

The Crystal Structure of Xylitol

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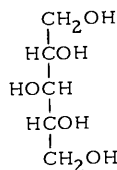
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The crystal structure of xylitol, $C_5H_{12}O_5$, has been determined by application of the tangent phase-refinement method. The space group is $P2_12_12_1$ with four molecules in a unit cell with $a=8.291$, $b=8.970$, $c=8.970$ Å. The molecules are unsymmetrical conformers with a non-planar carbon chain.

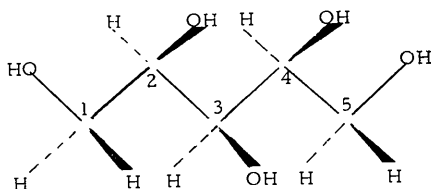
Introduction

Of the six pentitol and hexitol crystal structures that have been studied, all but ribitol have the molecules in the straight carbon-chain conformation (D,L-arabinitol by Hunter & Rosenstein, 1968; galactitol by Berman & Rosenstein, 1968; three forms of D-mannitol by Berman, Jeffrey & Rosenstein, 1968, and by Kim, Jeffrey & Rosenstein, 1968; ribitol by Kim, Jeffrey & Rosenstein, 1969). This distinction is associated with the avoidance of a fourth neighbour interaction of the type $O(n)\cdots O(n+2)$, which would occur in ribitol between O(2) and O(4) at about 2.5 Å, when the carbon atoms are linearly extended. The configurations of the three other polyols are such that this repulsive non-bonding interaction does not occur in the most symmetrical conformers.

Xylitol, $C_5H_{12}O_5$, I in the Fischer & Stahl (1891) convention, also has a close $O(2)\cdots O(4)$ distance in the straight carbon-chain conformation II. Both xylitol and ribitol have *meso* configurations by reason of a mirror plane of symmetry in the symmetrical conformation, e.g. through C(3) in II. Whereas ribitol crystallizes as a racemate of left and right-handed unsymmetrical conformers, xylitol has an enantiomorphous crystal structure in its stable orthorhombic form. The primary purpose of this investigation was to establish the molecular conformation.



I

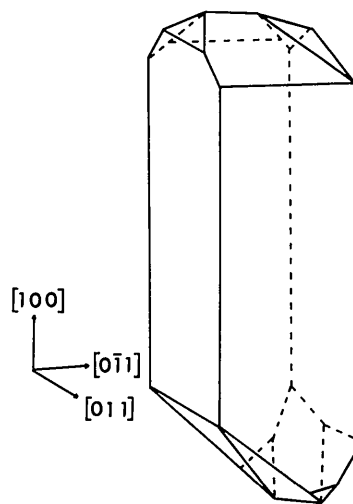


II

Crystal data

Two crystalline forms of xylitol have been reported by Wolfrom & Kohn (1942) and Carson, Waisbrot & Jones (1943): a metastable hygroscopic monoclinic form, m.p. 61°C, and a stable orthorhombic form, m.p. 94°C.

We obtained two different morphologies of the orthorhombic form, m.p. 92–94°C: needles elongated about a with $\{111\}$, $\{011\}$ from tetrahydrofuran, and well-developed prisms with $\{111\}$, $\{110\}$, $\{011\}$ from ethanol, as illustrated below.



The data obtained with Cu $K\alpha$ radiation from these crystals are as follows:

Orthorhombic,
 $a=8.291$ (2) Å
 $b=8.970$ (2)
 $c=8.970$ (5)
 $V=667.1$ Å³
 $D_m=1.520$ g.cm⁻³
 $D_x=1.515$ g.cm⁻³
 $Z=4$
 $\mu_{Cu K\alpha}=11.94$ cm⁻¹.

Space group $P2_12_12_1$, from systematic absences $h00$ with h odd, $0k0$ with k odd, $00l$ with l odd.

