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13α-HYDROXYMETHYLENEDEACETYLLAURENOBIOLIDE, A NEW GERMACRANOLIDE FROM *Tanacetopsis mucronata*

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The new sesquiterpene lactone 13-hydroxymethylenedeacetyllaurenobiolide was isolated from the aerial part of Tanacetopsis mucronata *S. Koval. (Asteraceae). Its structure was established using spectral data and X-ray structure analysis. The germacranolide macrocycle has the chair—chair conformation with the configuration* ${}_1D^{14}$, ${}^{15}D_5$.

Key words: *Tanacetopsis mucronata*, sesquiterpene lactone, 13-hydroxymethylenedeacetyllaurenobiolide, X-ray structure analysis.

The new sesquiterpene germacrane lactone (**1**), $C_{15}H_{22}O_4$, $[M]^+$ 266, mp 153-154°C, was isolated from the aerial part of *Tanacetopsis mucronata* (Regel et. Schmalh.) S. Koval. (Asteraceae) by rechromatography of fractions resulting from separation of the flavonoids [1].

The IR spectrum of **1** contains a broad band with separate maxima at 3282 and 3235 cm^{-1}, corresponding to absorption of interacting H-bonds of hydroxyls, a strong band for a γ-lactone carbonyl ring at 1753 cm^{-1}, and a weak band at 1671 cm^{-1} characteristic of a double bond.

The PMR spectrum of **1** has signals for protons of two tertiary methyls on a double bond (br.s at 1.48 ppm, 3H-14, 3H-15) and protons of a hydroxymethylene (br.q AB at 2.84 ppm, 2H-13). Signals of the remaining protons appear as multiplets: H-11, 2.2-2.6; H-6, 3.2-3.4; H-8, 4.00-4.3; H-5, 4.4-4.65; and H-1, 4.65-5.2 ppm. Protons of two hydroxyls that shift to weak field upon addition of trifluoroacetic acid are found at 6.4-7.00 ppm.

The literature teaches that such broadening and multiplicity in PMR spectra are characteristic of linear 7,8-*trans*-fused germacranolides that have structures related to the sesquiterpene lactone laurenobiolide (**2**) [2-6]. This is due to the presence in the solution of a mixture of several conformers, e.g., in the PMR spectra of deacetyllaurenobiolide (**2**) [7], dehydrodeacetyllaurenobiolide (**3**) [8], and 1α,10β-epoxydeacetyllaurenobiolide (mucrin) (**4**), which we isolated previously from *Tanacetopsis mucronata* [9, 10].

The pyrazoline derivatives were prepared by reaction with diazomethane in order to produce more clearly interpreted signals in the PMR spectra of this type of compounds. The conformations of the rings are relatively more stable [2-6].

According to the PMR spectra, **1** contains an exomethyl on the γ-lactone ring and a hydroxymethylene, which precludes the possibility of preparing the pyrazoline derivative. Nevertheless, based on the composition and a comparison of the spectral properties of **1** and lactones **2-4**, a more likely structure for the isolated compound **1** is proposed.

We performed an X-ray structure analysis (XSA) to determine the structure of the compound. Figure 1 shows the structure of **1** from the XSA. The structure and an analysis of the torsion angles in **1** show that the macrocycle has the chair—chair conformation with the ${}_1D^{14},{}^{15}D_5$ configuration (CH_3 groups on C4 and C10 are parallel and mutually β-*syn*-oriented whereas the endocyclic double bonds are staggered). This corresponds to the preferred conformation observed in solution for laurenobiolide [2].

