MOLECULAR AND CRYSTAL STRUCTURE OF THE SESQUITERPENE LACTONE KETOPELENOLIDE A

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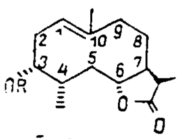
UCD 547.992:547.37+548.737

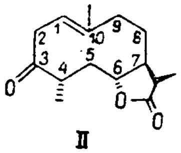
The boat-boat conformation of the germacrane ring of ketopelenolide A has been established by x-ray structural analysis.

In an investigation of the plant Artemisia absinthinium L. we isolated the known sesqiterpene germacrane lactones hydroxypelenolide (I) and ketopelenolides A (II) and B [1, 2]. As compared with the cyclodeca-1(10), 4(5)-diene germacrolides, these compounds lack the characteristic double bond in the 4(5) position. It has been shown by the x-ray structural method that, in spite of this absence, hydroxypelenolide adopts a chair-boat conformation (according to the structure of hydroxypelenolide p-bromobenzoate (Ia) [3]) — one of the four possible conformations: chair-chair (A), chair-boat (C), and boat-boat of two types (B and D) [4, 5].



I. R=H

Ia. R= p-COC_6H_4Br

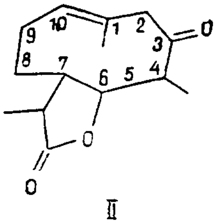


II

For this reason the conformation of the ten-membered ring in the molecule of (II) relative to those observed in other related germacrolides with a keto group in the C3 position appeared of interest.

An x-ray structural investigation has shown that the conformation of the germacrane ring in the molecule of (II) differs from the four possible ones shown above. The spatial structure of the (II) molecule is shown in Fig. 1 in a projection of the b,c plane; Table 1 gives the intracyclic torsion angles determining the conformation of the ten-membered ring in the (II) molecule and also literature examples for each conformation: A — sachosin (chair-chair); C — chimganidin (chair-boat); D — hallerol (boat-boat); and B — mucrin (boat-boat) [6-9]. A comparison of the torsion angles of the germacrane ring of the (II) molecule with those given in the literature for the four possible conformations shows an absence of symbaticity of these magnitudes.

Thus, the inclusion of a trigonal atom in the C-3 position (C=O group) leads to an appreciable change in the conformation of the whole germacrane ring. However, if a model of the molecule is inverted and the lactone ring is shifted into the 4(5) position, then the structure of (II) has a form almost identical with the B-form (boat-boat) conformation of laurenobiolide [10].



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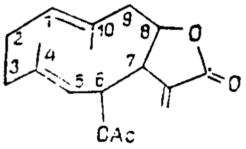

laurenobiolide

Institute of the Chemistry of Plant Substances, Uzbek SSR Academy of Science, Tashkent. Translated from Khimiya Prirodnykh Soedinenii, No. 3, pp. 342-346, May-June, 1990. Original article submitted July 6, 1989; revision submitted October 2, 1989.

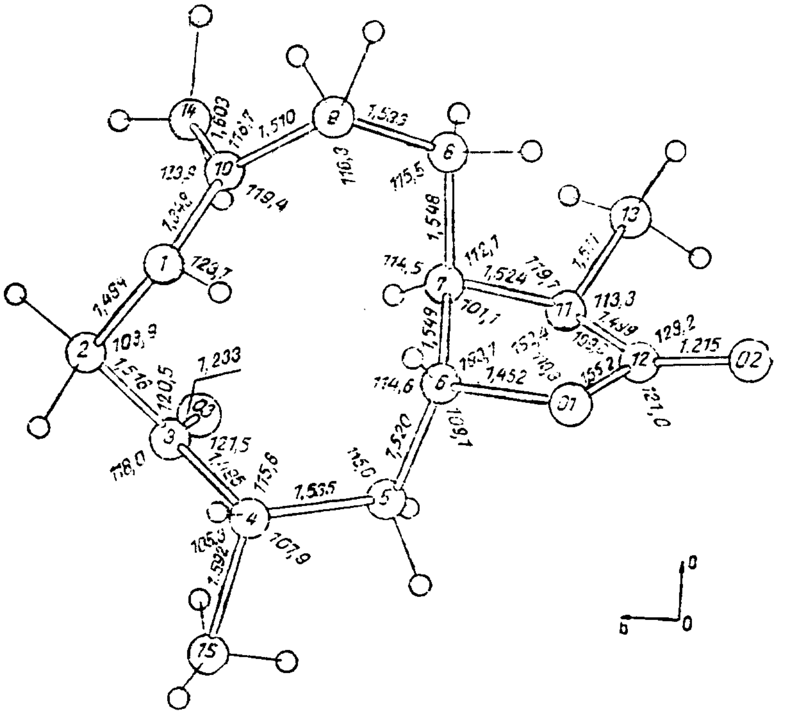

Fig. 1. Structure of the ketopelenolide A molecule.

