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EUDESMANOLIDES FROM *Artemisia lehmanniana*. CRYSTAL AND MOLECULAR STRUCTURES OF 1α-ACETOXY-4α-HYDROXY-5,7α,6,11β(H)-EUDESM-2,3-EN-6,12-OLIDE AND 1α-ACETOXY-3α-HYDROXY-5,7α,6,11β(H)-EUDESM-4,15-EN-6,12-OLIDE

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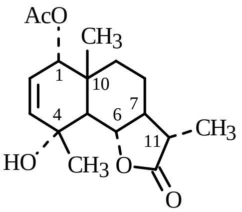
Two eudesmane sesquiterpene lactones of composition $C_{17}H_{24}O_5$ were isolated from the aerial part of Artemisia lehmanniana *Bunge. X-ray structure analysis established their crystal and molecular structures.*

Key words: *Artemisia*, eudesmanolides, x-ray structure analysis.

In continuation of research on terpenoids from plants of the *Artemisia* genus (Asteraceae) [1, 2], we isolated two eudesmane sesquiterpene lactones (**1** and **2**) with the same composition ($C_{17}H_{24}O_5$) from the aerial part of Lehmann wormwood (*Artemisia lehmanniana* Bunge) by rechromatography of previously obtained fractions [2].



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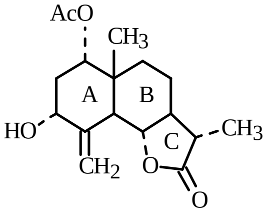

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The physicochemical constants and IR spectra of the isolated lactones were comparable with those of 1α-acetoxy-4α-hydroxy-5,7α,6,11β(H)-eudesm-2,3-en-6,12-olide and 1α-acetoxy-3α-hydroxy-5,7α,6,11β(H)-eudesm-4,15-en-6,12-olide, respectively [3]. However, because the PMR spectra of **1** and **2** taken on a Tesla BS 567A spectrometer at working frequency 100 MHz did not enable an unambiguous assignment of all proton signals, we performed an x-ray structure analysis (XSA) of the isolated lactones.

Figure 1 shows the molecular structures of **1** and **2**. The *trans* fusion of the A/B and B/C rings in **1** and **2** is evident. Ring A in **1** has the half-chair conformation with C5 and C10 deviating (by 0.29 and -0.45 Å, respectively) from the plane of the remaining four atoms (±0.01 Å). Ring B has the chair conformation. The six-membered rings in **2** have the chair conformation. Ring C in both molecules has the 7α-envelope conformation. Atom C7 deviates from the plane of the remaining four atoms by 0.62 Å.

The C1 acetate in both molecules has the α-axial orientation; the C10 methyl, β-axial; the C11 methyl, α-axial. The C4 hydroxyl in **1** is α-equatorial; the methyl, β-axial. The C3 hydroxyl in **2** has the α-axial orientation.

The bond lengths and angles in **1** and **2** (Table 1) are practically the same as in previously studied eudesmanolide isomers [1, 2]. The C1–C10 bond (site of ring A and B fusion) is characteristically lengthened (up to 1.582 Å) from the normal value [4].

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TABLE 1. Bond Lengths (r, Å) and Angles (ω, deg) in **1** and **2**

