

GRACILIN - A NEW SESQUITERPENE LACTONE FROM *Artemisia gracilescens*

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By extraction with acetone and chromatography of the resin on a column of type KSK silica gel the epigeal part of *Artemisia gracilescens* has yielded the new sesquiterpene lactone gracilin, for which the structure of 1-oxo-6 β , 7 α , 11 β (H)-eudesm-4(5)-en-6,12-olide is proposed.

The isolation from *Artemisia gracilescens* Krasch. et Iljin. of α -santonin, tauremisin, and artemisin has been reported previously [1, 2].

The extraction with acetone, followed by chromatography of the resulting resin in a column of type KSK silica gel at a ratio of total material to support of 1:20 and elution by hexane-CCl₄ (1:1), of the anthodia, leaves, and small stems of *A. gracilescens* gathered in the flowering phase in the valley of the River Tundyk, Karaganda province, Kazakh SSR, has yielded a crystalline substance (I) with the composition C₁₅H₂₀O₃, mp 104-105°C (hexane), $[\alpha]_D^{20} = 108.6^\circ$ (c 0.019; ethanol), which has proved to be a new sesquiterpene lactone and has been called gracilin. The IR spectrum of (I) has absorption bands in the regions of 1780 cm⁻¹ (C=O of a γ -lactone) and 1718 cm⁻¹ (keto group). In the PMR spectrum of (I) a doublet at 1.21 ppm (3 H, J = 7 Hz) relates to a methyl group at C11, and singlets at 1.30 and 1.94 ppm (3 H each) to an angular methyl group and a methyl group at a double bond, respectively. Because of the presence of the keto group in the vicinal position, the signal of the angular methyl group is shifted downfield. A doublet at 4.57 ppm (1 H, J = 10.5 Hz) relates to a lactone proton. The nature of the splitting of the signal of the lactone proton permitted the assumption that the lactone ring was located at C6 and C7, and the double bond at C4 and C5. From its PMR spectrum, the substance isolated was assigned to sesquiterpene lactones of the eudesmane type in the structure of which there is a keto group and a double bond. A comparison of the PMR spectrum of the substance isolated and of taurin, finitin, deoxy- Ψ -santonin [3, 4] showed an analogy of the structures of these eudesmanolides. However, the difference in their physicochemical constants permits us to discuss their stereoisomerism.

The structure of gracilin has been studied by x-ray structural analysis. Its oxime derivative, with the composition C₁₅H₂₁O₃N, mp 189-191°C (from alcohol) was obtained, and the IR spectrum of this showed absorption bands at (cm⁻¹) 3360 (OH group), 1780 (C=O of a γ -lactone), and 1680 (C=N-).

The structure of the gracilin oxime molecule is shown in Fig. 1. The averaged lengths of the bonds (Fig. 1) and the valence angles (Table 1) in the two independent molecules are the usual ones within the limits of error [5]. The lactone ring and the six-membered carbocycle B are trans-linked (the H6C6C7H7 torsional angle = -160(1)°). The oxime group at C1 and the methyl group at C11 have the α -orientation. A comparison of the intracyclic torsional angles in the two crystallographically independent molecules (1 and 2) (Table 2) shows that the conformations of rings A and C in them differ somewhat. Thus, the conformation of the six-membered carbocycle A in (1) and (2) is considerably distorted from the ideal half-chair and sofa shapes, but in (1) the conformation is closer to a distorted 1 α ,2 β -half-chair ($\Delta C_2^{4,5} = 10.1^\circ$ and $\Delta C_5^5 = 14.7^\circ$), while in (2) it is closer to a distorted sofa ($\Delta C_5^5 = 10.7^\circ$ and $\Delta C_2^{4,5} = 19.0^\circ$). The conformation of ring B in each of (1) and (2) is the chair conformation, the difference in the values of the corresponding torsional angles in the ring not exceeding 3.3°.

The chair conformation is somewhat distorted, the greatest disturbance of the symmetry of the ring being observed in the m plane passing through the C5 and C8 atoms ($\Delta C_5^5 = 11.5$

