5,6,7,8,8a-octahydro-β-2,5,5,8a-pentamethylnaphthalene-1-pentanoic acid) [7]. The H-atom and C-atom signals were assigned by using a combination of HSQC and HMBC experiments. Two methoxycarbonyl goups attached to C(4) and C(14), respectively, were established by the HMBC experiment indicating the long-range correlations (*Fig. 2*) Me(18) (δ(H) 1.35) and H–C(5) (δ(H) 3.17)/C(19) (δ(C) 178.7), and H–C(13) (δ(H) 3.07–3.09)/C(15) (δ(C) 172.6). A ketone C=O group gave a ^{13}C-NMR signal at δ(C) 211.2 ascribed to C(12), which was confirmed by the HMBCs Me(16) (δ(H) 1.18) and H–C(9) (δ(H) 3.25)/C(12). An α,β-unsaturated ketone moiety in ring *B* was confirmed by the HMBCs H–C(5) (δ(H) 3.17)/C(6) (δ(C) 197.4), and H–C(7) (δ(H) 5.86)/C(20) (δ(C) 22.2). A single-crystal X-ray study of **1** (*Fig. 3*) revealed that both Me groups Me(18) and Me(17) are positioned on the same (α) side of ring *A*. A combination of optical-rotation comparisons [8][9] and anomalous dispersion effects (see *Exper. Part*) confirmed the structure of **1** to be dimethyl (5β,9α,10α)-6,12-dioxolabd-7-ene-15,19-dioate with the absolute configuration (4*S*,5*S*,9*R*,10*S*,13*S*), and it was named loxocalyxin A.

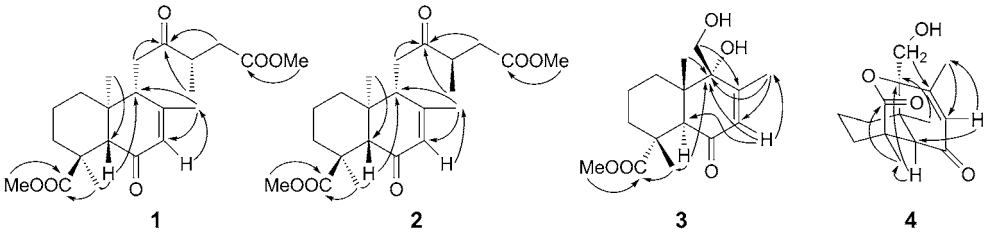

Fig. 2. *Key HMBC features of* **1**–**4**

Compound **2** was obtained as colorless crystals, $[\alpha]_D^{20} = -125$. The molecular formula, $C_{22}H_{32}O_6$, was deduced by HR-ESI-MS (*m/z* 415.2068 ($[M+Na]^+$)). The ^{1}H- and ^{13}C-NMR data (*Tables 1* and *2*) of **2** were rather similar to those of **1**, indicating

Table 1. *^{1}H-NMR Data* (600 MHz, $CDCl_3$) *of* **1**–**4**[a]). δ in ppm, J in Hz.

