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THE CRYSTAL STRUCTURE OF L-*chiro*-INOSITOL

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ABSTRACT

The crystal structure of L-*chiro*-inositol is monoclinic, $P2_1$, with $a = 6.867(3)$, $b = 9.133(4)$, $c = 6.217(3)$ Å, $\beta = 106.59(4)°$, $Z = 2$. The structure was solved by using MULTAN, and refined to $R = 0.028$ for 1065 intensities observed with Ni-filtered MoKα radiation. The molecule has the expected chair conformation, with puckering parameters $Q = 0.561$ Å, $\theta = 4.4°$, $\phi = 51.2°$. The non-hydrogen molecular symmetry is close to C_2, with deviations of less than 0.07 Å from a weighted fit. The intramolecular hydrogen-bonding forms infinite chains which are cross-linked through the weaker component of a three-center bond. The C–C bond lengths range from 1.515 to 1.528 Å, and the C–O bond lengths from 1.418 to 1.436 Å. The C–C–C angles range from 109.7 to 113.1°, and the C–C–O angles from 106.5 to 112.0°.

INTRODUCTION

The inositols are widely distributed in Nature, either as the free molecules or as phosphoric esters[1]. Hitherto, the crystal structures have been determined for the *meso* compounds, *myo*-inositol[2] and its dihydrate[3], its 2-phosphate monohydrate[4], its calcium bromide pentahydrate[5], its magnesium chloride tetrahydrate[6], for *epi*-inositol[7] and its strontium chloride pentahydrate[8], and for *muco*-inositol[9]. L-*chiro*-Inositol is reported to crystallize as a dihydrate from water, and anhydrous from alcohol[10].

The free L-*chiro*-inositol configuration has C_2 symmetry. This is not a crystallographic axis of symmetry in its crystal structure. Therefore, the molecules will be more or less distorted in the crystal by the intermolecular force-field of lower symmetry which is primarily due to intermolecular hydrogen-bonding.

This analysis was carried out to determine the extent of this distortion, and the pattern of the hydrogen-bonding structure in the crystal.

EXPERIMENTAL

Clear, plate-like crystals of the anhydrous form were obtained from Professor L. Anderson, University of Wisconsin. The crystallographic, experimental,

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TABLE I

CRYSTAL DATA AND X-RAY DIFFRACTION STRUCTURE ANALYSIS DATA FOR L-*chiro*-INOSITOL

$C_6H_{12}O_6$; mol. wt. = 180.16; m.p. = 247°C; $[\alpha]_D$ −64°; $P2_1$; $Z = 2$
Cell dimensions: = 6.867(3), b = 9.133(4), c = 6.217(3) Å, β = 106.59(4)°, based on 25 reflections with 15° $\leqslant \theta \leqslant$ 20°
$D_{obs} = 1.60$ g.cm^{-3}, $D_{calc} = 1.59$ g.cm^{-3}
Crystal dimensions: 0.35 × 0.25 × 0.20 mm
Radiation: Ni-filtered MoKα (λ = 0.7107 Å)
1146 intensities, for which 76 had $F_o < 3\sigma F_o$, were measured on a CAD-4 diffractometer
No corrections for absorption (μ = 0.96 cm^{-1}) or extinction
Refinement on $\omega(|F_o| - k|F_c|)^2$ where $\omega^{-1} = \sigma^2(I)_{counter} + (0.02F_o^2)$
Final refinement values: $R = 0.028$, $R_w = 0.032$, $S = 2.12$
Number of observations, 1065; number of parameters, 156
Final shifts <0.1 σ

TABLE II

ATOMIC POSITIONAL PARAMETERS AND EQUIVALENT ISOTROPIC THERMAL PARAMETERS[a] FOR THE CRYSTAL STRUCTURE OF L-*chiro*-INOSITOL