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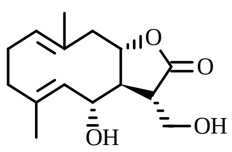
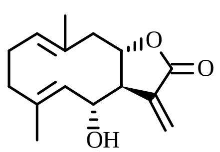
TABLE 1. Bond Lengths (r, E) and Angles (ω, deg) in **1**

Bond	r	Angle	ω	Angle	ω
O1-C6	1.449(3)	C12-O2-C8	111.2(2)	O2-C8-C7	104.2(2)
O2-C12	1.340(3)	C10-C1-C2	127.3(2)	C9-C8-C7	119.7(2)
O2-C8	1.466 (3)	C1-C2-C3	108.4(2)	C10-C9-C8	112.6(2)
O3-C12	1.202 (3)	C4-C3-C2	110.1(2)	C1-C10-C14	124.3(2)
O4-C13	1.419(3)	C5-C4-C3	118.7(2)	C1-C10-C9	120.4(2)
C1-C10	1.336(4)	C5-C4-C15	125.7(3)	C14-C10-C9	115.1(2)
C1-C2	1.491(4)	C3-C4-C15	115.1(2)	C12-C11-C13	109.5(2)
C2-C3	1.555(4)	C4-C5-C6	129.2(2)	C12-C11-C7	103.3(2)
C3-C4	1.509(4)	O1-C6-C5	108.2(2)	C13-C11-C7	118.4(2)
C4-C5	1.325(3)	O1-C6-C7	104.7(2)	O3-C12-O2	122.1(2)
C4-C15	1.496(4)	C5-C6-C7	113.7(2)	O3-C12-C11	127.7(2)
C5-C6	1.490(3)	C11-C7-C6	112.7(2)	O2-C12-C11	110.2(2)
C6-C7	1.544(3)	C11-C7-C8	101.6(2)	O4-C13-C11	114.2(2)
C7-C11	1.544(3)	C6-C7-C8	115.9(2)		
C7-C8	1.544(3)	O2-C8-C9	105.5(2)		
C8-C9	1.541(4)				
C9-C10	1.497(4)				
C10-C14	1.511(4)				
C11-C12	1.507(4)				
C11-C13	1.522(3)				



1



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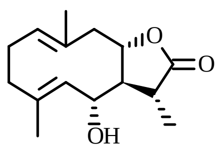

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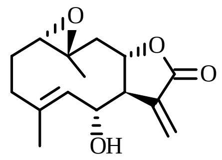

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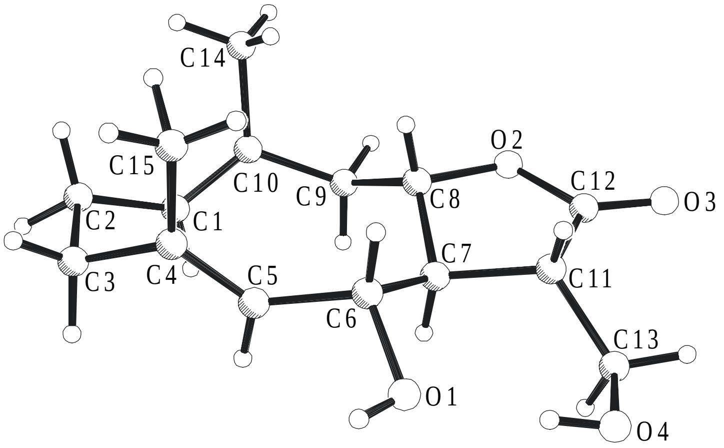

Fig. 1. Structure of **1** (placement of H atoms on hydroxyls indicates the nature of the intramolecular H-bond).

The positions of the hydroxyls on C13 and C6 are favorable for the formation of an intramolecular OH...O H-bond. The unshared pair of O1 interacts with the H atom of the C13 hydroxyl. This is evident in the distances O1...O4 (2.62 Å), O1...H (1.79 Å), and angle O1...H–O4 (165.8°).

The lengths of Csp^3—Csp^3 bonds in the carbon framework of the germacranolide on average are close to the normal value 1.540 Å. The endocyclic double bonds C1=C10 and C4=C5 have values of 1.336(4) and 1.325(3) Å, respectively. These are the same within experimental uncertainty (3σ) and do not differ from the standard values [11] observed in other types of bonds (Table 1).