H-Atom	**1**	**2**	**3**	**4**
CH_2(1)	1.59 (t*, J = 4.6, H_α), 1.24–1.28 (m, H_β)	1.59 (t*, J = 3.2, H_α), 1.25–1.32 (m, H_β)	1.63–1.66 (m*, H_α), 1.54–1.57 (m*, H_β)	2.45 (dd, J = 14.9, 4.6, H_α), 1.41 (dt, J = 14.4, 5.8, H_β)
CH_2(2)	1.60–1.63 (m*)	1.62 (dd, J = 2.9, 2.3)	1.58–1.60 (m*), 1.25 (br. s)	1.69–1.72 (m), 1.80–1.86 (m*)
CH_2(3)	1.60–1.63 (m*), 1.50 (ddd, J = 3.8, 4.5, 4.8)	1.71 (br. d, J = 13.3), 1.51 (ddd, J = 4.4, 4.9, 1.7)	1.49–1.57 (m*)	1.60 (dt, J = 13.3, 4.9), 1.94 (dd, J = 13.0, 4.8)
H–C(5)	3.17 (s)	3.19 (s)	3.79 (s*)	2.18 (s)
H–C(7)	5.86 (s)	5.87 (s)	5.78 (s)	5.91 (s)
H–C(9)	3.25 (dd, J = 8.6, 7.3)	3.27 (dd, J = 8.3, 8.2)		
CH_2(11)	2.77 (dd, J = 8.2, 6.3), 2.69 ($dddd$, J=1.3, 1.9, 1.7, 2.0)	2.78 (dd, J = 8.6, 8.2), 2.70 ($dddd$, J= 1.3, 1.9, 1.4, 2.0)	3.86 (d, J = 11.2), 3.78 (d*, 11.0)	4.10 (d, J = 12.1), 4.08 (d, J = 12.1)
Me(12)			2.05 (s)	2.16 (d, J = 0.9)
H–C(13) or Me(13)	3.07–3.09 (m)	3.06–3.16 (m)		1.15 (s)
CH_2(14) or Me(14)	2.85 (dd, J = 9.5, 7.4), 2.35 (ddd, J = 4.4, 4.5, 4.5)	2.85 (dd, J = 9.6, 9.7), 2.35 (ddd, J = 4.5, 4.6, 4.5)	1.38 (s)	
Me(15)			0.95 (s)	1.13 (s)
Me(16)	1.18 (d, J = 7.3)	1.17 (d, J = 7.3)		
Me(17)	0.88 (s)	0.89 (s)		
Me(18)	1.35 (s)	1.35 (s)		
Me(20)	1.77 (s)	1.74 (s)		
COOMe	3.63 (s)	3.65 (s)	3.65 (s)	
COOMe	3.63 (s)	3.64 (s)		

[a]) Asterisk (*) = overlapping signals.

Table 2. *^{13}C-NMR Data* (150 MHz, $CDCl_3$) *of* **1**–**4**. δ in ppm.

C-Atom	**1**	**2**	**3**	**4**
C(1)	37.2	37.2	30.5	36.2
C(2)	17.6	17.7	17.4	21.1
C(3)	36.9	37.1	36.9	40.5
C(4)	43.0	43.0	43.1	44.2
C(5)	59.7	59.7	52.5	64.9
C(6)	197.4	197.5	198.1	198.2
C(7)	127.4	127.6	128.0	127.4
C(8)	160.2	159.7	158.1	160.5
C(9)	49.1	48.6	74.8	85.5
C(10)	41.1	41.1	43.9	39.4
C(11)	38.3	39.1	61.5	62.0
C(12)	211.2	211.3	20.5	20.4
C(13)	42.4	41.9	179.3	22.5
C(14)	37.3	37.2	17.3	175.0
C(15)	172.6	172.7	17.8	25.0
C(16)	17.4	17.2		
C(17)	15.6	15.6		
C(18)	17.0	17.0		
C(19)	178.7	178.8		
C(20)	22.2	22.1		
COO*Me*	52.2	52.2	52.3	
COO*Me*	51.7	51.8		

that **2** was an analogue of **1**. An X-ray crystal-structure analysis (*Fig. 3*) of **2** revealed that the stereogenic center C(13) had (*R*)-configuration, indicating that compound **2** is an epimer of **1**. By the procedure applied to **1**, the absolute configuration of **2** was determined and its structure was elucidated as dimethyl 6,12-dioxo-*ent*-labd-7-ene-15,19-dioate with the absolute configuration (4*S*,5*S*,9*R*,10*S*,13*R*), and it was named 13-epiloxocalyxin A.