Atom	x/a	y/b	z/c	B_{eq} or B[b]
C-1	7060(2)	4660(2)	4532(2)	118(5) × 10^{-2}
C-2	6389(2)	3078(2)	3972(3)	109(5)
C-3	6543(2)	2583(3)	1680(2)	113(4)
C-4	8650(2)	2907(2)	1445(2)	106(4)
C-5	9286(2)	4484[c]	1983(2)	109(5)
C-6	9203(2)	4906(3)	4332(3)	119(5)
O-1	5673(2)	5619(2)	3018(2)	161(4)
O-2	4422(2)	2838(2)	4215(2)	194(4)
O-3	6172(2)	1037(2)	1517(2)	179(4)
O-4	8621(2)	2555(2)	−814(2)	179(4)
O-5	11280(2)	4620(2)	1745(2)	181(4)
O-6	10583(2)	4050(2)	6033(2)	187(4)
H-C-1	706(3)	486(3)	599(4)	16(4) × 10^{-1}
H-C-2	731(3)	249(3)	510(3)	17(4)
H-C-3	550(3)	310(2)	45(3)	7(3)
H-C-4	966(3)	229(3)	247(3)	10(4)
H-C-5	837(3)	511(2)	93(3)	14(4)
H-C-6	955(3)	589(2)	459(3)	10(4)
H-O-1	568(3)	632(3)	368(4)	16(4)
H-O-2	359(4)	355(3)	348(4)	24(5)
H-O-3	554(4)	87(3)	11(4)	25(5)
H-O-4	953(4)	308(3)	−94(4)	25(5)
H-O-5	1144(4)	541(4)	142(5)	29(6)
H-O-6	1149(4)	451(4)	656(4)	31(6)

[a] Fractional coordinates × 10^4 for non-hydrogen atoms, × 10^3 for hydrogen atoms. E.s.d. values given in parentheses refer to the least significant digit. [b] For non-hydrogen atoms, $B_{eq} = {}^4/_3\ (\Sigma_{ij} B_{ij} \vec{a}_i \cdot \vec{a}_j)$, calculated in Å^2 from the refined, anisotropic, thermal parameters; for hydrogen atoms, B (in Å^2). [c] Fixed parameter.

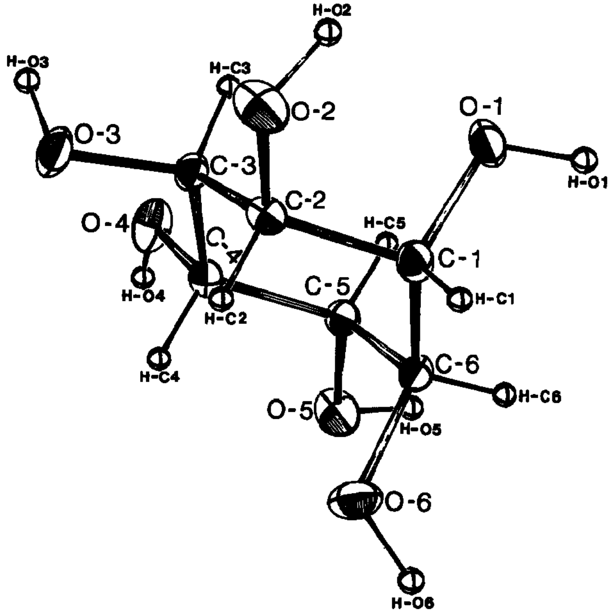

Fig. 1. Atomic notation and thermal ellipsoids at 50% probability for L-*chiro*-inositol.

structure-determination and refinement data are given in Table I. The intensities were measured by integrating $\omega/2\theta$ scans over 96 intervals[11,12]. The structure was solved by using MULTAN[13] on 245 E-values greater than 1.20. All twelve hydrogen atoms were located on the difference maps. The strong $11\bar{2}$ reflection, affected by extinction, was excluded from the final refinement. The final atomic parameters* are given in Table II. The atomic notation[14] and thermal ellipsoids are shown in Fig. 1.

DISCUSSION

As anticipated, the molecular conformation in the crystal is that with two axial and four equatorial hydroxyl groups, as shown in Fig. 1, this being, presumably, the preponderant conformer in aqueous solution. The two-fold axis of the isolated molecules passes through the mid-points of the C-1–C-6 and C-3–C-4 bonds.

The non-hydrogen atom molecular symmetry is very close to C_2, with deviations of 0.02 to 0.07 Å for the weighted fit[15]. If the methine hydrogen atoms are included, the deviations are 0.11 Å. The bond lengths and valence and torsion

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*Lists of structure factors, anisotropic thermal parameters, and hydrogen-bond distances and angles have been deposited with, and may be obtained from, Elsevier Science Publishers B.V., BBA Data Deposition, P. O. Box 1527, Amsterdam, The Netherlands. Reference should be made to BBA/DD/352/*Carbohydr. Res.*, 159 (1987) 211–216.