Attempts to obtain the lower melting monoclinic form from alcoholic solutions either at room temperature or close to 0°C have hitherto been unsuccessful. We invariably grow the orthorhombic crystals. It is interesting to note that although xylitol was first prepared as a syrup in 1891, there was no report of crystal-

lization until fifty years later, when it was the metastable form that was obtained first. Having now obtained the stable form, it is difficult to recover the metastable crystals. This behavior is reminiscent of that observed with D-mannitol, where polymorphism has been reported but it is difficult to reproduce the crys-

Table 1. Fractional atomic coordinates and anisotropic thermal parameters in xylitol

Key to atomic numbering is given in Fig. 1. The estimated standard deviations given in parentheses refer to the last decimal positions. The temperature factor expression used was

$$\exp [-(\beta_{11}h^2 + \beta_{22}k^2 + \beta_{33}l^2 + 2\beta_{12}hk + 2\beta_{13}hl + 2\beta_{23}kl)]$$

	<i>x</i>	<i>y</i>	<i>z</i>	β_{11}	β_{22}	β_{33}	β_{12}	β_{13}	β_{23}
C(1)	0.2832 (3)	0.5642 (3)	0.5648 (3)	0.0072 (3)	0.0072 (3)	0.0081 (3)	0.0004 (3)	-0.0001 (2)	-0.0011 (3)
C(2)	0.4513 (3)	0.5395 (2)	0.5030 (3)	0.0068 (3)	0.0048 (2)	0.0071 (2)	0.0006 (2)	-0.0010 (2)	-0.0011 (2)
C(3)	0.5783 (2)	0.5588 (2)	0.6249 (2)	0.0063 (3)	0.0053 (2)	0.0062 (2)	0.0003 (2)	-0.0006 (2)	-0.0007 (2)
C(4)	0.7508 (3)	0.5250 (2)	0.5724 (3)	0.0064 (3)	0.0054 (3)	0.0067 (2)	-0.0004 (2)	0.0008 (2)	-0.0010 (2)
C(5)	0.7741 (3)	0.3605 (3)	0.5436 (3)	0.0064 (3)	0.0055 (2)	0.0097 (3)	-0.0002 (3)	-0.0011 (2)	-0.0004 (2)
O(1)	0.1630 (2)	0.5342 (2)	0.4563 (2)	0.0057 (2)	0.0075 (2)	0.0110 (2)	-0.0009 (2)	0.0011 (2)	-0.0008 (2)
O(2)	0.4796 (2)	0.6415 (2)	0.3815 (2)	0.0086 (2)	0.0066 (2)	0.0062 (2)	0.0013 (2)	-0.0011 (2)	-0.0014 (2)
O(3)	0.5692 (2)	0.7093 (2)	0.6798 (2)	0.0094 (3)	0.0053 (2)	0.0072 (2)	-0.0002 (2)	-0.0002 (2)	0.0004 (2)
O(4)	0.8646 (2)	0.5667 (2)	0.6850 (2)	0.0068 (2)	0.0076 (2)	0.0082 (2)	-0.0007 (2)	0.0022 (2)	-0.0005 (2)
O(5)	0.9276 (2)	0.3289 (2)	0.4784 (2)	0.0063 (2)	0.0060 (2)	0.0097 (2)	0.0004 (2)	-0.0010 (2)	0.0008 (2)
H(C1)	0.267	0.494	0.650						
H'(C1)	0.273	0.669	0.599						
H(C2)	0.456	0.436	0.465						
H(C3)	0.556	0.488	0.708						
H(C4)	0.773	0.582	0.481						
H(C5)	0.766	0.305	0.640						
H'(C5)	0.688	0.326	0.473						
H(O1)	0.130	0.627	0.419						
H(O2)	0.518	0.591	0.308						
H(O3)	0.577	0.701	0.769						
H(O4)	0.908	0.662	0.662						
H(O5)	0.990	0.411	0.500						

