

## THE X-RAY CRYSTAL STRUCTURE OF 2,5-ANHYDRO-L-IDITOL

PETER KÖLL

*University of Oldenburg, Department of Chemistry, Organic Chemistry Laboratory, C.v. Ossietzky-Str. 9–11, D-2900 Oldenburg (Federal Republic of Germany)*

AND JURGEN KOPF

*University of Hamburg, Institute of Inorganic Chemistry, Martin-Luther-King-Platz 6, D-2000 Hamburg 13 (Federal Republic of Germany)*

(Received April 16th, 1985; accepted for publication, September 30th, 1985)

### ABSTRACT

The crystal and molecular structure of 2,5-anhydro-L-iditol (**1**) has been determined by X-ray diffraction using direct methods to a final residual value of  $R = 0.051$  for 1151 reflections. The crystals of **1** are orthorhombic, space group  $P2_12_12_1$ ,  $a = 739.9$  (4),  $b = 902.0$  (5),  $c = 1109.1$  (6) pm, with four molecules in the unit cell. In the crystal, the molecule does not show the expected  $C_2$  symmetry: the ring C–O bonds differ in length (145.0 vs. 143.6 pm) and the conformation of the tetrahydrofuran ring deviates slightly from the ideal  $^3T_4(L)$  arrangement (puckering parameters  $Q = 39.9$  pm,  $\Phi_1 = 95.5^\circ$ ). Molecules are interlinked by a network of strong intermolecular hydrogen-bonding involving all hydroxyl groups. Except for O-3, all oxygen atoms act as acceptors in this pattern.

### INTRODUCTION

In general, 2,5-anhydrohexitols and their derivatives can be considered as homomorphs of ketohexofuranosides and furanoid C-glycosides. They have recently attracted attention because they act as substrates for hexokinases and they inhibit the growth of some carcinoma-cells<sup>1–3</sup>. This is especially true for 2,5-anhydro-D-mannitol, for which a crystal structure analysis has been reported<sup>4</sup>. Also, 2,5-anhydro-L-iditol (**1**) is of interest as a precursor in the synthesis of muscarine analogues<sup>5</sup>. Both compounds are long known<sup>6,7</sup> and recently the enantiomer of **1** was described<sup>3</sup>.

Our interest in this class of compounds derived from studies of the dehydration products of hexitols at high temperatures<sup>8</sup> and from investigations on the conformations of anhydro sugars having furanoid structures<sup>9</sup>.

2,5-Anhydro-L-iditol (**1**) was prepared<sup>8</sup> together with 2,5-anhydro-D-mannitol by dehydration of D-glucitol. 2,5-Anhydro-L-iditol (**1**) has an axis of symmetry ( $C_2$ ). This is evident from the n.m.r. spectrum which shows only a

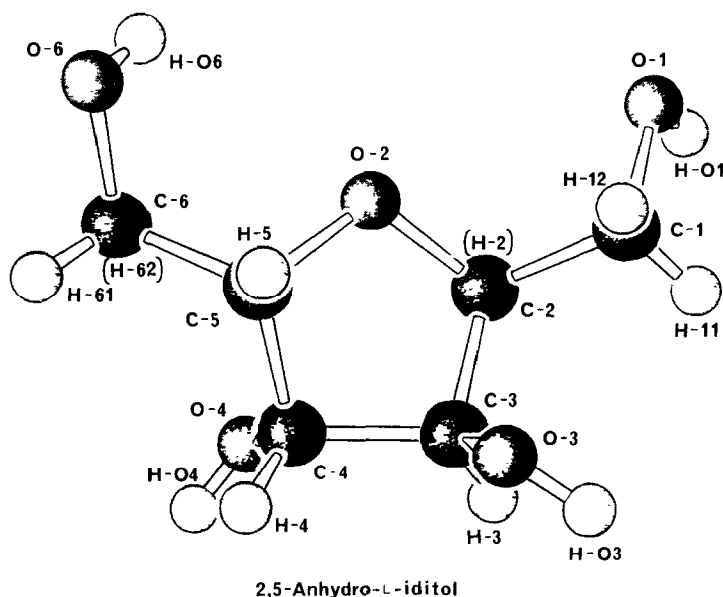


Fig. 1. SCHAKAL<sup>14</sup> representation of one molecule of 2,5-anhydro-L-iditol (**1**).

symmetry-reduced multiplicity of signals. The situation can be different in the crystalline state, especially, when intermolecular hydrogen-bonds are present.

