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1α-ACETOXY-11β(H),13-DIHYDRODOUGLANIN, A NEW EUDESMANOLIDE FROM *Artemisia lehmanniana*

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A new sesquiterpene lactone, 1α-acetoxy-11β(H),13-dihydrodouglanin, was isolated from Artemisia lehmanniana. *The structure was established by spectral data and an x-ray analysis.*

Key words: sesquiterpene lactone, *Artemisia lehmanniana* Bunge, x-ray structure analysis, 1α-acetoxy-11β(H),13-dihydrodouglanin.

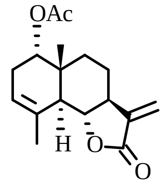
In continuation of the study of terpenes from *Artemisia* species (Asteraceae) [7], we isolated from the aerial part of Lehman wormwood (*A. lehmanniana* Bunge) [1] β-amyrin acetate, coumarin, isofraxidin, and a new eudesmane-type sesquiterpene lactone of composition $C_{17}H_{24}O_4$, M^+ 292, mp 114-115°C.

The IR spectrum of the lactone contains absorption bands of the carbonyl in the γ-lactone ring (1780 cm^{-1}), an ester carbonyl (1735, 1245 cm^{-1}), and a double bond (1645 cm^{-1}).

The mass spectrum exhibits peaks with *m*/*z* 232 $[M - 60]^+$ and 217 $[232 - CH_3]^+$, which are due to loss of acetic acid and methyl, and fragments (see Experimental) that are characteristic of the electron-impact decomposition of sesquiterpene lactones of the eudesmane type [4]. The conversion of the molecular ion with *m*/*z* 292 to the ion with *m*/*z* 232 $[M - 60]^+$ was determined using metastable defocusing.

The ^1H NMR spectrum (δ, ppm, $CDCl_3$) contains signals of two tertiary methyls (0.88, 3H, s, and 1.78, 3H, br. s), a secondary methyl (1.15, 3H, d, J = 8 Hz), an acetyl (2.00, 3H, s), and protons from lactone (3.88, 1H, q, J_1 = 10 Hz, J_2 = 12 Hz), gemacyl (4.56, 1H, d, J = 9 Hz), and olefine (5.22, 1H, br. s).

The spectral properties of the isolated sesquiterpene lactone are comparable to those of the lactones douglanin acetate **1** [2] and 11,13-dihydrosantamarin **2** [3] and suggest the structure **3** for it.



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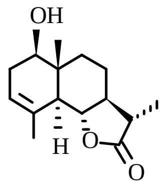

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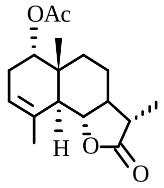

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An x-ray analysis was performed in order to unambiguously establish the structure. The eudesmane core consists of *A*/*B*- and *B*/*C*-*trans*-fused rings. The cyclohexene ring *A* adopts the rarely encountered 10β-half-chair conformation that is characteristic of eudesmanolides with a C3=C4 double bond [4-7]. The cyclohexane ring *B* has the common chair conformation. The lactone ring (6,7-*trans*) adopts the 7α-envelope conformation. The O-acetyl group on C1 is α-axial; the methyl group on C10, β-axial. The methyl group in the lactone ring has the α-orientation. The conformational parameters of the tricyclic system are practically the same as those of the previously examined eudesmanolide 9β-hydroxy-11β(H),13-dihydrosantamarin [7], although they differ in the substituents on C1 and C9 in the eudesmanolide core.

