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# CRYSTAL AND MOLECULAR STRUCTURE OF THE SESQUITERPENE LACTONE MUCRIN

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An x-ray structural investigation has been made of the sesquiterpene lactone mucrin, diffractometer: Cu K_{α} radiation, 942 reflections, direct method, R factor 0.083. The spatial structure of the molecule has been determined: the lactone ring is trans-linked with the germacrane ring, the epoxide group in the 1,10 position has the $1\alpha,10\beta$-orientation, and the hydroxy group in position 6 has the α-orientation.

We have previously reported the isolation from _Tanacetopsis mucronata_ of the sesquiterpene lactone mucrin, for which structure (I) has been proposed [1]. Continuing a study of the structure of mucrin, we have investigated its PMR spectrum. It is worth noting that mucrin acetate has the same structure as pyrethrosin [2, 3]
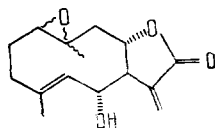
I

A comparative analysis of the PMR spectra in $CDCl_3$ of pyrethosin and mucrin acetate showed that they differed mainly by the magnitudes of the chemical shifts (CSs) of the 10-CH_3 and H-7 protons; the signal of the former was shifted downfield by 0.14 ppm and that of the latter upfield by 0.19 ppm. All these facts show that mucrin acetate differs from pyre-
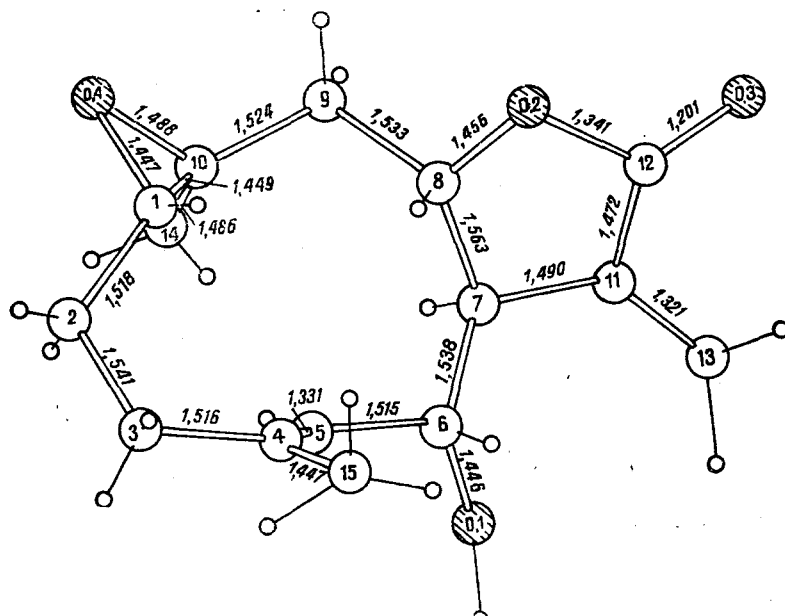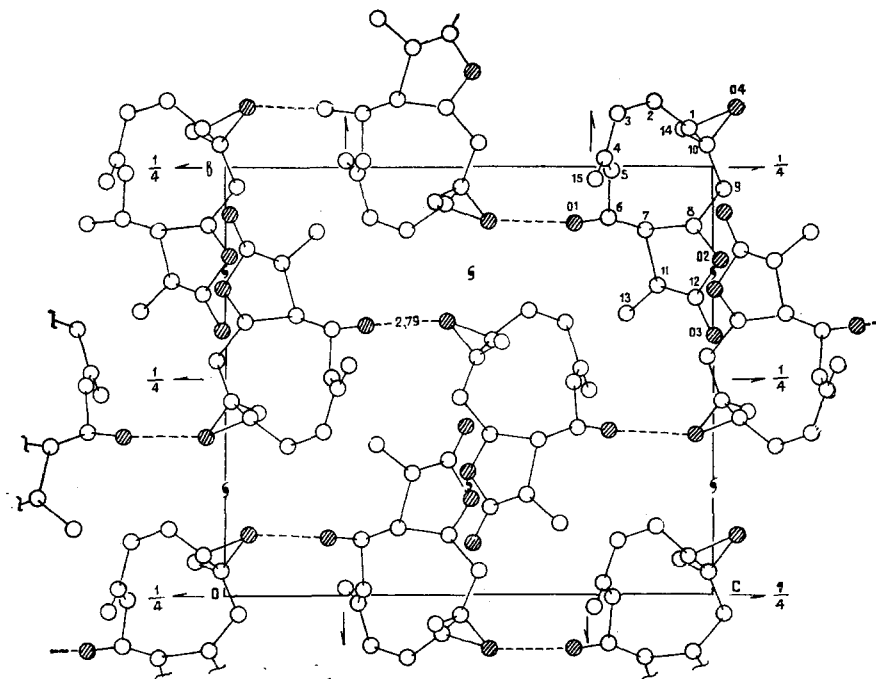
Fig. 1. Structure of the mucrin molecule.