## RESULTS AND DISCUSSION

The crystal and molecular structure of **1** was determined in the usual way by applying direct methods using MULTAN<sup>10</sup> and SHELX<sup>11</sup> programmes. Experimental data are shown in Table I. Table II gives the atomic coordinates for the carbon and oxygen atoms. The resulting three-dimensional structure of one of the equivalent molecules in the unit cell is shown in Fig. 1. This is a SCHAKAL representation<sup>12</sup>, in which the atom numbering scheme is also given. Bond lengths and bond angles involving carbon and oxygen atoms are summarised in Table III. For convenience in conformational discussions, selected torsion angles are also listed (Table IV)\*.

From the orthorhombic space-group  $P2_12_12_1$  and the number of molecules in the unit cell, it is evident that, in the crystalline state, **1** cannot adopt a symmetrical conformation. The conformation of the tetrahydrofuran ring is  $^3T_4(L)$  [corresponding to  $^2T_3(L)$  in normal furanoses and to  $^4T_3(D)$  for the enantiomer of **1**] which

\*Lists of observed and calculated structure amplitudes, atomic coordinates of the hydrogen atoms, anisotropic thermal parameters for carbon and oxygen atoms, and isotropic parameters for hydrogen are deposited with, and can be obtained from, Elsevier Science Publishers B.V., BBA Data Deposition, P.O. Box 1527, Amsterdam, The Netherlands. Reference should be made to No. BBA/DD/332/Carbo-hydr. Res., 147 (1986) 169–174.

TABLE I

## CRYSTALLOGRAPHIC DATA

Formula	C <sub>6</sub> H <sub>12</sub> O <sub>5</sub>
Mol. wt.	164.16
M.p.	117–118°
Space group	<i>P</i> 2 <sub>1</sub> 2 <sub>1</sub> 2 <sub>1</sub>
Cell constants	
<i>a</i>	739.9(4) pm
<i>b</i>	902.0(5) pm
<i>c</i>	1109.1(6) pm
$\alpha = \beta = \gamma$	90°
Volume	740.2(7) pm <sup>3</sup> × 10 <sup>6</sup>
<i>Z</i>	4
<i>F</i> (000)	352
Density (calc.)	1.47 g.cm <sup>-3</sup>
$\lambda$ (MoK $\alpha$ )	70.9261 pm
$\mu$ (MoK $\alpha$ )	0.84 cm <sup>-1</sup>
Reflections measured (3° ≤ 2 $\theta$ ≤ 60°)	1268
Reflections with <i>F</i> > 3 $\sigma$ ( <i>F</i> )	1151
Final residual factors	
<i>R</i>	0.051
<i>R<sub>w</sub></i> ( $w_i = 1.619/[\sigma^2(F) + 0.00003 \cdot F^2]$ )	0.048
Diffractometer	Hilger and Watts Y 290

TABLE II

FRACTIONAL POSITIONAL PARAMETERS OF CARBON AND OXYGEN ATOMS IN 2,5-ANHYDRO-L-IDITOL (1)  
(E.S.D. IN PARENTHESES)

Atom	<i>x</i>	<i>y</i>	<i>z</i>
C-1	1187(4)	5434(3)	5099(2)
C-2	98(3)	5071(3)	6207(2)
C-3	-372(4)	6404(3)	6989(2)
C-4	-2153(3)	5915(3)	7557(2)
C-5	-3059(3)	5149(3)	6499(2)
C-6	-4465(4)	4002(3)	6806(3)
O-1	1765(3)	4131(2)	4472(2)
O-2	-1622(2)	4439(2)	5848(2)
O-3	-749(3)	7670(2)	6269(2)
O-4	-1822(3)	4880(2)	8504(2)
O-6	-5235(3)	3367(2)	5750(2)

is slightly distorted in direction to *E*<sub>4</sub>(L). Puckering parameters<sup>13</sup> are *Q* = 39.9 pm and  $\Phi$  = 95.5° of which the first gives the amplitude of pseudorotation and the second the phase angle on the pseudorotation itinerary.

The <sup>13</sup>C-n.m.r. spectrum of **1** in solution shows<sup>14</sup> only three resonances, consistent with C<sub>2</sub> symmetry. The <sup>1</sup>H-n.m.r. spectrum also shows a high degree of symmetry, and the coupling constants indicate <sup>3</sup>*T*<sub>4</sub>(L) as the average conformation in solution<sup>15</sup>.