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

Bond	*r*	Angle	ω	Angle	ω
O1-C12	1.198(5)	C12-O2-C6	107.9(3)	C6-C7-C11	99.7(3)
O2-C12	1.365(5)	C16-O3-C1	118.3(3)	C7-C8-C9	107.6(3)
O2-C6	1.460(5)	O3-C1-C2	106.8(3)	C10-C9-C8	113.3(3)
O3-C16	1.333(5)	O3-C1-C10	109.3(3)	C1-C10-C9	110.6(3)
O3-C1	1.460(5)	C2-C1-C10	112.5(3)	C1-C10-C14	105.7(3)
O4-C16	1.190(5)	C3-C2-C1	113.3(4)	C9-C10-C14	108.2(4)
C1-C2	1.520(6)	C4-C3-C2	125.5(4)	C1-C10-C5	108.0(4)
C1-C10	1.527(5)	C3-C4-C15	120.5(4)	C9-C10-C5	112.1(4)
C2-C3	1.496(6)	C3-C4-C5	120.6(4)	C14-C10-C5	112.1(4)
C3-C4	1.320(6)	C15-C4-C5	118.8(4)	C12-C11-C13	113.4(4)
C4-C15	1.500(6)	C4-C5-C6	118.1(3)	C12-C11-C7	100.2(3)
C4-C5	1.525(5)	C4-C5-C10	110.8(3)	C13-C11-C7	117.4(4)
C5-C6	1.520(5)	C6-C5-C10	106.8(3)	O1-C12-O2	120.5(4)
C5-C10	1.562(5)	O2-C6-C7	102.7(3)	O1-C12-C11	129.2(4)
C6-C7	1.525(6)	O2-C6-C5	114.8(3)	O2-C12-C11	110.3(4)
C7-C8	1.508(6)	C7-C6-C5	111.9(3)	O4-C16-O3	123.9(4)
C7-C11	1.534(6)	C8-C7-C6	111.4(3)	O4-C16-C17	124.0(4)
C8-C9	1.534(6)	C8-C7-C11	122.4(3)	O3-C16-C17	112.1(4)
C9-C10	1.535(6)				
C10-C14	1.543(6)				
C11-C12	1.506(6)				
C11-C13	1.520(6)				
C16-C17	1.487(6)				

TABLE 2. Atomic Coordinates ($\times 10^4$) and Equivalent Isotropic Thermal Parameters U_{eq} ($Å^2 \times 10^3$) in **1**

Atom	*x*	*y*	*z*	U_{eq}
O1	6801(6)	10001(2)	2109(5)	74(1)
O2	5129(5)	8945(2)	2444(4)	52(1)
O3	5726(4)	6139(2)	3910(4)	51(1)
O4	6620(6)	5030(2)	2834(6)	96(1)
C1	4034(6)	6201(2)	2292(6)	47(1)
C2	2103(7)	6218(2)	3309(7)	54(1)
C3	1597(7)	6972(2)	4038(6)	51(1)
C4	2558(6)	7592(2)	3691(5)	43(1)
C5	4398(6)	7579(2)	2524(5)	39(1)
C6	4808(6)	8259(2)	1282(5)	41(1)
C7	6772(6)	8182(2)	324(6)	45(1)
C8	6655(7)	7550(2)	-1173(6)	53(1)
C9	6206(7)	6841(2)	-34(6)	52(1)
C10	4300(6)	6900(2)	1054(5)	41(1)
C11	7059(6)	8990(2)	-306(6)	51(1)
C12	6385(7)	9388(2)	1490(7)	54(1)
C13	9160(8)	9220(3)	-765(8)	74(1)
C14	2428(7)	6932(3)	-569(6)	53(1)
C15	1935(7)	8315(2)	4549(7)	58(1)
C16	6774(7)	5507(2)	4083(7)	51(1)
C17	8162(7)	5467(3)	6015(7)	59(1)

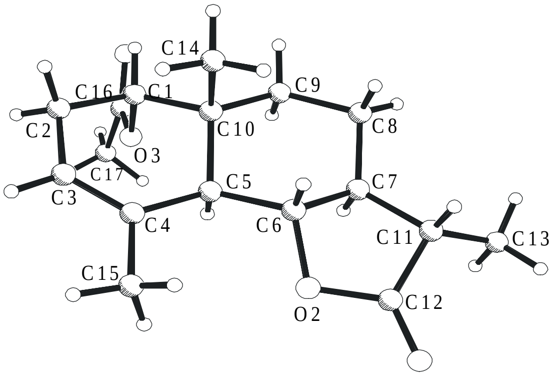

Fig. 1. Structure of 1α-acetoxy-11β(H),13-dihydrodouglanin.

The Csp^3–Csp^3 bonds in **3** are on the average shorter that the normal value of 1.540 Å and vary in the range 1.508-1.543 Å, except for the C5—C10 distance [1.562(5) Å] (Table 1). The observed elongation of the C5—C10 bond is typical of this bond in eudesmanolides [4-7]. The lengths of the C5—C10 bond in eudesmanolides are listed below (Å):

Mucrolide [4]	1.566(5)
4(15)α-Epoxyisoalantolactone [5]	1.551(4)
3β-Hydroxyeudesm-4(15),11(13)-dien-6,12-olide [6]	1.560(7)
9β-Hydroxy-11β(H),13-dihydrosantamarin [7]	1.568(3)
1α-Acetoxy-11β(H),13-dihydrodouglanin	1.562(5)

The lengths of the C3═C4 double bond and the C═O carbonyl are 1.320(5) and 1.194(6) Å, respectively. They are within experimental uncertainty of the normal lengths [8]. All other bond lengths have their typical values. The bond angles are consistent with those observed in other tricyclic eudesmanolides [4-7].

