

TOURNEFORIN, A NOVEL EUDESMANOLIDE FROM *Artemisia tournefortiana*

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A novel eudesmane sesquiterpene lactone, the structure of which was established by XSA, was isolated from Artemisia tournefortiana.

Key words: *Artemisia tournefortiana*, sesquiterpene lactone, eudesmanolide, tourneforin, XSA, NMR.

In continuation of systematic research on representatives of the Kazakhstan population of *Artemisia* [1, 2], we studied for the first time the chemistry of *A. tournefortiana* Rchb.

The aerial part was collected in July 2005 in Shetsk Region of Karaganda District during budding. A new sesquiterpene lactone, which we called tourneforin, was isolated. According to high-resolution mass spectrometry, its formula was C₁₅H₁₈O₃. The IR spectrum of the isolated compound had absorption bands consistent with the presence of a butenolide ring, double bonds, and an unconjugated carbonyl group. The presence of the last was confirmed by a resonance for C-9 at 213.25 ppm in the ¹³C NMR spectrum [3].

The PMR spectrum showed two 3H singlets for an angular methyl on C-10 at 1.17 ppm and an olefinic methyl on C-4 at 1.86 ppm. These indicated that there was a eudesmane carbon skeleton [4]. There were also two symmetric doublets at 5.65 and 6.35 ppm with SSCC 2.5 Hz from a C-11 exomethylene, a multiplet for methine proton H-7 centered at 3.65 ppm, and a doublet for lactone proton H-6 at 5.75 ppm with SSCC 4.0 Hz. This suggested a lactone ring with the *cis*-orientation. Two resonances as a doublet of doublets at 2.42 ppm with J_{8a,8b} = 14.0 and J_{7,8a} = 3.0 Hz and at 2.75 ppm with J_{8a,8b} = 14.0 and J_{7,8b} = 7.5 Hz were assigned to C-8 protons. This indicated that vicinal protons were absent on C-9 and confirmed that C-9 was a ketone [3].

The stereochemical position of the C-10 methyl could not be determined from the PMR spectra. Therefore, we performed an x-ray structure analysis (XSA) and found that the structure of tourneforin was that shown in Fig. 1, 9-oxo-6 α (H),7 α (H)-eudesm-4(5),11(13)-dien-12,6-olide.

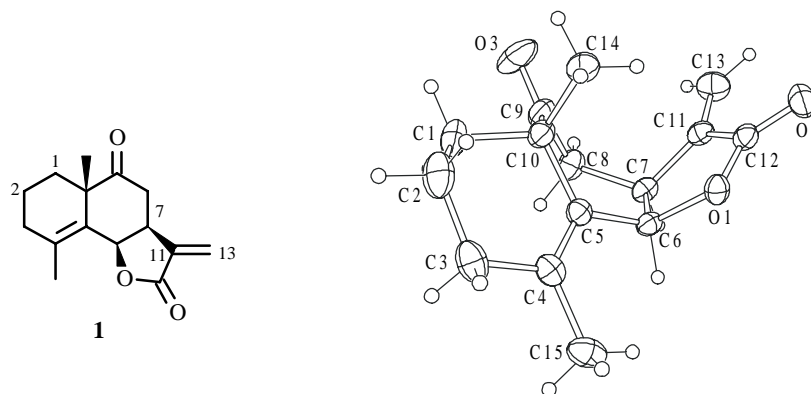
Bond lengths in **1** are within the normal range [5]. The *cis*-fused lactone ring is planar within a mean-square deviation of 0.036 Å of atoms from the plane. The conformation of the C5-C10 ring is close to a boat with atoms C5 and C8 deviating from the plane of the remaining atoms by 0.481(4) and 0.621(5) Å, respectively. Ring C1-C5,C10 is a distorted half-chair with C1 and C2 deviating by 0.515(6) and -0.230(6) Å. Intermolecular contacts include a slightly shortened [6] contact H...O for (C6)H...O2 of 2.56 Å. The Cambridge Structural Database [7] contains relatively few (a total of 11 compounds) structures of 6 α (H),7 α (H),10 β (C)-eudesman-12,6-olides. In general, these are derivatives of santonin [8-11] and eudesman-6,12-olides [12, 13].

We interpreted PMR and ¹³C NMR spectra of **1** (Table 1) using two-dimensional ¹H—¹H COSY and ¹³C—¹H COSY and COLOC spectra.

