CRYSTAL AND MOLECULAR STRUCTURES OF THE SESQUITERPENE LACTONE AJAFININ

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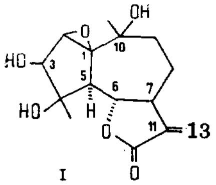
An x-ray structural analysis has been made with the aim of reliably determining the spatial structure of the sesquiterpene lactone ajafinin. It has been established that it has the structure and configuration of 1,2-α-epoxy-3α,4β,10β-trihydroxy-5,6β(H),7α(H)-guai-11(13)-en-6,12-olide.

On the basis of chemical transformations and spectral characteristics [1, 2], a guaiane structure has been proposed for the sesquiterpene lactone ajafinin, $C_{12}H_{20}O_6$, isolated from *Ajania fastigiata* Poljak., family Compositae, [1]. In addition, a double-resonance PMR experiment has shown the relative configurations of the C-5, C-6, and C-7 centers [2]. However, it was difficult to determine the remaining stereochemical aspects of the structure of ajafinin (the conformations of the rings, the linkage of rings A/B, and the configurations of the other five asymmetric centers of the molecule), and we have therefore performed an x-ray structural investigation.



I

Figure 1 shows the structure of one of the molecules of the sesquiterpene lactone ajafinin (I) in projection on the plane of the b,c axes. Lactone (I) crystallizes with two molecules in the independent part of the elementary cell, forming hydrates in a ratio of 1:1. The crystallographically independent but chemically equivalent molecules of ajafinin (Ia and Ib) have the same conformation of the rings and orientation of the substituents. The orientation of the substituents in the three asymmetric centers C5, C6, and C7, i.e., their relative configuration, agrees with the orientation indicated by PMR spectroscopy. The orientation of the other substituents is as follows: the oxygen atom in the epoxide ring adjacent to the 1,2-position and the hydroxy group in position 3 are α and the hydroxy groups in positions 4 and 10 are β (see Fig. 1). Thus, ajafinin is represented by the structure 1,2α-epoxy-3α,4β,10β-trihydroxy-5,6β(H),7α(H)-guai-11(13)-en-6,12-olide. The linkage of rings A/B is cis and that of rings B/C trans. A similar linkage of these three rings is observed in the dimeric lactones anabsin [3], absinthin [4], and artelein [5], the structures of which were established by x-ray structural analysis. However, in the diepoxidic monolactone chrysartemin B the linkage of these rings is trans [6]. The conformations of the rings can be judged from the figures in Table 1, which gives the main planes of fragments 1a and 1b of the molecules and the deviations of the atoms from them. It can be seen from Table 1 that in both molecules the five-membered rings A and C have the envelope conformation and the cyclopentane rings B the chair conformation.

The geometry (the bond lengths and the sizes of the valence angle) of the epoxide ring in (Ia) and (Ib) are close to those observed in the carotane ester lapidolin [7]. A comparative analysis of the interatomic distances and the valence angles of the molecules (Ia) and (Ib) revealed no anomalous deviations and showed their good agreement (average values) with the standard values (Table 2) [8].

The packing of the molecules is shown in Fig. 2 as a projection on the plane of the b,c axes. In the crystal an intermolecular H-bond of the O—H...O type is formed. The H atoms

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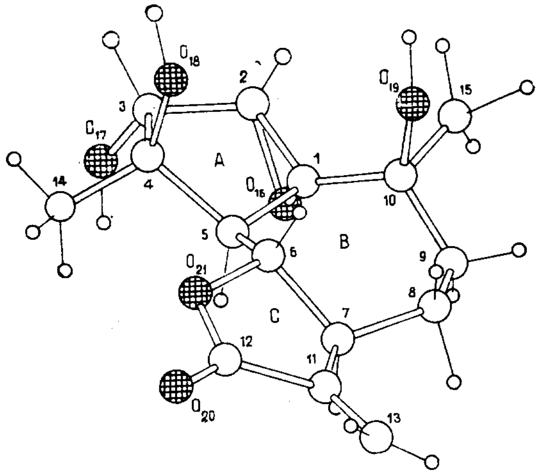

Fig. 1. Structure of one of the molecules of ajafinin (the missing H atoms have been inserted from geometric considerations).