Compound **3** was obtained as colorless crystals, $[\alpha]_D^{20} = +23$, with a molecular formula $C_{16}H_{24}O_5$, which was deduced by HR-ESI-MS (*m*/*z* 319.1510 ($[M+Na]^+$)) A broad-band absorption at 3428 cm^{-1} in the IR spectrum suggested the presence of OH groups. It also revealed the presence of C=O groups by the strong absorptions at 1718 and 1660 cm^{-1}. The presence of an α,β-unsaturated ketone moiety was supported by an absorption maximum at 234 nm in the UV spectrum. The ^{1}H-NMR spectrum (*Table 1*) disclosed resonances for three tertiary Me groups (δ(H) 0.95 (Me(15)), 1.38 (Me(14)) and 2.05 (Me(12)), an oxymethylene group (δ(H) 3.78 and 3.86 (*d*, $J = 11$ Hz, CH_2(11)), an olefinic H-atom at δ(H) 5.78 and a methoxycarbonyl group at δ(H) 3.65 (MeOOC–C(4)). The ^{13}C-NMR spectrum (*Table 2*) revealed 16 C-atom signals. Detailed comparison of the data of **3** with those of (3β,9α)-3,9,11-trihydroxydrim-7-en-6-one [10] showed it to differ only in the substitution pattern of ring *A*. This deduction was confirmed by the HMBC results (*Fig. 2*). The NOESY (*Fig. 4*) correlation Me(14)/Me(15) suggested the α-orientation for the methoxycarbonyl group. Therefore, compound **3** was determined as methyl 9,11-dihydroxy-6-oxodrim-7-en-13-oate and named loxocalyxin B, which was further confirmed by the X-ray crystallographic

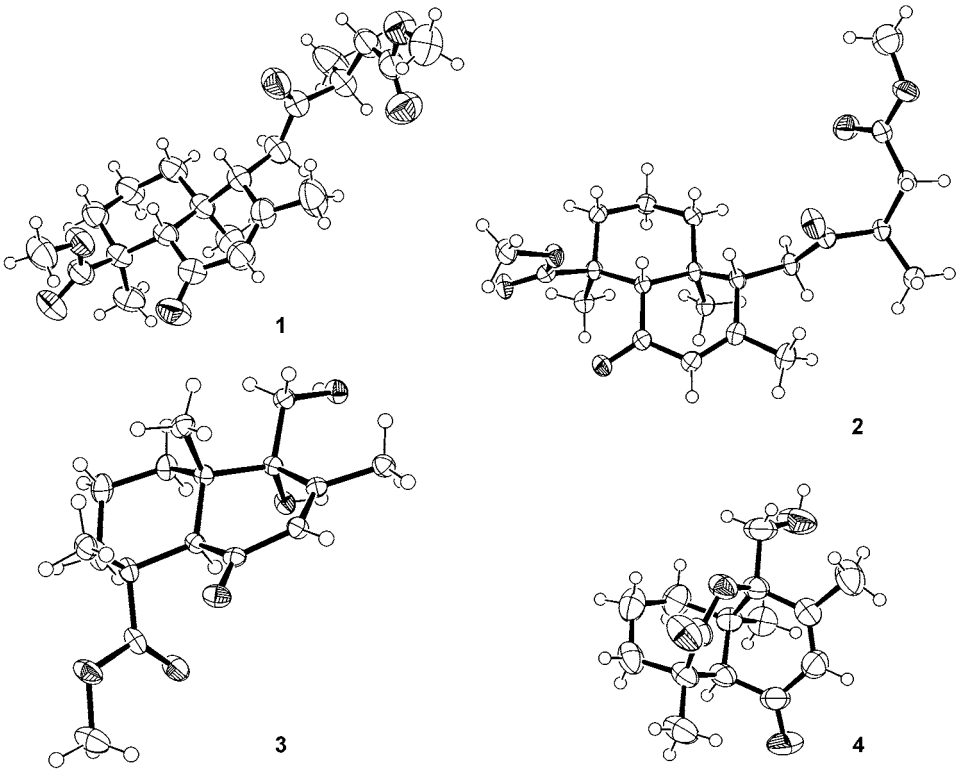

Fig. 3. *Single-crystal X-ray structures of* **1**–**4**

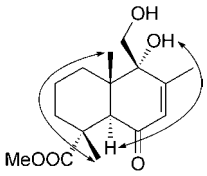

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Fig. 4. *Selected NOESY correlations of* **3**

analysis (*Fig. 3*). Alternatively, the absolute configuration (4*R*,5*R*,9*R*,10*S*) of **3** (*Fig. 1*) was determined by comparison of computated and experimental optical rotations.

