Chemistry of Natural Compounds, Vol. 40, No. 5, 2004

X-RAY STRUCTURE OF LAGOCHIRSINE

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UDC 547.944/945+548.737

The molecular structure of the lagochilin diterpenoid lagochirsine was determined by x-ray structure analysis. The crystallographic investigations were conducted on an automated four-circle STOE/STAD14 diffractometer at room temperature. The crystals were trigonal, space group $P3_2$ *(No. 145),* $C_{20}H_{32}O_5$, $a = b = 14.289(2)$ Å, $c = 8.2320(16)$ Å, $V = 1455.6(4)$ Å^3, $Z = 3$, $D_{calc} = 1.206$ g/cm^3, $R = 0.065$ ($R_w = 0.1368$).

Key words: lagochilin, lagochirsine, crystal structure, x-ray structure analysis.

Diterpenoids isolated from plants of the *Lagochilus* genus are highly physiologically active. They can be used as starting materials for preparing highly effective medicinal preparations [1]. In particular, the medicinal preparation "Lagoden," which is used for various hemorrhages, is based on the lactone lagochirsine, which is isolated from *L. hirsutissimus*, *L. setulosus*, and *L. gypsaceus*. The structure of lagochirsine was established by chemical transformations and PMR spectroscopy. However, its confirmational structure was not elucidated. The present article reports results of an x-ray structure analysis of lagochirsine.

Figure 1 shows the molecular conformation and atomic numbering. Asymmetry parameters that characterize the degree of deviation of this conformation from the ideal one were calculated using the RING program [3] in order to define more accurately the conformation of all rings. The six-membered cyclohexane lagochirsine rings A and B of starting lagochilin [4, 5] and lagochilin derivatives [6, 7] have a slightly distorted chair conformation [for ring A: $\Delta C_s = 2.8°$ (C2), $\Delta C_2 = 1.9°$ (C2-C3); for ring B: $\Delta C_s = 0.9°$ (C8), $\Delta C_2 = 0.8°$ (C7-C8)]. Atoms C4 and C1 deviate from the plane of C2-C3-C5-C10 by 0.68 and 0.65 Å, respectively; atoms C6 and C9 from that of C7-C8-C10-C5, by 0.70 and 0.71 Å, respectively.

The conformation of five-membered rings C and D is an envelope [ΔC_s (C12) = 4.4° and ΔC_s (C13) = 2.5°, respectively]. Atoms C11, C9, O5, and C13 in ring C are planar with a maximum least-squares deviation of 0.02 Å. Atom C12 deviates by 0.46 Å. Atoms C14, C16, O3, and C15 of ring D are planar with a maximum least-squares deviation of 0.01 Å. Atom C13 deviates by 0.45 Å. Rings A and B are *trans*-fused.

Methyls on C4 and C10 are axial; that on C8, equatorial.

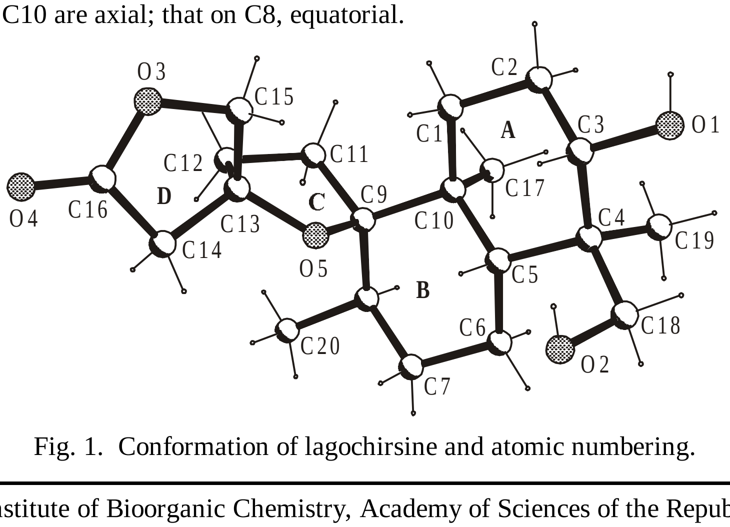

Fig. 1. Conformation of lagochirsine and atomic numbering.