The molecular packing and intermolecular contacts indicate that there are no significant intermolecular interactions. The molecules in the crystal are situated within van-der-Waals distances.

Thus, it is unambiguously established that the isolated eudesmanolide has the structure 1α-acetoxy-3,4-en,5,7α,6,11β(H)-eudesm-6,12-olide.

EXPERIMENTAL

IR spectra were recorded on a Perkin—Elmer system 2000 IR-Fourier spectrometer (KBr pellets); mass spectra, on a Kratos MS-25 GC—MS (GB) and MX-1310.

^{1}H NMR spectra were recorded on a Tesla BS 567 A spectrometer at working frequency 100 MHz with HMDS internal standard. Chemical shifts are reported on the δ-scale.

Isolation Method. The aerial part of *A. lehmanniana* (6 kg) was collected on June 30-31, 1994, during budding and flowering near Chechekty, Murgabskii region, Tadzhikistan Republic. It was extracted five times with $CHCl_3$ at a material:extractant ratio of 1:5. The combined extracts were evaporated and treated with 90% alcohol. The precipitate that formed was filtered off after 24 h. The filtrate was evaporated to give 222 g of solid that was placed on a silica-gel column in a 1:20 ratio. Elution with benzene and its mixtures with ethylacetate, pure ethylacetate, an ethylacetate—methanol mixture, and methanol gave fractions of 500 ml that were distributed as follows: 1-99 (benzene), 100-123 (benzene—ethylacetate, 19:1), 124-192 (benzene—ethylacetate, 14:1), 193-229 (benzene—ethylacetate, 4:1), 230-270 (benzene—ethylacetate, 2:1), 271-298 (benzene—ethylacetate, 1:1), 299-312 (benzene—ethylacetate, 1:2), 313-335 (ethylacetate), 336-358 (ethylacetate—methanol, 9:1), 359-415 (ethylacetate—methanol, 4:1), 416-431 (methanol).

β-Amyrin acetate is a white crystalline powder isolated from fractions 14-18, $C_{32}H_{52}O_2$, mp 239-240°C, M^+ 468. The triterpene was identified based on mass spectra and directly by comparision with an authentic sample [9]

Isofraxidin is a white crystalline powder isolated from fractions 44-47, $C_{11}H_{10}O_5$, M^+ 222, mp 141-143°C. The coumarin was identified based on mass spectra and directly by comparison with an authentic sample [10].

1α-Acetoxy-11β(H),13-dihydrodouglanin is a colorless crystalline substance isolated from fractions 24-34, $C_{17}H_{24}O_4$, M^+ 292, mp 114-115°C. Mass spectrum (*m/z*, intensity, %): 232 (100), 217 (34), 203 (4), 189 (6.5), 176 (8), 175 (6.5), 171 (10.5), 165 (3), 158 (31.5), 143 (55), 133 (10.5), 119 (24), 108 (6.5), 107 (16), 106 (14.5), 105 (31.5), 98 (6.5), 91 (18.5), 55 (16).

X-ray Structure Analysis. Unit-cell constants and intensities of 1872 independent reflections were measured on a CAD-4 Nonius diffractometer (Mo Kα-radiation, graphite monochromator, θ/2θ-scanning). Crystals of **3** are monoclinic, a = 6.634(5), b = 18.02(3), c = 6.644(4) Å, β = 97.02(6)°, V = 788(2) $Å^3$, d_{calc} = 1.232 g/cm^3, Z = 2 ($C_{17}H_{24}O_4$), space group $P2_1$. The structure was solved by direct methods and refined by anisotropic full-matrix least-squares techniques for nonhydrogen atoms. All H atoms with the exception of the hydroxyl H, which was located in a difference electron-density synthesis, were placed geometrically and fixed to the appropriate atom. A total of 1780 reflections with $I > 2\sigma(I)$ was used. The final agreement factors are R = 0.0625 and R_w = 0.1081. Atomic coordinates are listed in Table 2. All calculations were performed on an IBM-486 PC using the SHELXS-93 and SHELXL-93 programs.

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