Compound **4** was obtained as light yellow crystals, $[\alpha]_D^{20} = +206$, with a molecular formula $C_{15}H_{20}O_4$ which was deduced by HR-ESI-MS (*m*/*z* 287.1259 ($[M+Na]^+$)). Similar to **3**, the presence of OH and C=O groups were revealed by the strong absorptions at 3486, 1715, and 1671 cm^{-1}. The presence of an α,β-unsaturated ketone moiety was also supported by an absorption maximum at 239 nm in the UV spectrum. The ^1H- and ^{13}C-NMR spectra of **4** resembled those of **3**. A C=O of a lactone moiety gave a ^{13}C-NMR signal at δ(C) 175.0 attributed to C(14), which was supported by long-range correlations between H–C(5) (δ(H) 2.18) and Me(13) (δ(H) 1.15) with C(14)

(δ(C) 175.0) (*Fig. 2*). To the resonance of C(13) of **3** at δ(C) 179.3 corresponded the upfield-shifted δ(C) 175.0 of C(14) of **4**; C(9) was downfield-shifted from δ(C) 74.8 (**3**) to 85.5 (**4**) and C(15) from δ(C) 17.8 (**3**) to δ(C) 25.0 (**4**); moreover H–C(5) was upfield-shifted from δ(H) 3.79 (**3**) to δ(H) 2.18 (**4**). All these shifts indicated the presence of a lactone moiety at C(14) and C(9), and a new drimane-type skeleton with a *cis*-fused decalin ring system in **4** [11][12]. The HMBC data (*Fig. 2*) established, the relative configuration of **4** as (9α,10α)-11-hydroxy-6-oxodrim-7-eno-14,9-lactone, and the structure was named loxocalyxin C. This novel structure was consistent with the X-ray crystal-structure analysis (*Fig. 3*).

The quasimolecular ions $[M+H]^+$ at *m*/*z* 393 (pos. mode) and $[M-H]^-$ at *m*/*z* 391 (neg. mode) for loxocalyxin A (**1**) and 13-epiloxocalyxin A (**2**) were found in the petroleum ether phase obtained from an EtOH extract (see *Exper. Part*). Thus, **1** and **2** were considered as original compounds from *L. urticifolius*. Similarly, $[M+Na]^+$ at *m*/*z* 319 and $[M-H]^-$ at *m*/*z* 295 for loxocalyxin B (**3**) were detected in the AcOEt phase obtained from an EtOH extract which indicated the loxocalyxin B was also an original compound from *L. urticifolius*.

The authors gratefully acknowledge Prof. *S. R. Yi* for the collection and identification of the plant. We also appreciate Prof. *H. P. Xiao* for the single-crystal X-ray experiments. This work was financially supported by the grants from the *National Basic Research Program* (No. 2007CB512604), the *2010 Technological Talents Program of the Chinese Academy of Sciences* to *Y. Z.*, and the *National Natural Sciences Foundation of China* (No. 30973634).