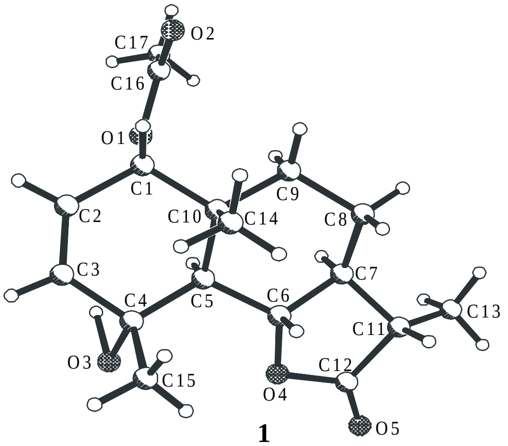
Bond	r**1**	r**2**	Angle	ω**1**	ω**2**
O1-C16	1.347 (6)	1.337 (5)	C(16)-O(1)-C(1)	117.8 (4)	116.8 (4)
O1-C1	1.461 (6)	1.465 (5)	C(12)-O(4)-C(6)	107.6 (3)	108.2 (4)
O2-C16	1.194 (7)	1.206 (6)	O(1)-C(1)-C(2)	106.6 (4)	108.7 (4)
O3-C4	1.443 (6)		O(1)-C(1)-C(10)	111.5 (4)	108.2 (4)
O3-C3		1.419 (6)	C(2)-C(1)-C(10)	113.0 (4)	113.4 (4)
O4-C12	1.364 (6)	1.346 (6)	C(3)-C(2)-C(1)	124.4 (5)	114.4 (4)
O4-C6	1.468 (5)	1.465 (6)	C(2)-C(3)-C(4)	124.7 (5)	110.2 (4)
O5-C12	1.198 (6)	1.203 (7)	O(3)-C(3)-C(4)		107.9 (4)
C1-C2	1.487 (7)	1.529 (8)	O(3)-C(3)-C(2)		113.9 (4)
C1-C10	1.531 (7)	1.544 (6)	O(3)-C(4)-C(3)	107.2 (4)	
C2-C3	1.319 (7)	1.524 (8)	O(3)-C(4)-C(5)	110.0 (4)	
C3-C4	1.503 (7)	1.508 (6)	C(3)-C(4)-C(5)	110.8 (4)	
C4-C5	1.531 (6)	1.499 (6)	O(3)-C(4)-C(15)	101.7 (4)	112.2 (4)
C4-C15	1.533 (7)	1.323 (7)	C(3)-C(4)-C(15)	111.5 (4)	122.2 (5)
C5-C6	1.513 (6)	1.507 (5)	C(5)-C(4)-C(15)	114.9 (4)	125.5 (4)
C5-C10	1.582 (6)	1.578 (6)	C(6)-C(5)-C(4)	116.3 (4)	116.1 (3)
C6-C7	1.507 (6)	1.508 (7)	C(6)-C(5)-C(10)	107.1 (4)	107.1 (3)
C7-C8	1.509 (7)	1.513 (8)	C(4)-C(5)-C(10)	113.5 (4)	109.7 (4)
C7-C11	1.524 (6)	1.540 (7)	O(4)-C(6)-C(7)	103.2 (4)	103.5 (4)
C8-C9	1.527 (7)	1.543 (8)	O(4)-C(6)-C(5)	114.5 (3)	113.9 (3)
C9-C10	1.551 (7)	1.527 (8)	C(7)-C(6)-C(5)	113.6 (4)	112.7 (4)
C10-C14	1.538 (7)	1.536 (7)	C(6)-C(7)-C(8)	109.6 (4)	110.0 (5)
C11-C13	1.507 (7)	1.516 (9)	C(6)-C(7)-C(11)	101.2 (4)	100.0 (4)
C11-C12	1.511 (7)	1.521 (8)	C(8)-C(7)-C(11)	122.0 (4)	123.2 (5)
C16-C17	1.493 (8)	1.479 (7)	C(7)-C(8)-C(9)	107.2 (4)	107.8 (4)
			C(8)-C(9)-C(10)	113.7 (4)	113.7 (4)
			C(1)-C(10)-C(14)	106.1 (4)	106.5 (4)
			C(1)-C(10)-C(9)	110.2 (4)	110.7 (4)
			C(14)-C(10)-C(9)	107.8 (4)	109.2 (5)
			C(1)-C(10)-C(5)	108.3 (4)	107.9 (4)
			C(14)-C(10)-C(5)	113.5 (4)	111.4 (4)
			C(9)-C(10)-C(5)	110.8 (4)	111.1 (4)
			C(13)-C(11)-C(12)	114.1 (5)	114.6 (6)
			C(13)-C(11)-C(7)	117.2 (4)	117.4 (5)
			C(12)-C(11)-C(7)	100.5 (4)	100.3 (4)
			O(5)-C(12)-O(4)	121.1 (5)	121.6 (6)
			O(5)-C(12)-C(11)	128.3 (4)	128.0 (5)
			O(4)-C(12)-C(11)	110.6 (4)	110.4 (5)
			O(2)-C(16)-O(1)	124.7 (5)	123.4 (4)
			O(2)-C(16)-C(17)	124.3 (6)	125.2 (4)
			O(1)-C(16)-C(17)	111.0 (5)	111.4 (4)