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TABLE 1. Bond Lengths (r) and Angles (φ) in Lagochirsine

Atom	r, Å	Atom	r, Å	Atom	φ, deg	Atom	φ, deg
O1-C3	1.431 (8)	C5-C6	1.550 (8)	C15-O3-C16	110.6 (5)	O5-C9-C11	104.1 (4)
O2-C18	1.427 (7)	C5-C10	1.557 (9)	C9-O5-C13	112.8 (5)	C10-C9-C11	113.3 (4)
O3-C15	1.436 (7)	C6-C7	1.529 (10)	C1-C10-C5	107.8 (5)	O5-C9-C8	107.7 (4)
O3-C16	1.345 (10)	C7-C8	1.528 (11)	C5-C10-C17	115.0 (5)	C8-C9-C10	110.2 (4)
O4-C16	1.208 (10)	C8-C9	1.531 (8)	C2-C1-C10	113.5 (5)	C8-C9-C11	112.9 (5)
O5-C9	1.458 (7)	C8-C20	1.531 (10)	C1-C2-C3	110.5 (5)	C1-C10-C9	109.7 (4)
O5-C13	1.432 (7)	C9-C10	1.589 (8)	O1-C3-C4	108.4 (4)	C1-C10-C17	109.2 (5)
C1-C10	1.543 (8)	C9-C11	1.546 (9)	O1-C3-C2	111.9 (5)	C5-C10-C9	107.6(4)
C1-C2	1.517 (10)	C10-C17	1.542 (9)	C2-C3-C4	112.3 (5)	C9-C10-C17	107.5 (5)
C2-C3	1.506 (10)	C11-C12	1.537 (9)	C3-C4-C18	107.9 (5)	C9-C11-C12	104.8 (5)
C3-C4	1.543 (7)	C12-C13	1.517 (10)	C3-C4-C5	107.4 (4)	C11-C12-C13	103.4 (5)
C4-C18	1.539 (10)	C13-C14	1.521 (8)	C5-C4-C19	115.9 (5)	O5-C13-C14	110.3 (5)
C4-C5	1.557 (8)	C13-C15	1.531 (8)	C18-C4-C19	104.7 (5)	O5-C13-C12	105.9 (4)
C4-C19	1.543 (8)	C14-C16	1.496 (10)	C3-C4-C19	110.8 (4)	C12-C13-C15	113.3 (5)
				C5-C4-C18	110.0 (4)	O5-C13-C15	110.7 (5)
				C6-C5-C10	111.6 (5)	C12-C13-C14	115.6 (5)
				C4-C5-C6	112. 8 (5)	C14-C13-C15	101.1 (4)
				C4-C5-C10	116.4 (4)	C13-C14-C16	104.3 (5)
				C5-C6-C7	108.9 (5)	O3-C15-C13	105.9 (5)
				C6-C7-C8	112.5 (6)	O3-C16-O4	120.5 (7)
				C9-C8-C20	114.6 (5)	O3-C16-C14	109.8 (6)
				C7-C8-C20	108.5 (6)	O4-C16-C14	129.7 (7)
				C7-C8-C9	111.1 (6)	O2-C18-C4	114.7 (5)
				O5-C9-C10	108.3 (5)		

TABLE 2. Intermolecular H-Bonds in the Crystal Structure of Lagochirsine

H-bond	Symmetry	O-H, (Å)	O...H, (Å)	O...O, (Å)	Angle, (°)
O1-H...O2	1-x + y, 1-x, -2/3 + z	0.75 (6)	2.04 (7)	2.739 (7)	155 (9)
O2-H - O1	1-x + y, 1-x, 1/3 = z	0.83 (6)	2.02 (6)	2.824 (7)	163 (5)

Lengths of Csp^3–Csp^3 bonds vary in the range 1.506(10) (C2–C3) to 1.589(8) (C9–C10) Å. Bond angles are normal and close to the standard values (Table 1).

The structure of lagochirsine contains seven asymmetric atoms: C3, C4, C5, C8, C9, C10, and C13. The quality of the prepared single crystals was insufficient to collect a data set enabling the determination of the absolute configuration. Therefore, we can only propose the configuration of the chiral centers: C3*S*, C4*R*, C5*S*, C8*R*, C9*R*, C10*S*, and C13*S*. These agree with the configurations of the analogous chiral centers in lagochilin and its derivatives [4-7].