TABLE 1. Main Planes of the Fragments of the Ajafinin Molecule and the Deviations of the Atoms (δ, Å) from These Planes

Plane	Atom	δ_{Ia}	δ_{Ib}
Ring *A*	C1	0,003	0,008
	C2	−0,003	−0,008
	C3	0,002	0,005
	C4	0,526	0,512
	C5	−0,002	−0,005
Ring *B*	C5*	−1,092	−1,173
	C6	0,027	0,006
	C7	−0,032	−0,007
	C8*	0,711	0,683
	C9	0,033	0,007
	C10	−0,027	−0,006
	C1*	−0,969	−1,034
Ring *C*	C6	0,027	0,030
	C7*	0,497	0,476
	C11	−0,027	−0,030
	C12	0,046	0,052
	O21	−0,046	−0,052

*Atoms not included in the calculation of the equations of the planes.

found experimentally permit the sequence of formation of H bonds to be traced. The hydroxy groups in positions 10 of the (Ia) molecules are close to the OH groups in positions 4 and 10 of the (Ib) molecules ($O19_{Ia}\ldots O18_{Ib}$ distance 2.90 Å, and $O19_{Ia}\ldots O19_{Ib}$ distance 2.81 Å), which leads to the formation of a backbone. One molecule of water of crystallization binds these backbones through a H-bond along a 2_1 screw axis (along the c axis), and a second molecule of water along the translation axis b.

EXPERIMENTAL

Single crystals of lactone (I) grown from ethyl acetate solution had the form of elongated prisms. The space group and the parameters of the elementary cell were established from precession photographs and were refined on a Syntex P2 diffractometer (Institute of Bioorganic Chemistry of the Academy of Sciences of the Uzbek SSR) using CuK_α radiation: a = 6.814(4), b = 14.015(6), c = 16.317(8), Å, γ = 103.98(4)°, d_{calc} = 1.254 g/cm³; space group $P2_1$. A three-dimensional set of intensities was obtained on the diffractometer mentioned, and in the calculations 2156 structural factors exceeding 2σ were used.

TABLE 2. Interatomic Distances (r, Å) and Valence Angles (ω, deg) of the Ajafinin Molecule

Distance	R_{Ia}	R_{Ib}	Angle	ω_{Ia}	ω_{Ib}	Angle	ω_{Ia}	ω_{Ib}
C1—C2	1,494(7)	1,486(7)	C2—C1—C5	106,1	106,4	C5—C6—O21	108,5	108,5
C1—C5	1,556(7)	1,557(6)	C2—C1—C10	122,6	123,0	C7—C6—O21	104,3	104,6
C1—C10	1,497(8)	1,516(7)	C2—C1—O16	59,3	59,2	C6—C7—C8	113,0	115,4
C1—O16	1,475(7)	1,44(2)	C5—C1—C10	126,3	125,7	C6—C7—C11	100,8	100,3
C2—C3	1,516(9)	1,420(8)	C5—C1—O16	108,2	103,4	C8—C7—C11	116,3	114,6
C2—O16	1,469(9)	1,450(7)	C10—C1—O16	114,9	114,9	C7—C8—C9	112,4	113,3
C3—C4	1,533(9)	1,535(7)	C1—C2—C3	109,8	109,5	C8—C9—C10	119,7	118,0
C3—O17	1,424(9)	1,435(7)	C1—C2—O16	59,7	59,1	C1—C10—C9	116,3	113,5
C4—C5	1,564(9)	1,553(7)	C3—C2—O16	110,3	110,8	C1—C10—C15	110,6	110,5
C4—C14	1,494(10)	1,500(7)	C2—C3—C4	104,3	104,6	C1—C10—O19	106,2	107,7
C4—O18	1,443(9)	1,448(7)	C2—C3—O17	112,3	110,6	C9—C10—C15	109,6	109,5
C5—C6	1,513(9)	1,531(6)	C4—C3—O17	114,4	113,9	C9—C10—O19	106,3	107,3
C6—C7	1,539(9)	1,541(7)	C3—C4—C5	104,1	104,3	C15—C10—O19	107,4	108,2
C6—O21	1,455(6)	1,462(5)	C3—C4—C14	112,1	113,4	C7—C11—C12	106,7	105,4
C7—C8	1,526(9)	1,499(7)	C3—C4—O18	103,6	104,0	C7—C11—C13	129,3	130,7
C7 C11	1,508(9)	1,523(7)	C5—C4—C14	116,1	115,2	C12—C11—C13	123,9	123,7
C8—C9	1,518(11)	1,526(8)	C5—C4—O18	108,9	106,3	C11—C12—O20	130,6	129,7
C9—C10	1,510(11)	1,517(7)	C14—C4—O18	111,2	112,6	C11—C12—O21	109,9	110,2
C10—C15	1,555(9)	1,522(7)	C1—C5—C4	103,9	103,9	O20—C12—O21	119,7	120,1
C10—O19	1,481(9)	1,456(6)	C1—C5—C6	113,5	112,5	C1—O16—C2	61,0	61,7
C11—C12	1,461(9)	1,484(8)	C4—C5—C6	113,5	114,8	C6—O21—C12	109,9	109,4
C11—C13	1,300(10)	1,308(7)	C5—C6—C7	113,8	112,4			
C12—O20	1,199(7)	1,216(6)						
C12—O21	1,348(7)	1,341(5)						