The molecular packing showed that the crystal structures of **1** and **2** have an O–H...O H-bond between the acetate carbonyl and the hydroxyl at C3 and C4, respectively. Molecules in the crystal of **1** are translated along the *a* axis, related by a H-bond, and form an infinite chain with the following properties: O2...O3 (x, -1 + y, z) 2.91 Å, H3...O2 2.29 Å, and angle O3–H...O2 125.4°. An infinite chain is also formed in **2** but along the monoclinic *b* axis. Molecules translated by the 2_1 screw axis are related by a H-bond: O2...O3 (1 - x, 0.5 + y, 1 - z) 2.86 Å, H3...O2 2.09 Å, and angle O3–H...O2 156.8°.

Thus, we found that sesquiterpene lactone **1** has the structure 1α-acetoxy-4α-hydroxy-5,7α,6,11β(H)-eudesm-2,3-en-6,12-olide; lactone **2**, 1α-acetoxy-3α-hydroxy-5,7α,6,11β(H)-eudesm-4,15-en-6,12-olide.

TABLE 2. Principal Crystallographic Parameters and Conditions of X-ray Structure Analysis for **1** and **2**

Compounds	**1**	**2**
Empirical formula	$C_{17}H_{24}O_5$	$C_{17}H_{24}O_5$
Molecular weight	308.36	308.36
System	Orthorhombic	Monoclinic
Space group	$P2_12_12_1$	$P2_1$
Z	4	2
a, Å	7.542 (2)	9.583 (2)
b, Å	10.622 (2)	6.901 (1)
c, Å	20.048 (4)	12.718 (3)
α	90	90
β	90	99.92 (3)
γ	90	90
V, $Å^3$	1606.1 (6)	828.5 (3)
ρ, g/cm^3	1.275	1.236
Crystal dimen., mm	0.98 × 0.53 × 0.20	0.73 × 0.60 × 0.40
Scan region, 2θ	$2.03 \leq \theta \leq 27.49°$	$1.63 \leq \theta \leq 27.49°$
μ_{exp}, cm^{-1}	0.930	0.890
Number of reflections Number of	2120	2032
reflections I > 2σ (I)	1381	1492
R1 [I > 2σ (I) and total]	0.0634 (0.1124)	0.0597 (0.0908)
wR2	0.1389 (0.1697)	0.1482 (0.1778)
Difference electron-density peaks	0.199 and -0.203 e. $Å^3$	0.176 and -0.196 e. $Å^3$



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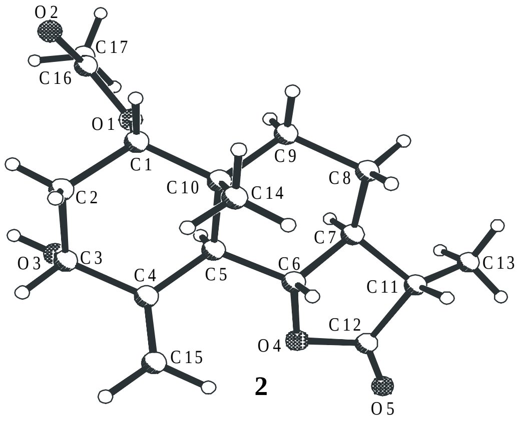

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Fig. 1. Structures of **1** and **2**.