TABLE III

ATOMIC DISTANCES (pm) AND BOND ANGLES (DEGREES) FOR CARBON AND OXYGEN ATOMS IN 2,5-ANHYDRO-L-IDITOL (**1**) (E S D IN PARENTHESES)

Distance		Angle	
C-1-C-2	150.5(4)	C-2-O-2-C-5	109.7(2)
C-2-C-3	152.3(3)	C-2-C-1-O-1	112.2(2)
C-3-C-4	152.6(4)	O-2-C-2-C-1	109.3(2)
C-4-C-5	151.8(3)	C-3-C-2-O-2	105.5(2)
C-5-C-6	150.6(4)	C-3-C-2-C-1	114.5(2)
C-1-O-1	143.1(3)	C-2-C-3-O-3	111.0(2)
C-2-O-2	145.0(3)	C-4-C-3-O-3	107.2(2)
C-3-O-3	142.1(3)	C-2-C-3-C-4	101.8(2)
C-4-O-4	142.6(3)	C-3-C-4-O-4	110.2(2)
C-5-O-2	143.6(3)	C-5-C-4-O-4	110.4(2)
C-6-O-6	142.3(3)	C-3-C-4-C-5	101.2(2)
		C-4-C-5-O-2	105.3(2)
		C-6-C-5-O-2	108.6(2)
		C-4-C-5-C-6	116.3(2)
		C-5-C-6-O-6	111.5(2)

TABLE IV

TORSION ANGLES (DEGREES) IN 2,5-ANHYDRO-L-IDITOL (**1**) (E S D IN PARENTHESES)

Bond	Angle	Bond	Angle
C-2-O-2-C-5-C-6	-142.3(2)	O-3-C-3-C-4-O-4	-166.4(2)
C-2-O-2-C-5-C-4	-17.1(3)	C-2-C-3-C-4-O-4	77.0(2)
C-5-O-2-C-2-C-1	-132.3(2)	C-2-C-3-C-4-C-5	-39.8(2)
C-5-O-2-C-2-C-3	-8.7(3)	O-3-C-3-C-4-C-5	76.9(2)
O-1-C-1-C-2-O-2	-68.6(3)	O-4-C-4-C-5-O-2	-81.0(2)
O-1-C-1-C-2-C-3	173.4(2)	C-3-C-4-C-5-O-2	35.6(2)
O-2-C-2-C-3-O-3	-83.2(2)	C-3-C-4-C-5-C-6	155.9(2)
C-1-C-2-C-3-O-3	37.1(3)	O-4-C-4-C-5-C-6	39.3(3)
C-1-C-2-C-3-C-4	150.8(2)	O-2-C-5-C-6-O-6	-62.0(3)
O-2-C-2-C-3-C-4	30.6(2)	C-4-C-5-C-6-O-6	179.5(2)

In contrast to the n.m.r. data, the X-ray data indicate that the conformation of **1** in the solid state is distorted from perfect  ${}^3T_4(L)$  which would correspond<sup>13</sup> to a phase angle of 90°. Symmetry-related atoms in the n.m.r. experiment are no longer equivalent in the X-ray experiment. Noteworthy, for example, is the difference in length of the two ring C-O bonds (145.0 and 143.6 pm, respectively) and the differences of related torsion angles, e.g., O-2-C-5-C-4-C-3 35.6° vs. O-2-C-2-C-3-C-4 30.6°.

These values are consistent with analogous observations in the X-ray investigation of 2,5-anhydro-D-mannitol<sup>4</sup>. This molecule adopts an equivalent distorted  ${}^4T_3(D) \sim {}^3T_4(L)$  conformation with all substituents in quasi-equatorial positions. Only the hydroxymethyl groups in **1** are in this favoured orientation, and HO-3 and HO-4 adopt quasi-axial positions.

TABLE V

HYDROGEN BONDS IN 2,5-ANHYDRO-L-IDITOL (1) (WEAK INTERACTIONS IN PARENTHESES)

Hydrogen bonds	Distances (pm)			Angle (degrees) O-H...O
	O-H	O...H	O...O	
O-1-H-O1 ··· O-6 (I) <sup>a</sup>	89.9	182.7	272.2	173.4
O-3-H-O3 ··· O-4 (II)	90.5	189.2	276.7	162.0
O-4-H-O4 ··· O-2 (III)	84.1	207.4	290.9	171.9
(O-4-H-O4 ··· O-6 (III))	84.1	287.8	332.0	(114.8)
O-6-H-O6 ··· O-1 (IV)	77.9	196.8	270.7	158.3
(O-6-H-O6 ··· O-2 (IV))	77.9	297.5	325.5	(104.2)

<sup>a</sup>Oxygen atoms in symmetry-related molecules in the crystalline lattice, as follows: (I)  $x + 1, y, z$ ; (II)  $-x, y + 1/2, -z + 3/2$ ; (III)  $-x - 1/2, -y + 1, z + 1/2$ ; (IV)  $x - 1/2, -y + 1/2, -z + 1$ .

