X-RAY-STRUCTURAL INVESTIGATION OF SESQUITERPENE ESTERS OF PLANTS OF THE GENUS Ferula.

II. CRYSTAL AND MOLECULAR STRUCTURE OF THE HUMULANE ALCOHOL FEXEROL

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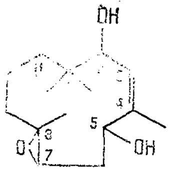
An x-ray structural investigation of the humulane alcohol fexerol has been carried out: diffractometer, CuKα radiation, 1426 reflections, direct method, R factor 0.105. The spatial structure of the fexerol molecule has been determined. The substituents in positions 2, 5, and 8 have the β orientation. The double bond in the 3-4 position has the cis configuration.

Fexerol — a humulane sesquiterpene alcohol — was isolated from the plant Ferula tschatkalensis [1]. On the basis of the results of IR, mass, and PMR spectroscopy and some chemical transformations, the following structure was proposed for fexerol [1, 2]:



The unambiguous determination of the stereochemistry of fexerol by spectroscopic — in particular PMR — methods, proved to be extremely laborious because of the presence in its structure of a labile 11-membered macrocyclic unit. To confirm the proposed structure and establish its stereochemistry, we have performed an x-ray structural investigation.

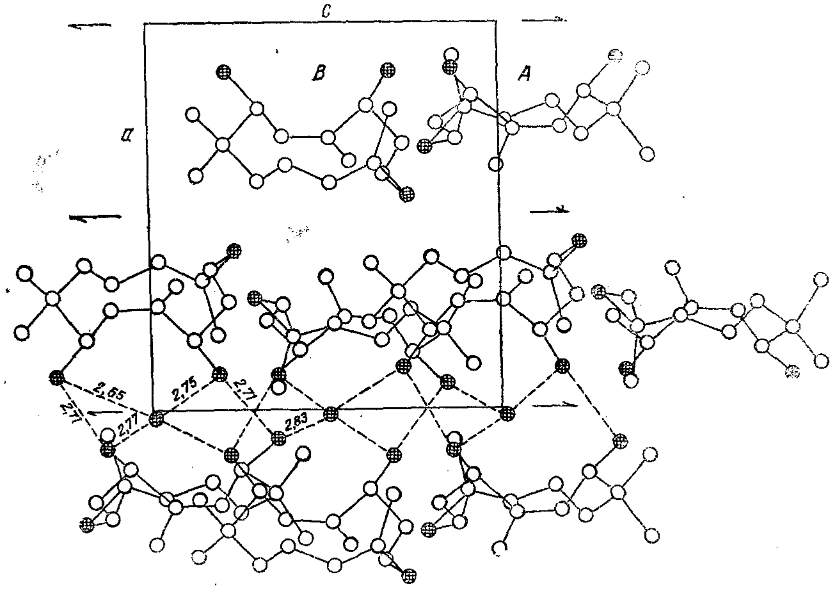


Fig. 1. Packing of fexerol molecules.

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TABLE 1. Torsional Angles of the Macrocycle (φ, deg)

Fragment	φ_A	φ_B
C(8)C(7)C(6)C(5)	−81,8	−85,9
C(7)C(6)C(5)C(4)	−66,5	−64,1
C(6)C(5)C(4)C(3)	118,5	119,1
C(5)C(4)C(3)C(2)	1,8	0,8
C(4)C(3)C(2)C(1)	−126,4	−127,4
C(3)C(2)C(1)C(11)	70,9	70,7
C(2)C(1)C(11)C(10)	71,6	69,4
C(1)C(11)C(10)C(9)	−153,6	−153,7
C(11)C(10)C(9)C(8)	90,9	94,3
C(10)C(9)C(8)C(7)	−83,9	78,7
C(9)C(8)C(7)C(6)	151,1	148,2

TABLE 2. Bond Lengths (r, Å) and Valence Angles (ω, deg)