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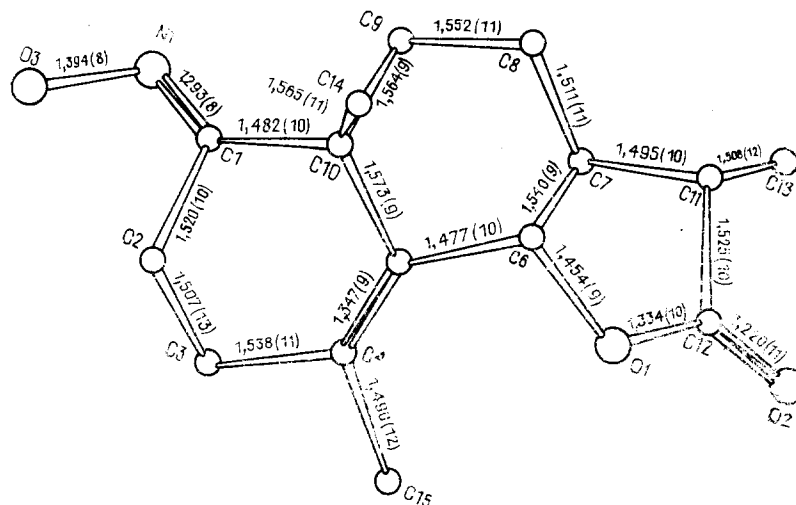


TABLE 2. Intracyclic Torsional Angles φ (degrees)

Angle	φ		Angle	φ	
	molec. A	molec. B		molec. A	molec. B
C1C2C3C4	46,5(8)	53,8(8)	C8C9C10C5	-50,9(8)	-50,2(7)
C2C3C4C5	-18,6(8)	-21,8(8)	C9C10C5C4	52,0(7)	53,4(7)
C3C4C5C10	-3,5(8)	-5,6(8)	C10C5C6C7	-61,5(7)	-63,9(7)
C4C5C10C1	-6,2(8)	-1,2(7)	C6C7C11C12	31,6(8)	33,3(8)
C5C10C1C2	33,4(8)	35,4(8)	C7C11C12O1	-15,5(8)	-20,4(7)
C10C1C2C3	-60,8(8)	-64,4(7)	C11C12O1C6	-9,5(7)	-2,4(7)
C5C6C7C8	67,8(9)	66,7(7)	C12O1C6C7	29,6(8)	23,8(8)
C6C7C8C9	-60,5(8)	-57,6(7)	O1C6C7C11	-37,8(8)	-35,7(7)
C7C8C9C10	56,2(8)	52,9(7)			

EXPERIMENTAL

The individuality of substances was checked by thin-layer chromatography (TLC) on Silufol plates in the hexane-ether (1:4) system. The revealing agent was 0.5% KMnO_4 in 0.5% H_2SO_4 . For analysis, the substance was dried in a vacuum pistol containing P_2O_5 over ethanol for 6-8 h. Specific optical rotations were measured on a SM-2 polarimeter in a tube 1 dm long with a volume of 10 ml.

IR spectra (tablets with KBr) were taken on a UR-20 spectrophotometer, and PMR spectra on a Bruker WP SY instrument (200 MHz) in deuteriochloroform with 0 - TMS, δ scale. The results of the elementary analyses of the compounds corresponded to the calculated figures.

Isolation of Gracilin. The anthodia and leaves of *A. gracilis* collected in the flowering phase in the valley of the R. Tundyk, Karaganda province, Kazakh SSR (5.5 kg) were exhaustively extracted with acetone. After evaporation of the solvent, 188 g of resin was obtained. Of this, 72 g was chromatographed on a column of type KSK silica gel in a ratio of total material to support of 1:20. When the column was eluted with hexane- CCl_4 (1:1), the eluate deposited a white amorphous substance. After three recrystallizations from hot hexane, a colorless crystalline substance was obtained with the composition $\text{C}_{15}\text{H}_{20}\text{O}_3$, mp 104-105°C, $[\alpha]_D^{20} - 108.6^\circ$ (c 0.019; EtOH). In TLC, a single spot was observed, with R_f 0.55. IR spectrum (cm^{-1}): 2990, 2960, 2930, 2850, 1780, 1718, 1450, 1370, 1350, 1320, 1310, 1280, 1250, 1190, 1150, 1120, 1050, 980, 910. PMR spectrum (multiplicity, ppm): 1.21 (3 H, d, $J = 7$ Hz); 1.30 (3 H, s); 1.94 (3 H, s); 4.57 (1 H, d, $J = 10.5$ Hz).

Synthesis of Gracilin Oxime. Gracilin (64 mg) was dissolved in absolute ethanol with heating, and then hydroxylamine (38 mg) and sodium acetate (44 mg) were added. The reaction mixture was heated at 70°C for 5 h and was then left overnight. The product was extracted with chloroform (3 \times 60 ml). The chloroform extract was washed twice with water. The solvent was distilled off under vacuum, leaving a crystalline mass. Recrystallization from hot ether gave a colorless crystalline substance with the composition $\text{C}_{15}\text{H}_{21}\text{O}_3\text{N}$, mp 189-191°C, R_f 0.60. IR spectrum (cm^{-1}): 3360, 3140, 2945, 2985, 1780, 1680, 1465, 1240, 1200, 1140.