Each hydroxyl in the lagochirsine crystal structure acts as a proton donor and acceptor (Table 2). Therefore, one lagochirsine molecule is H-bonded to four other molecules around the 3-fold axis to form infinite chains along the [001] direction (Fig. 2). In general, the observed crystal structure is rather loose (packing coefficient 65.5%).

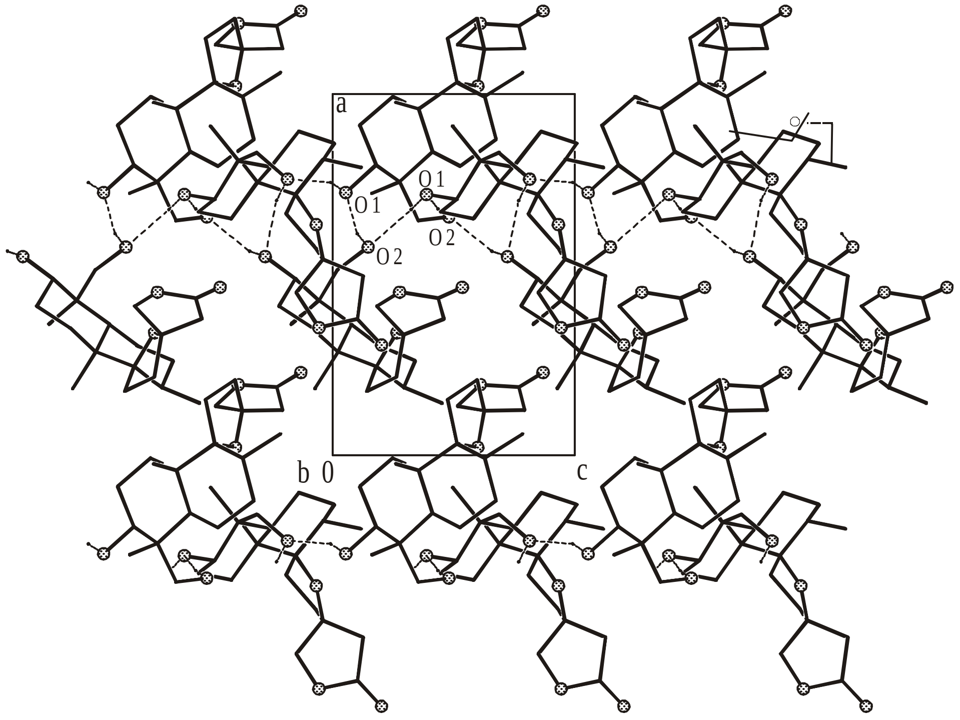

Fig. 2. Crystal structure of lagochirsine. A projection on the (101) plane. Dotted lines are H-bonds. Only H atoms involved in H-bonds are shown.

EXPERIMENTAL

The preparation and physicochemical properties of lagochirsine have been published [2]. Single crystals of lagochirsine were grown from acetone solution at room temperature. Crystallographic parameters of single crystals were determined and refined using 15 reflections on an automated four-circle STOE/STAD14 diffractometer at room temperature. The crystals are trigonal, space group $P3_2$ (No. 145), $C_{20}H_{32}O_5$, $a = b = 14.289(2)$ Å, $c = 8.2320(16)$ Å, V = 1455.6(4) Å^3, $Z = 3$, $D_{calc} = 1.206$ g/cm^3. Integrated intensities were measured by $\theta/2\theta$-scanning ($1.6 < \theta < 26.5°$) using graphite-crystal monochromatized Mo Kα-radiation. The total number of reflections was 2012. After calculating Lorentz and polarization corrections and removing weak reflections [$I < 2\sigma(I)$], the data set consisted of 1426 reflections. The structure was solved by direct methods using the SHELXS program set [8].

The structure was refined using the SHELXL-97 [9] program set. H atoms (with the exception of hydroxyls) were found geometrically (C–H distance 0.96 Å) and refined using the rider model. The discrepancy factor after final refinement of the positional and anisotropic thermal parameters was R = 0.065 ($R_w = 0.1368$). Table 2 contains interatomic distances and angles.

The structure is registered in the Cambridge Structural Database, No. CCDC 235925.

ACKNOWLEDGMENT

The work was performed under contract F-4.1.38 of the Center for Science and Technologies of the Coordinating Committee for Scientific-Technical Development in the Cabinet of Ministers of the Republic of Uzbekistan and with financial support of the Russian Foundation for Basic Research (license to use the Cambridge Structural Database).

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