Experimental Part

General. Column chromatography (CC): silica gel (SiO_2, 160–200 mesh; *Qingdao Marine Chemical Co.*, Qingdao, P. R. China), *MCI CHP-20* gel (75–150 μm; *Mitsubishi*), *ODS* (40–63 μm; *LiChroprep*) and *Sephadex LH-20* (*Pharmacia*). TLC: precoated plates *GF254* (*Qingdao Marine Chemical Co.*). M.p.: melting-point apparatus *X-6*, (*Beijing Fuka*); uncorrected. Optical rotation: *PE-241* polarimeter; the predicted optical-rotation values were calculated by using the B3LYP/6-311 + G (d) level of theory, and the *Boltzmann* formula was used to produce the sum of six different conformational optical rotations. UV Spectra: *Perkin-Elmer Lambda 35*; λ_{max} (log ε) in nm. IR Spectra: *Nicolet-MX-1* spectrometer; $\tilde{\nu}$ in cm^{-1}. NMR Spectra: *Bruker-AM-600* instrument; δ in ppm rel. to Me_4Si as internal standard, *J* in Hz. HR-MS: *MicrO TOF-Q II* mass spectrometers (*Bruker*, Germany); in *m*/*z*. ESI-MS: *Finnigan-LCQ^{DECA}* mass spectrometers; in *m*/*z*.

Plant Material. The plant was collected from Jinfoshan in Chongqing City, P. R. China, in July 2010, and identified as *L. urticifolius* by Prof. *S. R. Yi*. A voucher specimen was deposited with the Herbarium of the Chengdu Institute of Biology, Chinese Academy of Sciences.

Extraction and Isolation. The dried and powdered whole plant of *L. urticifolius* (6 kg) were extracted with MeOH at r.t. to give an extract (950 g) which was suspended in H_2O and extracted with petroleum ether and AcOEt (3 × 1 l, 3 h each) successively. The petroleum ether extract (80 g) was separated by CC (SiO_2 (5 × 50 cm); petroleum ether/acetone 30:1 → 1:1, 10 l): *β-sitosterol* (2.5–3.5 l; 1.5 g) and *Fractions 1–10*. *Fr. 4* (5 g) was subjected to CC (SiO_2 (4 × 40 cm), petroleum ether/acetone 20:1 → 1:1): phytol (850–1200 ml; 1 g). *Fr. 5* was subjected to CC (SiO_2 (3 × 50 cm), petroleum ether/acetone 15:1 → 1:1) (3β)-lanosta-7,9(11)-dien-3-ol (550–800 ml; 1 g). *Fr. 10* was subjected to CC (SiO_2 (3 × 40 cm), petroleum ether/acetone 15:1 → 1:1) and purified by CC (*Sephadex LH-20* (3 × 150 cm), $CHCl_3$/MeOH 1:1): **2** (1.5–1.6 l; 0.3 g). A fraction of 0.5 l (1.6–2.1 l; 1 g) from the CC (*Sephadex LH-20*) was purified by CC (*ODS* (40–63 μm, 3 × 30 cm, *LiChroprep*), MeOH/H_2O 4:7 → 8:2): **1** (450–600 ml; 0.2 g). The AcOEt extract (69 g) was separated by CC (*MCI CHP-20* (6 × 30 cm), MeOH/H_2O (7:3 (1 l), 8:2 (2 l), 9:1 (1 l), and 10:0 (1 l)): *Fractions 11–13*. *Fr. 12* (11 g) was subjected to CC

(SiO_2 (4×60 cm), with $CHCl_3$/MeOH 35:1 → 1:1): *Fr. 12.1* (1.2–1.5 l; 3 g). *Fr. 12.1* was subjected to CC (SiO_2 (3×40 cm), petroleum ether/AcOEt 20:1 → 1:1): **3** (650–800 ml, 0.2 g) and **4** (450–600 ml, 0.1 g).

Extraction for ESI-MS Analysis. The dried and powdered whole plant of *L. urticifolius* (1.2 g) was subjected to ultrasonic-wave extraction with EtOH at r.t. to give an extract (0.1 g), which was suspended in H_2O and extracted with petroleum ether and AcOEt successively. Both extracts of petroleum ether and AcOEt were subjected to CC (*MCI*) to remove chlorophyll, thus furnishing the extracts of the petroleum ether phase and the AcOEt phase for ESI-MS analysis.