TABLE III

BOND DISTANCES, VALENCE ANGLES, AND TORSION ANGLES IN L-*chiro*-INOSITOL[a]

Bond	*Bond length*	*Bond*	*Bond length*
C-1–C-2	1.525(2)	C-1–O-1	1.429(2)
C-2–C-3	1.528(2)	C-2–O-2	1.418(2)
C-3–C-4	1.524(2)	C-3–O-3	1.433(2)
C-4–C-5	1.515(2)	C-4–O-4	1.436(2)
C-5–C-6	1.527(2)	C-5–O-5	1.424(2)
C-6–C-1	1.527(3)	C-6–O-6	1.433(2)
Bonds	*Valence angle*	*Bonds*	*Valence angle*
C-1–C-2–C-3	113.1(1)	C-3–C-2–O-2	112.0(1)
C-2–C-3–C-4	110.6(1)	C-2–C-3–O-3	107.4(1)
C-3–C-4–C-5	112.6(1)	C-4–C-3–O-3	109.8(1)
C-4–C-5–C-6	111.3(1)	C-3–C-4–O-4	107.6(1)
C-5–C-6–C-1	109.7(1)	C-5–C-4–O-4	110.6(1)
C-6–C-1–C-2	110.0(1)	C-4–C-5–O-5	106.5(1)
C-2–C-1–O-1	109.4(1)	C-6–C-5–O-5	112.1(1)
C-6–C-1–O-1	109.6(1)	C-1–C-6–O-6	108.1(1)
C-1–C-2–O-2	111.0(1)	C-5–C-6–O-6	111.8(1)
Bonds	*Torsion angles*	*Bonds*	*Torsion angles*
C-6–C-1–C-2–C-3	−54.8(2)	C-3–C-4–C-5–C-6	56.2(2)
C-6–C-1–C-2–O-2	178.2(1)	C-3–C-4–C-5–O-5	178.7(1)
O-1–C-1–C-2–C-3	66.3(2)	O-4–C-4–C-5–C-6	176.6(1)
O-1–C-1–C-2–O-2	−60.6(2)	O-4–C-4–C-5–O-5	−60.9(2)
C-1–C-2–C-3–C-4	51.6(2)	C-4–C-5–C-6–C-1	−57.7(2)
C-1–C-2–C-3–O-3	171.4(2)	C-4–C-5–C-6–O-6	62.2(2)
O-2–C-2–C-3–C-4	177.9(1)	O-5–C-5–C-6–C-1	−176.9(1)
O-2–C-2–C-3–O-3	−62.2(2)	O-5–C-5–C-6–O-6	−57.0(2)
C-2–C-3–C-4–C-5	−52.1(2)	C-5–C-6–C-1–C-2	56.7(2)
C-2–C-3–C-4–O-4	−174.2(1)	C-5–C-6–C-1–O-1	−64.3(2)
O-3–C-3–C-4–C-5	−170.5(1)	O-6–C-6–C-1–C-2	−65.4(2)
O-3–C-3–C-4–O-4	67.4(2)	O-6–C-6–C-1–O-1	173.6(2)

[a] Bond lengths in Å; valence and torsion angles in degrees.

angles are shown in Table III. The variation over similar bonds or similar angles is comparable to that observed in the other cyclitol crystal-structures.

As in *myo*-inositol, the conformation is close to that of an ideal chair, with the puckering parameters[16] given in Table IV. In the phosphate and salt complexes of *myo*-inositol and *epi*- and *muco*-inositol, larger deviations of θ from 180° are observed. In the *myo*-inositols, this is due to crystal-field effects. In *epi*- and *muco*-inositol, it is a consequence of the repulsion of the syn-diaxial hydroxyl groups which are involved in intermolecular hydrogen-bonds. The degree of puckering, Q, and the deviations from the ideal chair, θ, are very similar to those observed in the crystal structures of the pyranoses and pyranosides[18].

TABLE IV

COMPARISON OF PUCKERING PARAMETERS OF THE CYCLOHEXANE RING OF INOSITOL STEREOISOMERS IN THEIR CRYSTAL STRUCTURES[a]

Isomer	Q	θ
L-Inositol	0.561	4.4
myo-Inositol (I)	0.593	3.0
myo-Inositol (II)	0.574	3.9
myo-Inositol · 2 H_2O	0.584	1.8
myo-Inositol 2-phosphate · H_2O	0.580	6.1
myo-Inositol · $MgCl_2$ · 4 H_2O	0.563	9.9
myo-Inositol · $CaBr_2$ · 5 H_2O	0.568	6.4
epi-Inositol	0.582	6.8
epi-Inositol · $SrCl_2$ · 5 H_2O	0.588	6.0
muco-Inositol	0.566	10.4

[a] Values for Q in Å; for θ, in degrees. The ideal chair is defined as that with $\theta = 0°$. When $\theta \sim 0°$, differences in the third parameter, ϕ, are insignificant[17].

