

MOLECULAR AND CRYSTAL STRUCTURE OF THE SESQUITERPENE LACTONE  
AUSTRICIN

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UDC 548.373:547.314

An x-ray structural study has been made of the sesquiterpene lactone austricin: diffractometer, MoK $\alpha$  radiation, 1147 reflections, direct method, R = 0.045. The spatial structure of the molecule has been determined. The conformation of the pentane carbocycle is 1 $\alpha$ -envelope, of the heptane ring 1,10 $\beta$ , 7 $\alpha$ -chair, and of the lactone ring 7 $\alpha$ -envelope. The lactone ring is trans-linked with the guaiane skeleton.

The isolation from the epigeal part of *Artemisia austriaca* Jacq. (Austrian wormwood) and of *Artemisia sericea* Web. (silky wormwood) of a crystalline substance with the composition

TABLE 1. Valence Angles  $\omega$  (deg)

Angle	$\omega$	Angle	$\omega$
C6O1C12	108,7 (3)	C6C7C8	114,1 (3)
C2C1C5	107,1 (3)	C6C7C11	100,8 (3)
C2C1C10	127,0 (3)	C8C7C11	118,7 (3)
C5C1C10	125,8 (3)	O4C8C7	106,5 (3)
O3C2C1	126,9 (3)	O4C8C9	108,7 (3)
O3C2C3	126,9 (4)	C7C8C9	111,9 (3)
C1C2C3	106,1 (3)	C8C9C10	113,5 (3)
C2C3C4	112,7 (4)	C1C10C9	121,3 (3)
C3C4C5	111,2 (3)	C1C10C14	124,8 (3)
C3C4C15	125,9 (4)	C9C10C14	113,9 (3)
C5C4C15	122,9 (3)	C7C11C12	101,0 (3)
C1C5C4	102,7 (3)	C7C11C13	118,0 (4)
C1C5C6	108,2 (3)	C12C11C13	112,3 (4)
C4C5C6	113,8 (3)	O1C12O2	120,7 (4)
O1C6C5	111,3 (3)	O1C12C11	110,5 (4)
O1C6C7	102,6 (3)	O2C12C11	128,7 (4)
C5C6C7	116,5 (3)		

TABLE 2. Torsion Angles (deg)  
in the Rings

Angle	$\varphi$	Angle	$\varphi$
C5C1C2C3	-2,8 (4)	C7C8C9C10	79,3 (4)
C1C2C3C4	1,2 (4)	C8C9C10C1	-66,7 (4)
C2C3C4C5	0,9 (3)	C9C10C1C5	2,2 (4)
C3C4C5C1	-2,6 (4)		
C4C5C1C2	3,2 (4)	C7C6O1C12	26,7 (4)
		C6O1C12C11	-2,7 (4)
C10C1C5C6	59,5 (4)	O1C12C11C7	-22,4 (4)
C1C5C6C7	-79,8 (4)	C12C11C7C6	36,6 (4)
C5C6C7C8	70,8 (4)	C11C7C6O1	-39,0 (4)
C6C7C8C9	-64,7 (4)		

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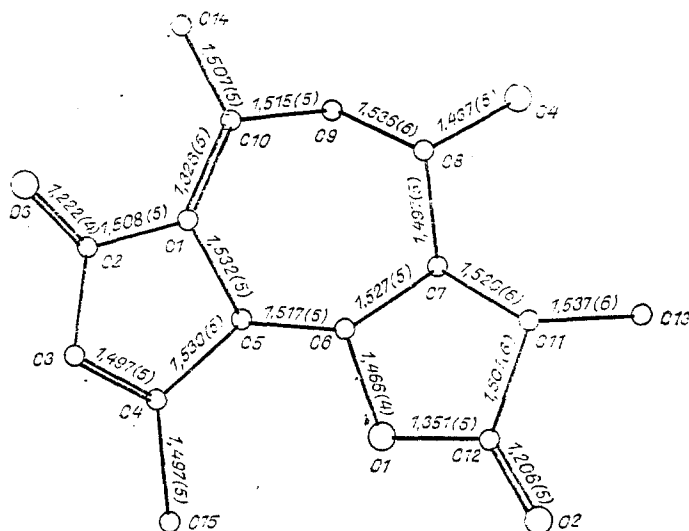


Fig. 1. Structure of the austricin molecule.