Fig. 2. Packing of the mucrin molecules.

throsin by the orientation of the epoxy group and of the methyl group at C_{10} and C_1, and this, in its turn, is possible when the conformation of the ten-membered ring and the mutual configuration of the endocyclic double bond relative to the Cl—C10 bond are different. In the CD spectrum of mucrin a negative Cotton effect appears in the 213-nm region and a positive one at 202 nm [4]. This indicates a substantial change in the conformation of the ten-membered ring relative to trans-trans-germacranolides with the chair-chair conformation and the $_1D^{14}$, $^{15}D_5$ configuration, while the chair-boat conformation with $^1D_{14}$, $_{15}D^5$ configuration is excluded on the basis of the change in the CSs of the H-6, H_a-13 and H_b-13 protons when the hydroxyl at C6 is acetylated [5]. The boat-boat conformation with the $_1D^{14}$, $_{15}D^5$ configuration, in which the equatorial orientation of H-6 was to be expected, is excluded on the basis of the SSCC values of the H-6 proton with H-5 and H-7, which amount to 9 and 10 Hz, respectively, and contradict an axial-equatorial interaction.

TABLE 1. Torsional Angles (ω, deg) of the Mucrin Molecule

Angle	ω	Angle	ω
1 2 3 4	40,1	9 10 1 2	149,5
2 3 4 5	34,3	10 1 2 3	—114,7
3 4 5 6	—170,5	7 11 12 O3	—5,1
4 5 6 7	114,9	7 8 O2 12	6,6
5 6 7 8	—46,2	8 O2 12 11	—1,2
6 7 8 9	110,6	O2 12 11 7	—5,0
7 8 9 10	—68,7	12 11 7 8	8,6
8 9 10 1	—62,1	6 7 11 12	131,4

TABLE 2. Valence Angles (φ, deg) of the Mucrin Molecule

Angle	φ	Angle	φ
2 1 10	125,6	7 8 O2	105,0
2 1 O4	118,8	9 8 O2	106,4
10 1 O4	61,8	8 9 10	113,8
1 2 3	110,4	9 10 1	116,9
2 3 4	115,8	9 10 O4	114,5
3 4 5	119,3	9 10 14	116,2
3 4 15	115,4	1 10 14	123,9
5 4 15	125,3	14 10 O4	111,7
4 5 6	127,1	1 O4 10	59,2
5 6 7	110,9	7 11 12	128,5
5 6 O1	111,7	7 11 13	130,2
7 6 O1	106,5	12 11 13	120,8
6 7 8	113,8	11 12 O2	108,8
6 7 11	112,1	11 12 O3	129,5
8 7 11	103,1	O2 12 O3	121,6
7 8 9	118,9	12 O2 8	113,2

TABLE 3. Coordinates of the Atoms ($\times 10^4$, for H $\times 10^3$) in the Structure of Mucrin