TABLE 1. Intracyclic Torsion Angles in the Molecules of Ketopelenolide A (I) and (VI), Saschosin (II), Chimganidin (III), Hallerol (IV), and Mucrin (V)*

Angle	I	II	III	IV	V	VI*	Angle†
C1C2C3C4	−65.4	43.6	−46,2	−37,0	40,1	39,2	C7C8C9C10
C2C3C4C5	22.4	−90 6	86,1	94,0	34,3	59,8	C6C7C8C9
C3C4C5C6	−69.9	146,8	−168.2	−158.0	−170,5	−154.3	C5C6C7C8
C4C5C6C7	92,2	−108,3	96,5	90,2	114,3	92,2	C4C5C6C7
C5C6C7C8	−154,3	102.0	40,8	56.0	−46,2	−69,9	C3C4C5C6
C6C7C8C9	59 8	−116,9	−130.2	−116.2	110,6	122,4	C2C3C4C5
C7C8C9C10	39.2	83,4	65.8	78,7	−68 7	−65,4	C1C2C3C4
C8C9C10C1	−107.4	−89.9	60,0	−92 4	−62,1	−79.8	C10C1C2C3
C9C10C1C2	157,0	168,8	−167 0	162.7	149,5	157,0	C9C10C1C2
C10C1C2C3	−79.5	−115,0	110,6	−71,8	−114.7	−107,4	C8C9C10C1

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*In this table, Roman numerals do not correspond with those found in the text — Publisher.

†For the transformed molecule of (II) (see text).

This visual closeness is confirmed by the numerical values of the torsion angles, i.e., the transformed values of the torsion angles of the (II) molecule are symbatic with the angles observed in mucrin (compare columns 5 and 6 in Table 1). Consequently, it may be assumed that, without taking the position of the lactone ring into account, the germacrane ring in ketopelenolide A has the boat-boat conformation (B-form).

The lactone ring, trans-linked with the germacrane ring at the C6-C7 bond has an envelope conformation with symmetry C_s: the departure of the C7 atom from the plane of the other four atoms of the ring amounts to 0.562 A. The methyl group at C11 has the β-orientation.

The values of the bond lengths and valence angles in the (II) molecule (see Fig. 1) are the usual ones (the mean square deviations for the bond lengths and valence angles are not more than 0.009 Å and 0.6°, respectively).

TABLE 2. Coordinates of the Atoms (× 10^4; for H, × 10^3) in the Structure of (II)

Atom	*x*	*y*	*z*	Atom	*x*	*y*	*z*
C1	6283(11)	6284(4)	8693(3)	H2.2	378	750	889
C2	4979(15)	6908(4)	9231(4)	H4	703	575	1015
C3	3676(11)	6175(4)	9708(3)	H5.1	580	410	1056
C4	5091(11)	5509(4)	10177(3)	H5.2	279	425	1005
C5	4705(11)	4410(4)	10050(3)	H6	756	425	917
C6	5633(9)	4021(4)	9321(3)	H7	265	450	879
C7	3820(8)	4020(3)	8686(2)	H8.1	601	339	786
C8	4907(11)	4075(4)	7905(3)	H8.2	300	400	766
C9	6401(11)	4985(5)	7748(3)	H9.1	692	475	721
C10	5294(10)	5879(4)	8092(3)	H9.2	817	534	738
C11	2572(8)	3050(3)	8821(2)	H11	132	300	936
C12	4502(10)	2417(3)	9116(3)	H13.1	6	310	814
C13	1209(11)	2573(4)	8203(3)	H13.2	298	225	784
C14	2984(10)	6199(4)	7775(3)	H13.3	22	200	850
C15	4337(16)	5753(5)	11001(3)	H14.1	201	675	808
O1	6213(6)	2935(2)	9404(2)	H14.2	224	613	718
O2	4695(8)	1532(2)	9101(2)	H14.3	113	589	823
O3	1529(7)	6093(3)	9662(2)	H15.1	278	515	1103
H1	795	587	884	H15.2	589	533	1067
H2.1	613	725	968	H15.3	580	600	1129

EXPERIMENTAL

Colorless crystals of (II) in the form of elongated prisms were grown from alcohol and were first investigated by the photo method.

The space group and parameters of the elementary cell were determined from precession x-ray diagrams. These parameters were subsequently refined on a Syntex $P2_1$ diffractometer using CuK_α radiation: a = 5.704 (1), b = 13.661 (8), c = 18.133 (7) A; d_{calc} = 1.182 g/cm^3; space group $P2_12_12_1$; Z = 4.

The intensities of the reflections were measured on the same diffractometer. In the primary treatment of the results, weak reflections with $I \leq 2\sigma$ were rejected. The final set contained 971 independent nonzero reflections. The structure was determined by the direct method using a program of the Rentgen-75 complex [11] in the automatic regime. From the best phase variant an E-series was constructed in which all 18 nonhydrogen atoms were localized (R = 0.30). The structure was refined first by successive approximations of electron density (ED) series (R = 0.25) and by the method of least squares (MLS) in the isotropic approximation (R = 0.17) and in a subsequent full-matrix MLS with allowance for the anisotropic temperature vibrations of the nonhydrogen atoms to R = 0.10. At this stage, a ED difference synthesis was calculated and all the H atoms were localized. The final value of the divergence factor after four iterations of MLS taking the H atoms into account was 0.075. The coordinates of the atoms are given in Table 2.

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