$C_{15}H_{18}O_4 \cdot H_2O$ , mp 149-151°C (ethanol), which was identified by its physicochemical constants and spectral characteristic as the sesquiterpene lactone austricin (I), has been reported previously [1, 2]. In order to obtain accurate information on the spatial structure of (I) we have made an x-ray structural investigation of a crystal of its monohydrate.

The structure of the molecule of (I) is shown in Fig. 1. The lengths of the bonds and the valence angles (Table 1) in rings A and B are close to the corresponding values for pumilin (II) [3], 8-acetyl-9-deacetyl-pumilin-9-methacrylate (III) [4], and lactucin (IV) [5], and those in ring C with the corresponding values of  $\alpha,\beta$ -unsaturated  $\gamma$ -lactones (see, for example [6]). Only an increase in the C7C11C13 valence angle to 118.0(4)° needs to be mentioned.

The conformation of ring A is a highly flattened envelope: the C2, C3, and C4 atoms and the exocyclic O3 atom are present in one plane with an accuracy of  $\pm 0.005$  Å, and the C1 and C15 atoms depart from it in the  $\alpha$ -direction by 0.05 and 0.07 Å, respectively. The O3, C2, C1, C10 conjugated system is actually planar [the corresponding torsion angle is 1.9(4)°].

The linkage of rings A and B is characterized by the torsion angles C2C1C5C4 of 3.2(4)° and C10C1C5C6 of 59.5(4)°. In the molecules of (II), (III), and (IV), the conformation of ring A is also a highly flattened envelope with the departure of the C1 atom from the plane of the other atoms of the ring in the  $\alpha$ -,  $\alpha$ - and  $\beta$ -directions, respectively. The torsion angles characterizing the linkage of rings A and B in them vary only slightly: C2C1C5C4 7.9, 3.3, and -1.1°, and C10C1C5C6 64.0, 62.5, and 53.1°, respectively, i.e., the types of linkage in (I)-(IV) are practically identical. The very small difference in the nature of the linkage is obviously due to the conformational rigidity of the flattened five-membered ring A.

The conformation of ring B is a slightly distorted chair (Table 2): the C5, C6, C8, and C9 atoms are coplanar to within  $\pm 0.02$  Å, and the C1, C7, and C10 atoms depart from their plane by 1.05, 0.70, and 1.09 Å in the  $\beta$ -,  $\alpha$ -, and  $\beta$ -directions, respectively. The molecules of (I), (III), and (IV) also have similar conformations of the seven-membered carbocycles, and the C5C1C10C9 torsional angles at the C=C double bond in (I-IV) are 2.7, 4.5, 6.5, and 6.1°, respectively. The hydroxy group at C8 in (I) has the equatorial orientation.

The conformation of the lactone ring C in (I) - an envelope (the C6, O1, C11 and C12 atoms are present in one plane with an accuracy of  $\pm 0.01$  Å, while the C7 atom departs from it by 0.62 Å, in the  $\alpha$ -direction) - differs considerably from the conformations of the corresponding rings in (II-IV), probably because of the presence of each of the latter of an endocyclic double bond conjugated with the  $\gamma$ -lactone grouping. The methyl group at C11 has the quasi-equatorial  $\alpha$ -orientation. The linkage of rings B and C is trans [H6C6C7H7 torsion angle -175(3)°].

The molecules of (I) and the water of crystallization (arranged randomly over two positions - O(w)1 and O(w)2 - are linked by O4-H...O(w)1 (x, y, z) hydrogen bonds (O...O, O-H, H...O distances 2.84, 0.64 and 2.25 Å, respectively; O-H...O angle 154.4°), O4-H...O(w)2 (x, y, z) (O...O and H...O distances 2.69 and 2.07 Å, respectively; O-H...O angle 163.4°), O(w)1-H...O2 (x, y, 1 + z) (O...O distance 2.80 Å), O(w)2-H...O2 (x, y, 1 + z) (O...O distance

TABLE 3. Coordinates of the Atoms ( $\times 10^4$ ); for the (w)2 and H Atoms,  $\times 10^3$