TABLE 3. Coordinates of the Atoms (×10^4 for H × 10^3) of the Ajafinin Molecules

Atom	Molecule Ia			Molecule Ib		
	x/a	y/b	z/c	x/a	y/b	z/c
C1	2559(9)	7536(5)	9427(5)	3715(7)	3735(4)	9972(3)
C2	1870(11)	7376(5)	8562(5)	5312(8)	4464(4)	9532(4)
C3	3382(12)	8006(5)	7931(5)	4801(8)	4446(4)	8624(4)
C4	5334(10)	8308(5)	8434(4)	2532(8)	3954(4)	8584(4)
C5	4580(10)	8389(4)	9331(4)	2165(7)	3220(4)	9313(3)
C6	6101(10)	8275(5)	10027(4)	—0007(7)	2951(4)	9637(3)
C7	5515(11)	8503(5)	10902(4)	—0370(8)	2091(4)	10252(3)
C8	4219(12)	7615(5)	11342(4)	0107(9)	2375(5)	1112(3)
C9	2129(12)	7275(5)	10966(5)	2346(9)	2835(4)	11278(3)
C10	1906(10)	6862(4)	10108(5)	3275(8)	3317(4)	10877(3)
C11	7571(11)	8940(5)	11267(4)	—2590(8)	1617(3)	10084(3)
C12	8935(11)	9298(5)	10583(4)	—2953(8)	1891(4)	9229(4)
C13	8121(17)	9019(7)	12032(5)	—4005(9)	1116(4)	10564(4)
C14	6751(14)	9205(7)	8148(5)	1862(9)	3512(4)	7763(3)
C15	—0306(11)	6259(6)	9971(6)	5189(9)	4122(5)	11335(4)
O16	0941(6)	8000(3)	9034(3)	5653(5)	3527(3)	9791(2)
O17	2683(7)	8809(3)	7660(3)	6041(6)	3938(3)	8170(2)
O18	6188(7)	7463(4)	8428(3)	1569(5)	4734(2)	8803(2)
O19	3230(5)	6166(3)	10060(2)	1824(5)	4422(2)	10954(2)
O20	10636(7)	9794(3)	10577(3)	—4405(6)	1585(3)	8787(3)
O21	7990(5)	8997(3)	9870(2)	—1370(5)	2583(2)	8955(2)
H2	076	677	838	388	505	479
H3	367	758	750	476	491	329
H5	443	915	946	201	248	917
H6	366	246	500	041	643	488
H7	480	907	079	019	858	518
H8	493	703	136			
H8′	382	771	187	024	156	129
H9	140	667	120	301	296	193
H9′				299	252	118
H13	226	133	751	357	906	614
H14	333	020	328	224	400	737
H15	003	641	942	465	539	697
H15′	053	428	522	334	508	622
H17	323	955	770	464	669	317
H18	172	540	866			
H19	276	591	970	213	515	094
O_w	9372(6)	5307(3)	7574(3)	—8156(7)	0249(4)	8852(4)
H_w	100	449	202	124	512	259

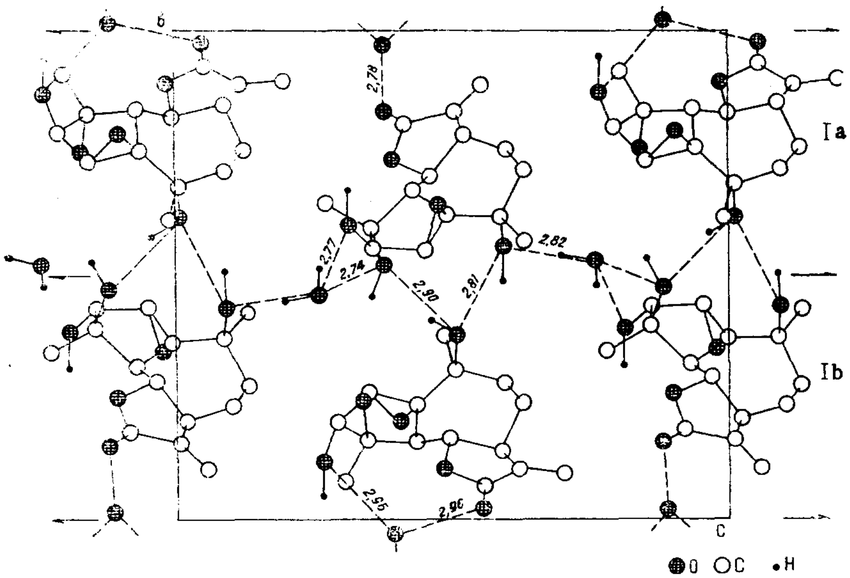

Fig. 2. Packing of the molecules. To illustrate the formation of H-bonds clearly, only the active hydrogen atoms found experimentally are shown.