Bond	r_A	r_B	Angle	ω_A	ω_B
C(1)—C(2)	1,535(14)	1,587(11)	C(1)C(2)C(3)	113,7(8)	112,4(7)
C(1)—C(13)	1,578(13)	1,501(13)	C(1)C(2)O(1)	109,9(7)	106,5(7)
C(1)—C(12)	1,543(14)	1,579(14)	O(1)C(2)C(3)	106,0(8)	109,1(7)
C(1)—C(11)	1,553(15)	1,541(11)	C(2)C(3)C(4)	131,2(8)	129,1(9)
C(2)—O(1)	1,449(13)	1,495(10)	C(3)C(4)C(5)	122,5(7)	123,6(9)
C(2)—C(3)	1,485(12)	1,482(14)	C(3)C(4)C(14)	123,6(9)	123,5(9)
C(3)—C(4)	1,373(15)	1,335(14)	C(14)C(4)C(5)	113,7(9)	112,9(9)
C(4)—C(14)	1,552(12)	1,554(16)	C(4)C(5)C(6)	113,2(8)	114,2(8)
C(4)—C(5)	1,552(13)	1,557(14)	C(4)C(5)O(2)	109,7(7)	108,4(7)
C(5)—O(2)	1,468(12)	1,457(10)	O(2)C(5)C(6)	108,1(8)	107,9(8)
C(5)—C(6)	1,527(15)	1,523(13)	C(5)C(6)C(7)	111,9(9)	109,8(8)
C(6)—C(7)	1,484(16)	1,512(12)	C(6)C(7)O(3)	118,9(9)	119,3(9)
C(7)—O(3)	1,433(13)	1,444(11)	C(6)C(7)C(8)	123,3(9)	121,5(9)
C(7)—C(8)	1,491(12)	1,502(14)	C(7)O(3)C(8)	62,4(6)	62,7(7)
O(3)—C(8)	1,446(9)	1,444(12)	O(3)C(8)C(7)	58,4(6)	58,7(6)
C(8)—C(15)	1,514(13)	1,482(16)	O(3)C(8)C(15)	115,4(7)	116,2(9)
C(8)—C(9)	1,555(14)	1,576(13)	O(3)C(8)C(9)	117,6(9)	113,6(7)
C(9)—C(10)	1,483(16)	1,548(14)	C(15)C(8)C(9)	113,5(8)	115,0(9)
C(10)—C(11)	1,528(12)	1,534(13)	C(7)C(8)C(9)	118,8(7)	117,9(9)
			C(7)C(8)C(15)	121,9(9)	122,5(9)
			C(8)C(9)C(10)	112,1(9)	108,3(7)
			C(9)C(10)C(11)	115,1(8)	116,0(9)
			C(10)C(11)C(1)	118,6(7)	117,6(7)
			C(11)C(1)C(12)	109,4(8)	107,7(7)
			C(11)C(1)C(2)	109,2(9)	107,8(7)
			C(2)C(1)C(13)	112,7(8)	112,7(7)
			C(2)C(1)C(12)	109,5(8)	110,3(7)
			C(12)C(1)C(13)	106,6(9)	108,9(8)
			C(11)C(1)C(13)	109,5(8)	109,3(7)
			O(3)C(7)C(8)	59,2(5)	58,7(6)

Fexerol crystallizes with two molecules in independent parts of the elementary cell. Figure 1 shows both molecules in a projection on the (101) plane. The geometry of these molecules is determined by the torsional angles of the 11-membered macrocycle, the values of which are given in Table 1. On comparing the corresponding torsional angles in the A and B molecules it is possible to observe that the two molecules, on the whole, have the same geometry. A slight divergence in the values of the torsional angles is observed in the fragments with the following bonds: C(8)—C(9), 5.2°; C(6)—C(7), 4.1°; and C(10)—C(11), 3.7°; while in the other torsional angles the divergence is within the limits of experimental error.

In the A and B molecules, the hydroxy groups in positions 2 and 5 and the methyl group in position 8 have the β orientation. The dienic fragment has the cis form, which is somewhat unusual, since in other 11-membered macrocycles it has the trans form [3].

It is known that, in the stereochemical respect, an epoxide group is analogous to a double bond [4] and, therefore, the C(6)—C(7) and C(8)—C(9) bonds adjoining the epoxide group are close to the trans form. The value of the C(6), C(7), C(8), C(9) torsional angle averages 150°C, and this is close to that in the diepoxyhumulanes [3]. The lengths of the bonds and the values of the valence angles are given in Table 2. The lengths of the ordinary C_{sp^3}—C_{sp^3}

TABLE 3. Coordinates (× 10^4) of the Atoms of the Fexerol Molecule

Atom	Molecule A			Molecule B		
	x/a	y/b	z/c	x/a	y/b	z/c
C(1)	7805(9)	7516(6)	8266(11)	7000(7)	2934(5)	2977(9)
C(2)	8450(8)	8117(6)	7433(9)	7951(8)	2207(6)	2030(9)
C(3)	7531(9)	8891(7)	6728(10)	7309(8)	1602(7)	1310(10)
C(4)	7407(9)	9136(6)	5381(13)	7308(8)	1412(5)	0014(12)
C(5)	8323(9)	8596(6)	4268(10)	8000(10)	1842(6)	1107(11)
C(6)	7640(10)	8196(7)	3175(12)	7111(9)	2412(6)	2174(11)
C(7)	7127(10)	7460(6)	3724(12)	6197(10)	3236(6)	1510(11)
C(8)	7932(9)	6503(7)	3963(0)	6551(8)	4112(6)	1292(10)
C(9)	7591(10)	5950(7)	5166(13)	5936(9)	4731(6)	0044(11)
C(10)	8111(9)	6170(6)	6475(11)	6665(9)	4307(6)	—1257(11)
C(11)	7213(8)	6947(7)	7284(10)	6094(7)	3646(5)	—2050(10)
C(12)	8811(11)	6860(8)	9175(13)	7766(9)	3459(6)	−3879(11)
C(13)	6733(9)	8095(7)	9247(13)	6223(8)	2505(7)	−3889(10)
C(14)	6410(9)	10009(7)	4843(15)	6624(11)	0733(7)	0627(13)
C(15)	9332(10)	6192(7)	3569(14)	7768(10)	4248(8)	1794(15)
O(1)	9199(7)	8528(6)	8317(7)	8965(6)	1636(4)	2940(7)
O(2)	8975(6)	9207(4)	3598(8)	8932(6)	1102(4)	1804(7)
O(3)	7041(7)	6729(5)	2841(9)	5633(7)	4043(5)	2316(8)
O_W	10088(5)	9622(3)	188(7)			

bonds range between 1.49 and 1.59 Å. The scatter in the lengths of the C_{sp^3}—C_{sp^2} and C—O bonds is small. On the whole, all the bond lengths agree with the standard values within the 3σ limits [5, 6]. The values of the valence angles in Ia and Ib are close to those generally adopted, within the limits of experimental error [3, 5, 6].