Dimethyl (5β,9α,10α)-6,12-Dioxolabd-7-ene-15,19-dioate (=*(β*S,*1*R,*4a*S,*5*S,*8a*S*)-1,4,4a,5,6,7,8,8a-Octahydro-5-(methoxycarbonyl)-β,2,5,8a-tetramethyl-γ,4-dioxonaphthalene-1-pentanoic Acid Methyl Ester*; **1**): Colorless crystals (MeOH). M.p. 83–85°. $[\alpha]_D^{20} = -159$ ($c = 1.3$, $CHCl_3$); *Gaussian* calculation, −140.1. UV ($CHCl_3$): 242. IR (KBr): 2934, 1729, 1703, 1657, 1439, 1335, 1176, 1144. ^{1}H- and ^{13}C-NMR: *Tables 1* and *2*. HR-ESI-MS: 415.2071 ($[M+Na]^+$; calc. 415.2091).

*Dimethyl 6,12-Dioxo-*ent*-labd-7-ene-15,18-dioate* (=*(β*R,*1*R,*4a*S,*5*S,*8a*S*)-1,4,4a,5,6,7,8,8a-Octahydro-5-(methoxycarbonyl)-β,2,5,8a-tetramethyl-γ,4-dioxonaphthalene-1-pentanoic Acid Methyl Ester*; **2**): Colorless crystals (MeOH/Me_2O/$CHCl_3$); M.p. 82–83°. $[\alpha]_D^{20} = -125$ ($c = 1.3$, $CHCl_3$); *Gaussian* calculation, −143.7. UV($CHCl_3$): 237. IR (KBr): 2928, 1733, 1715, 1657, 1432, 1379, 1202, 1187. ^{1}H- and ^{13}C-NMR: *Tables 1* and *2*. HR-ESI-MS: 415.2068 ($[M+Na]^+$; calc. 415.2091)

Methyl 9,11-Dihydroxy-6-oxodrim-7-en-13-oate (=*(1*R,*4a*S,*5*R,*8a*R*)-1,2,3,4,4a,5,8,8a-Octahydro-5-hydroxy-5-(hydroxymethyl)-1,4a,6-trimethyl-8-oxonaphthalene-1-carboxylic Acid Methyl Ester*; **3**): Colorless crystals (acetone). M.p. 159–160°. $[\alpha]_D^{20} = +23$ ($c = 4.0$, $CHCl_3$); *Gaussian* calculation, +19.1. UV ($CHCl_3$): 234. IR (KBr): 3428, 2928, 1733, 1718, 1660, 1451, 1433, 1404, 1379, 1140, 1111, 1089, 1057. ^{1}H- and ^{13}C-NMR: *Tables 1* and *2*. HR-ESI-MS: 319.1510 ($[M+Na]^+$, $C_{22}H_{32}O_6Na^+$; calc. for 319.1516).

(9α,10α)-11-Hydroxy-6-oxo-drim-7-eno-14,9-lactone (=*(1*S,*4a*R,*5*S,*8a*R*)-1,2,3,4,4a,5,8,8a-Octahydro-5-hydroxy-5-(hydroxymethyl)-1,4a,6-trimethyl-8-oxonaphthalene-1-carboxylic Acid δ-Lactone*; = *(1*S,*4a*R,*5*S,*8a*R*)-1,3,4,4a,5,8a-hexahydro-5-(hydroxymethyl)-1,4a,6-trimethyl-5,1-(epoxymethano)naphthalene-8,10(2*H*)-dione*; **4**): Light yellow crystals (acetone). M.p. 183–184°. $[\alpha]_D^{20} = +206$ ($c = 2.1$, $CHCl_3$); *Gaussian* calculation (+185.8). UV ($CHCl_3$): 239. IR (KBr): 3486, 2935, 1715, 1671, 1450, 1379, 1274, 1126, 978. ^{1}H- and ^{13}C-NMR: *Tables 1* and *2*. HR-ESI-MS: 287.1259 ($[M+Na]^+$, $C_{15}H_{20}O_4Na^+$; calc. 287.1254).