The hydroxyl hydrogen atoms do not comply with the molecular symmetry. The hydrogen-bond geometry is shown in Fig. 2, with the covalent O–H distances normalized to[19] 0.97 Å. It consists of infinite chains, as is common in the alditols and in most polyhydroxy compounds having only hydroxyl functional groups[20]. The infinite chains are cross-linked by the intramolecular component of a three-center bond from O-4–H to O-6 and O-5 in the adjacent chains. Fig. 3 shows a stereoview of the crystal structure.

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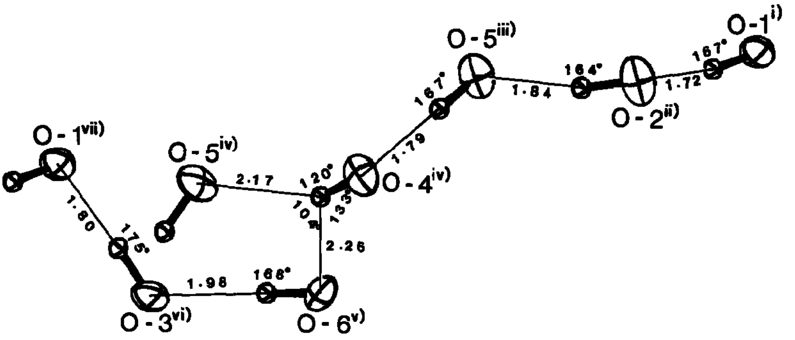

Fig. 2. Hydrogen bonding in the crystal structure of L-*chiro*-inositol. [The H---O distances (Å) and O–H---O angles (degrees) were obtained by normalizing the O–H covalent bond distances to the standard values of 0.97 Å. Symmetry code: (i) x, y, z; (ii) $1 - x, \frac{1}{2} + y, 1 - z$; (iii) $2 - x, \frac{1}{2} + y, 1 - z$; (iv) $x, 1 + y, 1 + z$; (v) $x, 1 + y, z$ (vi) $2 - x, \frac{3}{2} + y, 1 - z$; and (vii) $1 + x, 1 + y, 1 + z$.]

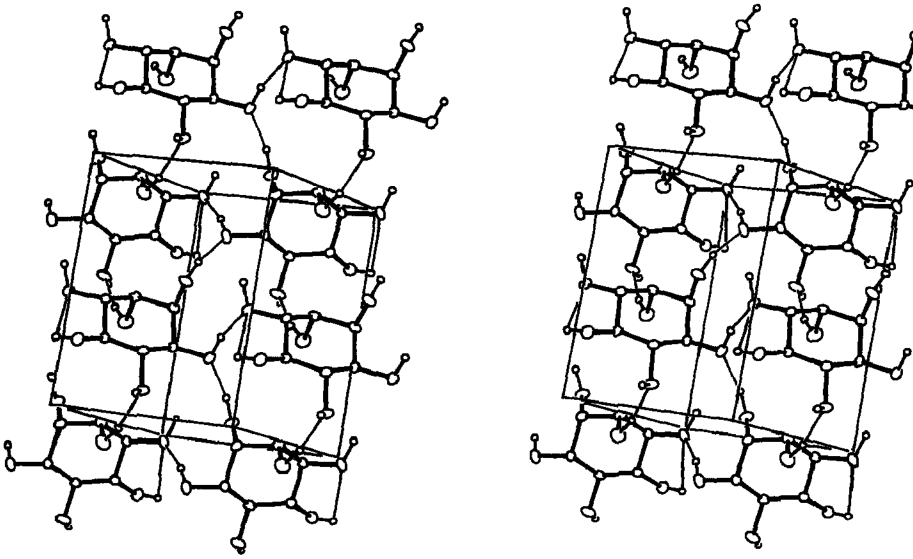

Fig. 3. Stereodiagram of L-*chiro*-inositol, by ORTEP[21]. [View is down the *c* axis, with hydrogen bonds shown by thin lines. Methine hydrogen atoms are omitted.]

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