Atom	x	y	z	Atom	x	y	z
O1	7279 (2)	3338	6098 (2)	O (w) 2	498 (1)	289 (2)	1188 (1)
O2	5325 (3)	4404 (6)	4347 (3)	H (O) 4	504 (3)	292 (4)	988 (3)
O3	12123 (2)	2389 (4)	11259 (3)	H3	1213 (2)	223 (4)	865 (2)
O4	4985 (2)	2717 (3)	9253 (3)	H5	831 (3)	50 (4)	778 (3)
C1	9597 (3)	1823 (5)	9761 (4)	H6	828 (2)	430 (4)	808 (3)
C2	11169 (3)	2164 (5)	10088 (4)	H7	601 (2)	180 (4)	746 (2)
C3	11328 (4)	2127 (6)	8739 (4)	H8	686 (2)	411 (4)	970 (2)
C4	10086 (3)	1848 (6)	7649 (4)	H9.1	711 (3)	121 (4)	1101 (3)
C5	8838 (3)	1677 (5)	8145 (3)	H9.2	712 (3)	32 (4)	974 (3)
C6	7739 (3)	3124 (5)	7630 (3)	H11	565 (3)	531 (5)	723 (3)
C7	6311 (3)	2839 (5)	7798 (4)	H13.1	337 (4)	428 (7)	706 (4)
C8	6425 (3)	2904 (6)	9303 (4)	H13.2	346 (3)	449 (6)	554 (4)
C9	7357 (4)	1425 (6)	10197 (4)	H13.3	348 (3)	281 (5)	587 (3)
C10	8961 (3)	1750 (5)	10682 (4)	H14.1	972 (4)	67 (5)	1270 (4)
C11	5359 (4)	4155 (6)	6745 (4)	H14.2	922 (3)	297 (5)	1253 (3)
C12	5924 (4)	4038 (7)	5586 (4)	H14.3	65 (2)	210 (4)	1248 (3)
C13	3717 (4)	3300 (8)	6186 (5)	H15.1	945 (3)	63 (5)	575 (3)
C14	9723 (4)	1973 (6)	12265 (4)	H15.2	924 (4)	234 (8)	546 (5)
C15	9897 (4)	1650 (7)	6129 (4)	H15.3	62 (3)	182 (5)	600 (3)
O (w) 1	6046 (4)	4323 (7)	11965 (4)				

2.68 Å), O(w)1-H...O4 (1 - x, 0.5 + y, 2 - z) (O...O distance 2.92 Å), and O(w)2-H...O3 (-1 + x, y, z) (O...O distance 2.72 Å) and form two-dimensional lattices in the crystal.

#### EXPERIMENTAL

The parameters of the cell and the intensities of the 1329 reflections were measured on a Hilger-Watts four-circle diffractometer ( $\lambda$  MoK $\alpha$ , graphite monochromator,  $\theta/2\theta$  scanning,  $2\theta \leq 60^\circ$ ). The crystals of the monohydrate of (I) were monoclinic,  $a = 10.0595(8)$ ,  $b = 7.7273(9)$ ,  $c = 10.213(1)$  Å,  $\beta = 112.747(7)^\circ$ ,  $V = 732.2(1)$  Å<sup>3</sup>,  $M = 280$ ,  $d_{\text{calc}} = 1.272$  g/cm<sup>3</sup>,  $z = 2$  (C<sub>15</sub>H<sub>18</sub>O<sub>4</sub>·H<sub>2</sub>O), sp. gr. P2<sub>1</sub>. In the calculations use was made of 1147 independent reflections with  $I \geq 2\sigma$ . The structure was interpreted by the direct method. Refinement was carried out by the block-diagonal MLS in the anisotropic approximation for the nonhydrogen atoms. The molecule of the water of crystallization was located randomly over two positions and these were refined with weights of 0.75 and 0.25 [O(w)1 and O(w)2, respectively]. The H atoms for it were not revealed. The other hydrogen atoms were localized in a difference synthesis and their positions were refined in their isotropic approximation. The final divergence factors were  $R = 0.045$  and  $R_w = 0.036$ . All the calculations were made on an Eclipse S/200 computer by means of the INEXTL programs [7]. The coordinates of the atoms are given in Table 3.

#### SUMMARY

The spatial structure of the sesquiterpene lactone austrocin has been determined by the x-ray structural method as 8 $\alpha$ -hydroxy-2-oxo-5 $\alpha$ ,6 $\beta$ ,7 $\alpha$ ,11 $\beta$ (H)-guaia-1(10),3-dien-6,12-olide.

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