EXPERIMENTAL

IR spectra were recorded on a Perkin—Elmer System 2000 IR-Fourier spectrometer (KBr disks). PMR spectra were recorded on a Tesla BS 567A spectrometer at working frequency 100 MHz with GMDS internal standard. Chemical shifts are given on the δ-scale.

The method for isolating the terpenoids from *A. lehmanniana* Bunge has been described [2].

1α-Acetoxy-4α-hydroxy-5,7α,6,11β(H)-eudesm-2,3-en-6,12-olide was colorless needle-like crystals isolated from eluates 183-192, $C_{17}H_{24}O_5$, $[M]^+$ 308, mp 182-183°C, R_f 0.44 (hydrocarbons:ethylacetate, 1:1, double elution). IR spectrum (KBr, ν, max): 3551 (7.78), 3430 (40.50), 3023 (20.87), 2981 (12.89), 2953 (15.96), 2902 (37.38), 2879 (18.96), 1762 (3.18), 1728 (3.20), 1657 (48.31), 1459 (37.01), 1441 (31.35), 1416 (25.35), 1393 (19.48), 1373 (7.03), 1341 (27.08), 1331 (35.22), 1316 (41.67), 1289 (19.37), 1273 (8.44), 1240 (3.25), 1227 (3.85), 1196 (8.20), 1162 (4.02), 1135 (18.02), 1122 (11.77), 1063 (6.09), 1053 (10.59), 1023 (3.44), 992 (3.12), 967 (27.35), 957 (17.71), 941 (12.55), 927 (18.42), 921 (19.78), 898 (52.86), 882 (26.36), 867 (34.29), 844 (55.56), 785 (57.35), 766 (20.98), 738 (38.42), 695 (70.57), 659 (65.30), 644 (48.76), 621 (44.72), 606 (43.65), 558 (56.53), 544 (44.87), 517 (39.78).

1α-Acetoxy-3α-hydroxy-5,7α,6,11β(H)-eudesm-4,15-en-6,12-olide was a colorless substance partly cottony (cellulosic) and partly cubic crystals isolated from eluates 211-215, $C_{17}H_{24}O_5$, $[M]^+$ 308, mp 187-189°C, R_f 0.36 (hydrocarbons:ethylacetate, 1:1, double elution). IR spectrum (KBr, ν, max): 3433 (30.93), 3096 (68.74), 2980 (56.09), 2945 (53.72), 2900 (67.76), 2872 (56.58), 1764 (12.51), 1706 (7.56), 1663 (54.60), 1460 (53.51), 1431 (50.47), 1385 (34.16), 1363 (49.23), 1341 (56.23), 1276 (15.10), 1250 (35.07), 1225 (46.41), 1197 (36.34), 1163 (43.02), 1147 (48.41), 1127 (35.53), 1081 (23.79), 1046 (29.33), 1021 (25.76), 1000 (34.44), 976 (29.35), 956 (52.06), 944 (46.92), 918 (56.69), 903 (35.87), 863 (56.84), 847 (58.84), 789 (66.82), 752 (64.07), 724 (67.76), 674 (63.88), 648 (66.80), 605 (59.47), 520 (61.60), 505 (61.98), 466 (63.83), 420 (72.33).

X-Ray Structure Analysis. Unit-cell constants of crystals of **1** and **2** were determined and refined on a Stoe Stadi-4 diffractometer (T = 295 K, graphite monochromator). Table 2 lists the principal parameters of the XSA and calculations. The three-dimensional intensity data set was collected on the same diffractometer by $\omega/2\theta$-scanning using Mo Kα-radiation. Absorption corrections were not applied.

Structures of **1** and **2** were solved by direct methods using SHELXS-97 programs and refined by full-matrix isotropic and anisotropic least-squares methods. The structures were refined using SHELXL-97 programs. Coordinates of H atoms were determined experimentally from a difference electron-density synthesis and refined isotropically. Data from the XSA were deposited as CIF files in the Cambridge Structural Database (CCDC 249892 and 249893).

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