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TABLE 1. ^{13}C NMR and PMR Spectra of **1** (CDCl_3 , δ , ppm, TMS = 0)

C atom	δ_{C}	δ_{H}	Cross-peaks in ^{13}C - ^1H COLOC 2D spectrum (10 Hz)
1	34.07 t	1.53 m (H-1A); 1.58 m (H-1B)	3H-15; 2H-2
2	17.68 t	1.63 m (H-2A); 1.77 m (H-2B)	2H-3
3	32.24 t	2.13 m (2H)	3H-14
4	139.75 s	-	3H-14
5	128.19 s	-	3H-14; 3H-15; 2H-3
6	75.01 d	5.75 d (4.0)	H-9A; H-13B
7	37.38 d	3.65 m	-
8	40.79 t	2.42 dd (14.0, 3.0); 2.75 dd (14.0, 7.5)	-
9	213.25 s	-	3H-15; H-8A; H-8B; H-7
10	47.09 s	-	3H-15; H-6
11	137.89 s	-	H-8A
12	169.41 s	-	H-6; H-13B
13	123.92 t	5.56 (A) d (2.5); 6.35 (B) d (2.5)	-
14	17.68 q	1.17 (3H, s, Me-10)	-
15	24.50 q	1.86 (3H, s, Me-4)	-

Fig. 1. Molecular structure of **1**.

EXPERIMENTAL

Melting points were determined on a Boetius instrument. Optical rotation was measured (at 580 nm) on a Polamat A polarimeter. IR spectra in KBr disks were recorded on a Thermo Nicolet Avatar 360 instrument; NMR spectra in CDCl_3 , on a Bruker DRX-500 spectrometer (operating frequency 500.13 MHz for ^1H ; 125.76 MHz, ^{13}C) with TMS internal standard on the δ -scale. Column chromatography used KSK SiO_2 (<0.3 mm fraction). TLC used Sorbfil plates and aqueous KMnO_4 (1%) for development.

Isolation of 9-Oxo-6 α ,7 α (H)-eudesm-4,11(13)-dien-12,6-olide (1). Raw material (0.5 kg) was extracted by soaking in CHCl_3 (8 L) at 75°C. The extraction was repeated four times (4×8 L). The combined extracts were filtered. Solvent was removed in vacuo. The resulting dry solid (0.15 kg) was treated three times with $\text{EtOH}:\text{H}_2\text{O}$ (2:1) at 70°C. Precipitated ballast substances were separated by decantation. The solution was filtered. The filtrate was extracted with CHCl_3 (4×0.5 L). The CHCl_3 extracts were combined and evaporated to dryness to afford total substances (59 g), chromatography of which over SiO_2 (petroleum ether and a petroleum ether: EtOAc gradient with the latter increasing from 0 to 20%) afforded **1** (2 g, 0.4%) as colorless crystals, mp 170-172°C, $[\alpha]_{\text{D}}^{25} +29.4^\circ$ (c 0.68, CHCl_3).

Mass spectrum (EI, 70 eV, m/z , I_{rel} , %): 246 (97) $[\text{M}]^+$, 131 (50), 203 (100), 159 (19), 157 (42), 137 (22), 131 (45), 109 (27), 105 (23), 93 (23), $\text{C}_{15}\text{H}_{18}\text{O}_3$.

IR spectrum (KBr, ν_{max} , cm^{-1}): 1740 (γ -lactone C=O); 1716 (C=O); 1658, 1656, 1319, 1278, 1264, 1214, 1145, 953, 863, 818, 677. Table 1 lists the ^{13}C NMR and PMR spectra.

The XSA was performed on a Bruker P4 diffractometer (Mo K α -radiation, graphite monochromator, $\theta/2\theta$ -scanning) at room temperature. Absorption corrections were applied empirically. The structure was solved by direct methods using the SHELXS-97 program and was refined by anisotropic least-squares methods using the SHELXL-97 program. Positions of H atoms were found geometrically and refined using the rider model. Crystallographic data: rhombic system, space group $P2_12_12_1$, $a = 6.3648(6)$, $b = 9.2590(8)$, $c = 21.795(2)$ Å, $V = 1284.4(2)$ Å³, $C_{15}H_{18}O_3$, $Z = 4$, $d_{\text{calc}} = 1.274$ g/cm³, $\mu = 0.88$ cm⁻¹, transmission $T_{\text{min}}/T_{\text{max}} = 0.913/0.979$, scanning range $2\theta < 52^\circ$, size $0.17 \times 0.2 \times 0.9$ mm. Refinement parameters: $wR_2 = 0.1198$, $S = 1.024$ (over all 1435 reflections), $R_1 = 0.0410$ [$1192 I \geq 2\sigma(I)$], 163 refined parameters. The absolute configuration of the studied molecule could not be established because of the lack of a heavy atom in it. The relative configuration of all asymmetric centers in **1** is shown although it apparently corresponds to the absolute one because of the $\alpha(H)$ - configuration at C-7.

The results were deposited in the Cambridge Crystallographic Data Centre (No. CCDC 645287) and can be obtained without charge from the address <http://www.ccdc.cam.ac.uk/cgi-bin/catreq.cgi>.

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