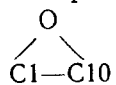| Atom	x	y	z	Atom	x	y	z
C1	1618(10)	— 971(5)	4592(4)	H1	32	— 76	466
C2	1294(11)	— 1753(5)	3817(5)	H2.1	250	—194	364
C3	152(10)	—1257(6)	3067(5)	H2.2	49	—225	400
C4	575(9)	— 137(5)	2837(4)	H3.1	—113	—134	316
C5	2265(9)	197(4)	2877(4)	H3.2	— 56	—175	254
C6	2909(7)	1302(4)	2808(4)	H5	316	— 28	303
C7	3759(7)	1662(4)	3716(3)	H6	170	173	268
C8	2642(8)	1394(5)	4581(4)	H7	508	125	372
C9	3341(9)	555(5)	5238(4)	H8	126	128	449
C10	3331(9)	— 542(5)	4845(4)	H9.1	262	60	583
C11	3919(6)	2828(4)	3771(3)	H9.2	470	69	535
C12	3208(8)	3170(4)	4652(5)	H13.1	— 166	125	237
C13	4545(9)	3492(5)	3161(5)	H13.2	365	141	144
C14	5068(9)	— 923(5)	4484(4)	H14.1	415	425	335
C15	—930(7)	498(7)	2545(6)	H14.2	476	350	247
O1	4286(6)	1418(3)	2122(2)	H14.3	558	— 57	406
O2	2532 6)	2351(3)	5098(3)	H15.1	620	— 64	489
O3	3170(7)	4039(3)	4980(4)	H15.2	477	—175	415
O4	2434(7)	—1330(3)	5425(2)	H15.3	—175	— 25	222
				HO1	—126	55	315

In order to determine the proposed structure and stereochemistry of mucrin reliably, we have carried out an x-ray structural investigation, which has enabled its structure to be refined in the form of (II):

II

51
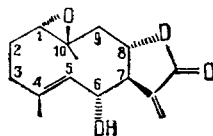
A spatial illustration of the mucrin molecules is shown in Fig. 1 (as a projection of the O11 plane). The lactone ring in the C7—C8 position is, as was assumed previously [1], trans-linked with the germacrane ring. The epoxy group occupying the 1,10 position has the 1α,10β-orientation, and the hydroxy group in position 6 is 6α-oriented.

The conformation of the germacrane ring is characterized by the torsional angles given in Table 1. The values of the torsional angles with the participation of the endocyclic 1,10-epoxy group (stereochemically equivalent to a double bond) (149.5°) and the 4,5-enic bond (170.5°) permits mucrin to be assigned to the trans-trans-germacranolides [6].

When the molecule is projected onto a plane perpendicular to the mean square plane of the germacrane ring it is possible to observe that the epoxide fragment $\begin{smallmatrix} & O & \\ \diagup & & \diagdown \\ C1 & \!\!\!-\!\!\! & C10 \end{smallmatrix}$ and the C4=C5 bond are parallel while the C14 and C15 methyl groups have the anti arrangement. It follows from this that the germacrane ring has the boat-boat conformation — one of the four theoretically possible for trans-trans-germacranolides — with a configuration of the $^1D_{14}$, $^{15}D_5$ type. This is the first time that such a conformation and configuration of the ten-membered ring in natural germacronolides has been detected by the x-ray structural method.

The conformation of the germacrane ring of mucrin found in the crystalline state agrees completely with that suggested on the basis of spectral characteristics. This fact permits the statement that mucrin has the same conformation in solution and in the crystalline state, although germacranolides with lactone rings in the 7-8 position are considered to be fairly labile [7].

The intracyclic distances, greatly shortened in comparison with the sums of the van der Waals radii, C1···C4 (2.90 Å), C1···C5 (2.95 Å) and C5···C10 (3.13 Å) are similar to those observed in hallerol [7] and chimganidin [8].