The present data reveal that the hydroxymethyl groups at positions 2 and 5 adopt *-gauche* dispositions (relevant torsion angles,  $-68.6^\circ$  and  $-62.0^\circ$ , respectively). This finding is in contrast to the data on the *D-manno* analogue in which a  $-g, +g$  arrangement is observed<sup>4</sup>. The relevant structural relationships between 2,5-anhydrohexitols and ketofuranoses have been discussed<sup>4</sup> with respect to these observations.

Strong, intermolecular forces are the apparent cause of the molecular distortions observed. These forces arise from different types of hydrogen-bonding interactions (Table V) in which all hydroxyl groups act as donors and, except for O-3, all oxygen atoms act as acceptors. Thus, HO-1 interacts with O-6 of another molecule and HO-3, which is bonded to O-3 with no acceptor function, also shows only a strong interaction with O-4 of a neighbouring molecule. The two remaining hydroxyl groups, HO-4,6, form, in addition to strong forces to other oxygen atoms (O-2 and O-1, respectively), further weak interactions that are given in parentheses (in Table V). Therefore, these last two hydrogen bonds are unsymmetrical bifurcated<sup>16</sup>.

## EXPERIMENTAL

The title compound **1** was crystallised from ethanol-ether and obtained as transparent crystals with m.p.  $117-118^\circ$ ,  $[\alpha]_D^{20} +9.0^\circ$  (water); lit.<sup>7</sup> m.p.  $117-118^\circ$ ,  $[\alpha]_D^{20} +9.7^\circ$ . The X-ray structure determination was direct by using conventional methods. Details are given in Table I and the text. Data were collected at room temperature.

## REFERENCES

- 1 W. L. DILLS, JR., T. R. COVEY, P. SINGER, S. NEAL, AND M. S. RAPPAPORT, *Carbohydr. Res.*, **99** (1982) 23-31, and references therein.
- 2 R. D. GUTHRIE, I. D. JENKINS, J. J. WATTERS, M. W. WRIGHT, AND R. YAMASAKI, *Aust. J. Chem.*, **35** (1982) 2169-2173, and references therein.

- 3 D. A. OTERO AND R. SIMPSON, *Carbohydr. Res.*, 128 (1984) 79–86, and references therein.
- 4 S. F. WATKINS, K. A. ABOUD, R. J. VOLL, T. A. W. KOERNER, JR. AND E. S. YOUNATHAN, *Carbohydr. Res.*, 119 (1983) 49–55.
- 5 J. KUSZMANN AND I. PELCZER, *Carbohydr. Res.*, 89 (1981) 103–120.
- 6 B. C. BERA, A. B. FOSTER, AND M. STACEY, *J. Chem. Soc.*, (1956) 4531–4535.
- 7 L. VARGHA, T. PUSKAS, AND E. NAGY, *J. Am. Chem. Soc.*, 70 (1948) 261–262.
- 8 P. KOLL AND M. OELTING, *Tetrahedron Lett.*, 24 (1983) 2557–2558; K. BOCK, C. PEDERSEN, AND H. THØGERSEN, *Acta Chem. Scand., Ser. B*, 35 (1981) 441–449.
- 9 P. KOLL, H.-G. JOHN, AND J. KOPF, *Justus Liebigs Ann. Chem.*, (1982) 639–650; P. KOLL, H. KOMANDER, AND B. MEYER, *ibid.*, (1983) 1310–1331; P. KOLL, A. FORTSCH, AND J. KOPF, *J. Carbohydr. Chem.*, 2 (1983) 189–200; J. KOPF AND P. KOLL, *Carbohydr. Res.*, 135 (1984) 29–46.
- 10 P. MAIN, M. M. WOOLFSON, L. LESSINGER, G. GERMAIN, AND J. P. DECLERCQ, *MULTAN, A System of Computer Programs for the Automatic Solution of Crystal Structures from X-Ray Diffraction Data*, Universities of York (Great Britain) and Louvain (Belgium), 1974.
- 11 G. M. SHELDRICK, *SHELX-76, Programs for Crystal Structure Determination*, University of Cambridge, 1976.
- 12 E. KELLER, *Chem. Unserer Zeit*, 14 (1980) 56–60.
- 13 D. CREMER AND J. A. POPLE, *J. Am. Chem. Soc.*, 97 (1975) 1354–1358.
- 14 K. QUE, JR., AND G. R. GRAY, *Biochemistry*, 13 (1974) 146–153.
- 15 H. THØGERSEN, Thesis, Technical University of Denmark, 1980.
- 16 G. A. JEFFREY AND S. TAKAGI, *Acc. Chem. Res.*, 11 (1978) 264–270.