The packing of the molecule is shown in Fig. 1 in a projection on the plane of the a and c axes. The hydroxy groups in the A and B molecules participate in intermolecular H bonds of the O—H...O type [the $O(1)_A...O(2)_B$ and $O(2)_A...O(1)_B$ distances amount to 271 Å], which favors the formation of islets arranged along the c axis. The water molecule detected close to the special position is arranged along a 2_1 screw axis passing through the origin of coordinates. In its turn, it forms H-bonds with these islets, "linking" them along the c axis in an infinite helix (see Fig. 1). Because of the absence of experimental values of the coordinates of the H atoms in the active OH groups participating in the H bonds, the mechanism of the formation of the hydrates remains unclear, since six possible positions of the four H-bonds with each of the oxygen atoms exist [7].

EXPERIMENTAL

Colorless crystals of fexerol in the form of elongated prisms were grown from ether solution and were first investigated by the photo method. The space group and the parameters of the elementary cell were determined from precession x-ray diagrams. These parameters were subsequently refined in a Syntex $P2_1$ diffractometer using CuK_α radiation: a = 10.889(4); b = 15.189(5); c = 9.838(3) Å; γ = 73.693(3)°; d_{calc} = 1.213(2) g/cm³; space group $P2_1$; z = 4. A three-dimensional set of experimental reflections was obtained in the same diffractometer. In the primary treatment of the group, weak reflections with $I \leq 2\sigma$ were excluded. The final group of structural amplitudes amounted to 1426 independent nonzero reflections.

The structure was determined by the direct method using the Roentgen-75 program [8]. After the normalization of the structural amplitudes, in order to determine phases by means of the program, 351 amplitudes with $E \geq 1.16$ were selected. It was impossible to interpret the structure in the automatic regime. After numerous variations of the coordinates and the reference reflections, we found the solution, the reference group then consisting of the reflections shown below:

	h	k	l	E
coordinate	3	5	2	2,93
	1	8	5	3,02
	6	−6	1	2,59
reference	1	1	2	2,04
	2	−4	3	1,92
	7	2	4	2,46
	1	10	5	2,51
	3	3	4	2,53

From the best variant of the signs, an E series was constructed in which 28 out of the 36 nonhydrogen atoms were found (R factor 0.37). For a more accurate localization of the atoms, several ρ(xyz) syntheses were calculated, in one of which all the nonhdyrogen atoms of fexerol were revealed (R factor 0.36). Then the structure was refined by successive electron-density syntheses and the presence of the molecule of water of crystallization was revealed (R factor 0.23). The structure was refined further by the method of least squares (MLS) in the anisotropic approximation to R 0.105. The coordinates of the atoms of molecules 1A and 1B from the last stage of the MLS are given in Table 3. Attempts to determine the coordinates of the H atoms from a difference synthesis were unsuccessful.

SUMMARY

The spatial structure of fexerol has been determined unambiguously by x-ray structural analysis.

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THE STRUCTURE OF ARTELEIN — A DIMERIC LACTONE OF A NEW TYPE FROM Artemisia leucodes

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The structure of a dimeric lactone of a new type from Artemesia leucodes, artelein, has been established unambiguously on the basis of an analysis of the results of IR, high-resolution mass, PMR, and ^{13}C NMR spectroscopy of the substance itself and an x-ray structural investigation of its acetyl derivative.

We have continued the study of the chemical composition of the leaves and flower heads of Artemesia leucodes Shrenk collected in the flowering phase in the environs of Mount Alintau, Chimkent province, Kazakh SSR [1-3]. By chromatographing the lactone resin from an ethanolic extract of the plant we have isolated a new lactone with mp 465°C which we have called artelein (I).

In the mass spectrum of artelein the maximum peak is that of an ion with m/z 263 (100%) while the relative intensity of the peak of an ion with m/z 262 amounts to 48% and it corresponds to the formula $C_{15}H_{18}O_4$. The IR spectrum (Fig. 1) contains strong absorption bands of the carbonyl of a γ-lactone ring (1760 cm^{-1}), of a cyclopentanone (1735 cm^{-1}), and of a hydroxy group (3510 cm^{-1}). Artelein is readily acetylated under mild conditions. The IR spectrum of artelein acetate (II) lacks the band characteristic for the vibrations of a hydroxyl and shows the C=O band of an acetate (1728 cm^{-1}).

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