TABLE 2. Crystallographic Data, Experimental Values, and Refinement Parameters for **1**

Empirical formula	$C_{15}H_{22}O_4$
Molecular weight	266.33
Temperature, K	110
Space group	$P3_2$, Z = 3
a, Å	10.785 (2)
b, Å	10.785(2)
c, Å	10.209(3)
a, deg	90
b, deg	90
g, deg	120
V, $Å^3$	1028.4(4)
r, g/cm^3	1.290
Absorption coefficient, µ (Mo) mm	0.092
Crystal dimensions, mm	0.3×0.1×0.1
Range of θ, deg	2.18-30.01
Total number of reflections	2984
Number of reflections [I > 2σ(I)]	2194
R-factor [I > 2σ(I)]	R1 = 0.0440, wR2 = 0.0620
R-factor (whole dataset)	R1 = 0.0960, wR2 = 0.1035

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

Atom	x	y	z	U_{eq}
O1	7703 (2)	2516(2)	153(2)	39(1)
O2	12666(2)	4406(2)	277(2)	42(1)
O3	12980(2)	5263(2)	-1753(2)	49(1)
O4	8567(2)	3563(2)	-2202(2)	42(1)
C1	10195(3)	1342(3)	3838(3)	34(1)
C2	9257(3)	1141(3)	4985(3)	40(1)
C3	7854(3)	1049(3)	4479(3)	41(1)
C4	8199(3)	2238(3)	3514(2)	33(1)
C5	8295(3)	2002(3)	2255(2)	31(1)
C6	8815(3)	3035(3)	1142(2)	32(1)
C7	10129(2)	3143(3)	432(2)	29(1)
C8	11516(2)	3747(3)	1250(2)	32(1)
C9	11829(3)	2720(3)	2044(3)	34(1)
C10	11327(3)	2561(3)	3432(2)	32(1)
C11	10624(3)	4192(3)	-736(2)	30(1)
C12	12201(3)	4697(3)	-835(3)	36(1)
C13	9919(3)	3634(3)	-2063(2)	33(1)
C14	12120(4)	3890(3)	4265(3)	45(1)
C15	8593(4)	3654(4)	4113(4)	53(1)

The packing and intermolecular contacts in **1** indicate the presence of an O...H–O H-bond. The crystal contains a H-bond between molecules along the 3_2 screw axis. This forms an infinite chain along the *c* axis. The geometric parameters of the intermolecular H-bond are: O1...O4, 2.75 Å; O4...H–O1, 1.97 Å; O1–H...O4, 171.5°.

Thus, XSA unambigusouly established the crystal and molecular structure of the new lactone that has the structure 1(10),4(5)-dien-6α-hydroxy-13α-hydroxymethylene-6β,8β,11β(H),5α,7α(H)-germacr-8,12-olide.

EXPERIMENTAL

IR spectra were recorded on a Perkin—Elmer System 2000 IR-Fourier spectrometer (KBr pellets). Mass spectra were recorded on a Cratos GB MS-25 RF GC—MS. PMR spectra were recorded on a Tesla BS 567A spectrometer at working frequency 100 MHz with internal standard HMDS. Chemical shifts are given in the δ-scale.

Isolation of 13α-Hydroxymethylenedeacetyllaurenobiolide (1). Polar fractions (21-25) obtained during isolation of flavonoids [1] were combined (1.57 g) and rechromatographed over KSK silica gel (1:40, compound—carrier). Elution by hexane—ethylacetate (1:2) gave **1** as colorless needle-like crystals with mp 153-154°C and composition $C_{15}H_{22}O_4$.

X-ray Structure Analysis. Single crystals of **1** were grown from ethanol, are transparent, and are shaped as elongated prisms. Unit-cell constants and intensities of reflections were determined on a Smart 1000 CCD Bruker multichannel diffractometer (ω-scanning in 0.3° steps along ω, 10 s exposure per frame). We used Mo Kα-radiation (graphite monochromator). The resulting dataset was processed using SAINT [12]. Absorption corrections were made using the program SADABS [13].

Table 2 contains the principal crystallographic data and conditions for the XSA.

The structure of **1** was solved using direct methods and refined by isotropic—anisotropic least-squares methods using the program SHELXTL PLUS 5.0 [14]. H atoms, with the exception of the hydroxyl H, which was found from a difference electron-density synthesis, were assigned geometrically in fixed positions. Table 3 lists coordinates of nonhydrogen atoms in **1**.

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