Crystal-Structure Determinations. Diffraction data (φ and ω scans) were collected on a *Bruker AXS Apex Duo CCD* with graphite-monochromated CuK_α radiation (λ 1.54178 Å) at 298 K for the structures of **1** and **4**. The total number of independent reflections measured was 3496, of which 3435 were observed ($|F|^2 > 2\sigma|F|^2$) for **1**, and the total number of independent reflections measured was 3820, of which 3721 were observed ($|F|^2 > 2\sigma|F|^2$) for **4**. A *Siemens-P4* four-circle diffractometer with an incident beam graphite monochromator (MoK_α radiation, λ 0.71073 Å) in ω-scan mode was used for the structure determination of **1**–**4**. The structures were solved by direct methods with SHELXS-97 [13] and refined against F^2 on all data by full-matrix least-squares with SHELXL-97 following established refinement strategies. All non-H-atoms were refined anisotropically. The cif files were disposed by Ortep3v2 and gimp 2.6.11.0 (see *Fig. 3*). CCDC-841577 to CCDC-841580) (**1**–**4**) contain the supplementary crystallographic data for this paper. These data can be obtained free of charge *via* http://www.ccdc.cam.ac.uk/data_request/cif.

X-Ray Crystal Data of **1**. $C_{22}H_{32}O_6$, orthorhombic, $P2_12_12_1$, M_r 392.48; unit cell dimensions, $a =$ 9.9258(4), $b = 14.1974(6)$, $c = 15.6110(7)$ Å, $\alpha = \beta = \gamma = 90°$, $V = 2199.91(16)$ Å^3, $Z = 4$, $d = 1.185$ g/cm^3, $F(000) = 848$; crystal size $0.20 \times 0.15 \times 0.12$ mm; θ range for data collection from 4.21° to 67.70°; $wR_2 =$ 0.0965 for 3496 independent reflections and 260 variables; $S = 1.033$.

X-Ray Crystal Data of **2**. $C_{22}H_{32}O_6$, M_r 392.48, orthorhombic, $P2_12_12_1$; unit cell dimensions, $a =$ 9.4120(16), $b = 14.381(3)$, $c = 15.979(3)$ Å, $\alpha = \beta = \gamma = 90°$, $V = 2162.8(6)$ Å^3, $Z = 4$, $d = 1.205$ Mg/m^3, $F(000) = 848$; Crystal size $0.54 \times 0.21 \times 0.16$ mm; θ range for data collection from 3.11° to 27.49°; $wR_2 =$ 0.0983 for 4946 independent reflections and 254 variables; $S = 1.003$.

X-Ray Crystal Data of **3**. $C_{16}H_{24}O_5$, M_r 296.35, monoclinic, $P2_1$; unit-cell dimensions, $a = 8.168(4)$, $b = 6.573(3)$, $c = 14.169(6)$ Å, $\alpha = 90°$, $\beta = 95.270(6)°$, $\gamma = 90°$, $V = 757.4(6)$ Å^3, $Z = 2$, $d = 1.299$ Mg/m^3,

$F(000) = 320$; crystal size $0.63 \times 0.60 \times 0.13$ mm; θ range for data collection from 2.77° to 29.14°; $wR_2 =$ 0.0691 for 2177 independent reflections and 202 variables; $S = 1.000$.

X-Ray Crystal Data of **4**. $C_{15}H_{20}O_4$, M_r 264.31, monoclinic, $P2_1$; unit-cell dimensions, $a = 12.7740(3)$, $b = 7.0990(2)$ (19), $c = 15.5107(3)$ Å, $\alpha = 90°$, $\beta = 107.2470(10)°$, $\gamma = 90°$, $V = 1343.31(6)$ Å^3, $Z = 2$, $d = 1.307$ g/cm^3, $F(000) = 568$; crystal size $0.26 \times 0.24 \times 0.20$ mm; θ range for data collection from 3.62° to 67.77°; $wR_2 = 0.0988$ for 3820 independent reflections and 351 variables; $S = 1.046$.

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