The search for a model of the structure was performed by the direct method using the Roentgen-75 program [9]. Calculation was begun in the automatic regime but the structure could not be interpreted. It was decided to decrease the number of normalized amplitudes participating in the TPSRs — a gradual decrease in the number of E_{hkl}'s in the TPRs (from 440 to 200 in steps of 50) in the automatic regime enabled a model of the molecule to be determined. In an electron-density (ED) synthesis constructed from the whole group of reflections we found all the missing basis atoms of the (Ia) and (Ib) molecules, and also those of the two molecules of water of crystallization.

The structure was refined first by successive approximations of the ED and by the method of least squares (MLS) in the isotropic approximation (R = 0.148), and then in the full-matrix MLS, taking into account the anisotropy of the thermal vibrations of the nonhydrogen atoms, to R = 0.105. At this stage a difference ED synthesis was made and the positions of 32 H atoms were found. The final value of the discrepancy factor after several iterations of the MLS taking the H atoms into account was 0.069. The coordinates of the basic atoms and of the H atoms found experimentally are given in Table 3.

SUMMARY

The spatial structure of the sesquiterpene lactone ajafinin has been found by x-ray structural analysis; it corresponds to 1,2α-epoxy-3α,4β,10β-trihydroxy-5,6β(H),7α(H)-guai-11(13)-en-6,12-olide.

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CYCLIZATION OF CEMBRANE DITERPENOIDS.

IV. STEREOSELECTIVE PHOTOCHEMICAL CYCLIZATION OF A NORCEMBRANE KETONE

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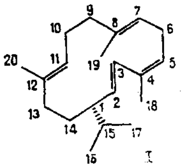
The possibility has been shown for the first time of the occurrence of an intramolecular [2 + 2]-cycloaddition for a derivative of a cembrane diterpenoid. The structure of the product, which was a higher isoprenolog of the bourbonane sesquiterpenoids, was established by the x-ray structural analysis of its epoxide.

The diterpene hydrocarbons cembrene (I) and isocembrene (II) are capable, under the action of electrophilic reagents, of undergoing intramolecular cyclization with the formation of tricyclic derivatives [1-3]. The first stage of the cyclizations, as is assumed, is the formation of a bond between the C_2 and C_{11} atoms. Such a process can take place if the C_2 and C_{11} double bonds in the reacting molecule or in an intermediate ion are sufficiently close in space. We have established that a cyclization similar in direction (the participation of a C_{11} double bond) can also be brought about photochemically. A suitable substrate for such cyclization has proved to be the ketone (III) [4] in which the C_2 double bond is activated by the neighboring keto group. This ketone has been obtained previously from isocembrene (II) by autooxidation or by its treatment with potassium permanganate in aqueous pyridine solution [4]. It has been found that a more convenient method for its synthesis is the oxidation of isocembrene with the Jones reagent by a procedure used previously [5] for cembrene. The ketone (III) was obtained in this way with a yield of 25%. When its pentane solution was irradiated with the light of a high-pressure mercury lamp, a mixture of products was formed that could be separated satisfactorily by chromatography on silica gel. A preliminary analysis of the PMR spectra of these products show that three of them had monocyclic carbon skeletons while one was a cyclization product. This compound (yield 14.0%, calculated on the ketone (III) that had reacted), which is the object of the present communication, was obtained in the form of colorless crystals with mp 35.5-36.5°C. According to its UV spectrum, its molecule did not contain an α-enonic system, while in the IR spectrum the band of an unconjugated carbonyl was observed (1710 cm^{-1}). The ^{13}C NMR spectrum showed the signals of three sp^2-hybridized carbon atoms (213.45 ppm, singlet, C=O; 122.07 ppm, doublet, $-CH=$, and 137.94 ppm, singlet, $-\overset{|}{C}=$). The signals of the other 16 carbon atoms were present in the 17-57 ppm region (see the Experimental part).



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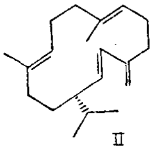
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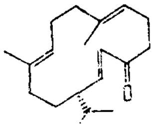
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According to its mass spectrum, the substance obtained was an isomer of the initial ketone. In view of the ^{13}C NMR results, it was possible to conclude that it had a tricyclic carbon skeleton and was most probably a product of intramolecular [2 + 2]-cycloaddition with the participation of the C_2 double bond. On the basis of spectral characteristics alone it did not appear possible to draw an unambiguous conclusion concerning the structure of the product

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