TABLE 3. Coordinates of the Nonhydrogen Atoms ($\times 10^4$) of the Two Crystallographically Independent Molecules of Gracilin Oxime

Atom	x	y	z	x	y	z
Molecule 1			Molecule 2			
C1	8902(7)	2015(9)	2866(3)	7045(7)	2390(10)	-0003(3)
C2	10442(8)	2216(13)	3270(4)	5565(7)	1711(13)	-0301(4)
C3	10845(7)	0570(12)	3634(4)	5790(9)	0196(12)	-0727(4)
C4	9656(7)	-0132(10)	3997(3)	6832(7)	0611(9)	-1288(3)
C5	8245(7)	0346(10)	3855(3)	7749(6)	1939(9)	-1196(3)
C6	6966(7)	-0290(10)	4191(3)	8764(7)	2509(9)	-1662(3)
C7	5785(7)	-1111(11)	3675(3)	10361(7)	2265(8)	-1351(3)
C8	5117(7)	0161(13)	3155(4)	10687(7)	3415(9)	-0730(3)
C9	6387(7)	0870(11)	2767(3)	9635(7)	3017(9)	-0215(3)
C10	7698(7)	1632(9)	3257(3)	7968(7)	3031(9)	-0527(3)
C11	4839(8)	-1041(10)	4155(4)	11159(7)	2436(10)	-1964(3)
C12	6008(8)	-2305(11)	4794(4)	10046(8)	1702(10)	-2522(3)
C13	4015(10)	-3184(13)	3869(5)	12643(7)	1664(12)	-1927(4)
C14	7238(10)	3303(11)	3585(4)	7447(8)	4870(10)	-0696(4)
C15	10222(9)	-1402(14)	4550(5)	6603(9)	-0592(12)	-1858(4)
O1	7235(5)	-1379(9)	4746(3)	8706(5)	1703(8)	-2348(2)
O2	5117(7)	-3233(11)	5263(3)	10246(6)	1171(9)	-3106(2)
O3	9795(6)	2602(9)	1856(3)	6564(5)	1730(9)	1056(2)
N1	8623(7)	2156(8)	2183(3)	7558(5)	2373(8)	0630(3)

The x-ray spectral experiment was performed on Syntex P2₁ automatic four-circle diffractometer (λ MoK α , graphite monochromator, $\theta/2\theta$ scanning, $2\theta \leq 50^\circ\text{C}$). The crystals were monoclinic, $a = 9.206$ (3), $b = 7.987$ (2), $c = 19.487$ (7) Å, $\beta = 97.89^\circ$, $d_{\text{calc}} = 1.23$ g/cm³, $Z = 4$ (C₁₅H₂₂NO₃), sp. gr. P2₁.

In the calculations we used 2362 reflections with $I \geq 2\sigma$. The structure was interpreted by the direct method using the MULTAN-78 program [6] and was refined by the full-matrix MLS in the anisotropic approximation for nonhydrogen atoms by the SHELX-76 program [7]. The H atoms were assigned geometrically. All the calculations were performed on an ES-1022 computer. The final divergence factors were $R = 0.081$ and $R_w = 0.092$. The coordinates of the non-hydrogen atoms are given in Table 3.

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SYNTHESIS OF BICYCLOHOMOFARNESANE DERIVATIVES FROM BIS(8 α ,13-EPOXY-14,15-BISNORLABD-12-EN-12-YL)METHANE — A PRODUCT OF THE OZONOLYSIS OF SCLAREOL

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A seven-stage method of obtaining a new odoriferous product with a strong amber odor analogous to ambroxide from sclareol has been developed. It includes odoriferous oxide compounds of the tetrahydrofuran series: (VIII), (IX), (XIII), and (XIV). The key stages in the synthesis of this product are the ozonolytic cleavage of sclareol with the formation of bis(8 α ,13-epoxy-14,15-bisnorlabd-12-en-12-yl)methane (II), its ozonolysis to bis(8 α -acetyl-12-oxo-13,14,15,16-tetranorlabdan-12-yl)methane (III), and the alkaline cleavage of the latter.

Previously, in the investigation of the ozonolysis of sclareol (I) we [1] established that when the reaction was performed in methanol and the ozonolysis product was treated with anhydrous ammonium chloride an 80% yield was obtained of bis(8 α ,13-epoxy-14,15-bisnorlabd-12-en-12-yl)methane (II)

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