The lactone ring has a conformation close to planar (the departure of the atoms from the mean square plane of the ring amounts to not more than 0.05 Å).

No anomalies are observed in the value of the valence angles (Table 2) and distances (Fig. 1) (the mean square deviations in the values of the valence bonds and angles are not more than 0.008 Å and 0.5°, respectively).

The packing of the mucrin molecules is shown in Fig. 2 as a projection on the bc plane. The hydroxy and epoxide groups participate in intermolecular H-bonds, the O1—H···O4 distance being 2.79 Å. The mucrin molecules, bound by screw axes of the 2_1 [1/4, 0, Z] type form chains along the c axis.

EXPERIMENTAL

Colorless crystals of mucrin with a rhombic form were grown from ethyl acetate—hexane solution and were first investigated by the photographic method. The space group and the parameters of the elementary cell were established from precession x-ray diagrams. Subsequently, these parameters were refined on a Syntex P2$_1$ diffractometer using Cu K$_\alpha$ radiation: a = 7.505(2), b = 12.851(3), c = 14.637(3) Å; d_{calc} = 1.5 g·cm^{-3}; space group P2$_1$2$_1$2$_1$; Z = 4.

A three-dimensional set of experimental reflection intensities was obtained on the same diffractometer. In the primary treatment of the group, weak reflections with I ≤ 2σ were excluded. The final group comprised 942 independent nonzero reflections. Their structure was determined by the direct method by means of the Rentgen-75 program [9] in the automatic regime. Analysis of the E-synthesis revealed all 19 nonhydrogen atoms (R = 0.321). The structure was then refined by the method of least squares (MLS) with allowance for the anisotropy of the thermal vibrations of the nonhydrogen atoms to R = 0.098. At this stage, an electron density difference synthesis was calculated and the positions of all the H atoms were localized.

The final value of the divergence factor after four cycles of MLS taking the H atoms into account was 0.083. The coordinates of the atoms are given in Table 3.

CONCLUSIONS

The structure of the sesquiterpene lactone mucrin has been refined and its stereochemistry has been established unambiguously by the x-ray structural method; it is 6-hydroxy-

1,10-epoxy-1β,5α,6β,7α,8β(H)-germacra-4(5),11(13)-dien-8,12-olide. The boat-boat conformation has been established for the ten-membered ring with a configuration of the $^1D_{14}$, $^{15}D_5$ type, and this is the first time that this has been detected in natural trans-trans-germacranolides.

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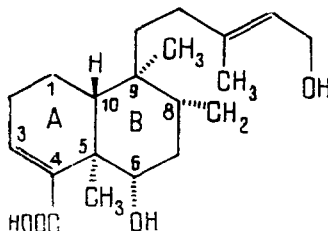9. V. N. Andrianov, Z. Sh. Safina, and B. L. Tarnopol'skii, Zh. Strukt. Khim., 15, 911 (1974).

CRYSTAL AND MOLECULAR STRUCTURE OF SALVICIN — A DITERPENOID ACID
OF THE CLERODANE SERIES

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The spatial structure of the diterpenoid salvicin has been determined by x-ray structural analysis. The trans-linkage of rings A/B proposed previously has been confirmed. This indicates that rings A and B in related diterpenoids — salvin and salvinin — also have the trans-linkage.

Salvicin $C_{20}H_{32}O_4$ has been isolated previously from the epigeal part of Pulicaria sal-viifolia (family Compositae). A comparative analysis of the PMR spectra of salvicin and compounds close to it in structure [1, 2] enabled the most probable orientation of the substituents to be determined and a possible type of linkage of the rings to be suggested. However, the question of the linkage of the rings is an extremely complex one and solution on the basis of the results of PMR spectroscopy alone cannot be considered definitive, with the exception of cases of a direct correlation with known compounds [3, 4]. In the majority of cases [5-7], reliable information on the nature of the linkage of the rings can be obtained by x-ray structural analysis. We have therefore performed an x-ray structural inves-