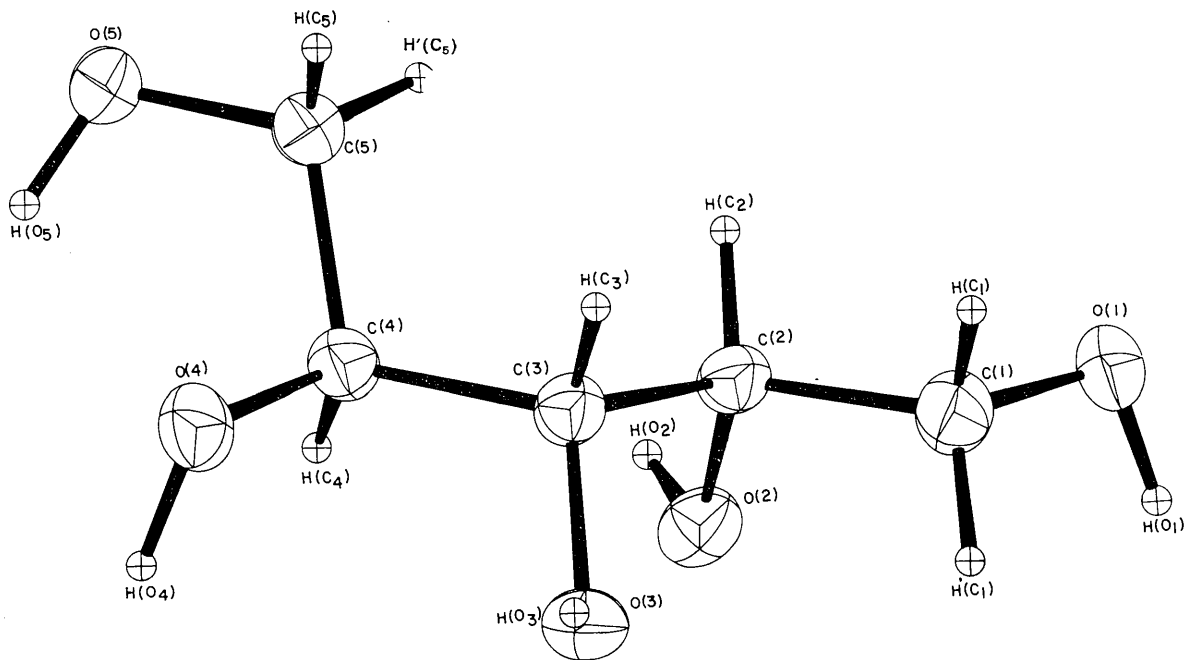


Fig. 1. Molecular conformation observed in the crystal structure of xylitol, showing atomic numbering used and the anisotropic thermal ellipsoids.

Table 2. Observed and calculated structure factors

Columns are: index, |0|F_obs|, |0|F_calc|, 10A_ealc, 10B_ealc.

* Indicates unobserved reflections.

Table with multiple columns containing numerical data for structure factors. The table is organized into rows and columns, with some cells containing multiple values separated by spaces. The data represents observed and calculated structure factors for various reflections.

tals (Berman, Jeffrey & Rosenstein, 1968; Kim, Jeffrey & Rosenstein, 1968). The availability of appropriate nuclei in the laboratory is clearly a determining factor, as is well-known to carbohydrate chemists.

Experimental

The unit-cell parameters were measured on a Picker four-circle diffractometer with $\text{Cu } K\alpha$ radiation (1.5418 \AA) from fifteen strong $h00$ and $0kl$ reflections and refined by least squares. The intensities were measured from an acicular crystal $0.5 \times 10.10 \times 0.10 \text{ mm}$ using $\text{Cu } K\alpha$ radiation with the Picker diffractometer in the $\theta/2\theta$ scanning mode. The scan width was varied from 2° at $2\theta=10^\circ$ to 3.25° at $2\theta=130^\circ$. Of the 904 reflections possible, 672 were recorded of which 15 had intensities less than two standard deviations above background. No absorption corrections were applied in converting the intensities to structure amplitudes.

Structure determination and refinement

The phases of the 105 largest normalized structure factors were determined by application of the tangent phase-refinement method (Karle & Hauptman, 1956) using an IBM 7090 version of the Hall (1968) direct phasing methods. The indices of the five starting re-

flections, their phases and $|E_{HKL}|$ values were as follows: $7\ 2\ 0, \pi/2, 2.83$; $0\ 7\ 2, \pi/2, 2.66$; $6\ 0\ 3, \pi/2, 2.32$; $0\ 5\ 1, \pi/2, 3.27$; $7\ 7\ 1, \pi, 2.66$. The ten highest peaks on the resulting E map were consistent with a chemically reasonable model. Structure factor calculations based on this model with a uniform isotropic temperature factor gave an initial R value of 0.30 for 672 reflections.

The structure was refined isotropically by three cycles of block-diagonal least squares to $R=0.09$, and anisotropically to $R=0.04$ using an IBM 1130 program by Shiono (1968). All hydrogen atoms were located in difference syntheses. A final refinement with full-matrix least squares (Shiono, 1966) included all parameters except those of the hydrogen atoms. The final parameters are given in Table 1 and the corresponding structure factors in Table 2. The final R value was 0.034. The thermal parameters are illustrated by an *ORTEP* plot in Fig. 1.

Description of the structure

The conformation of the molecule is shown in Fig. 1. As in ribitol, the carbon chain is non-planar. Atoms C(1) to C(4) lie in one plane to within 0.025 \AA . If this plane is extended to include O(1) and O(4), the deviations remain small, as shown in Table 3.

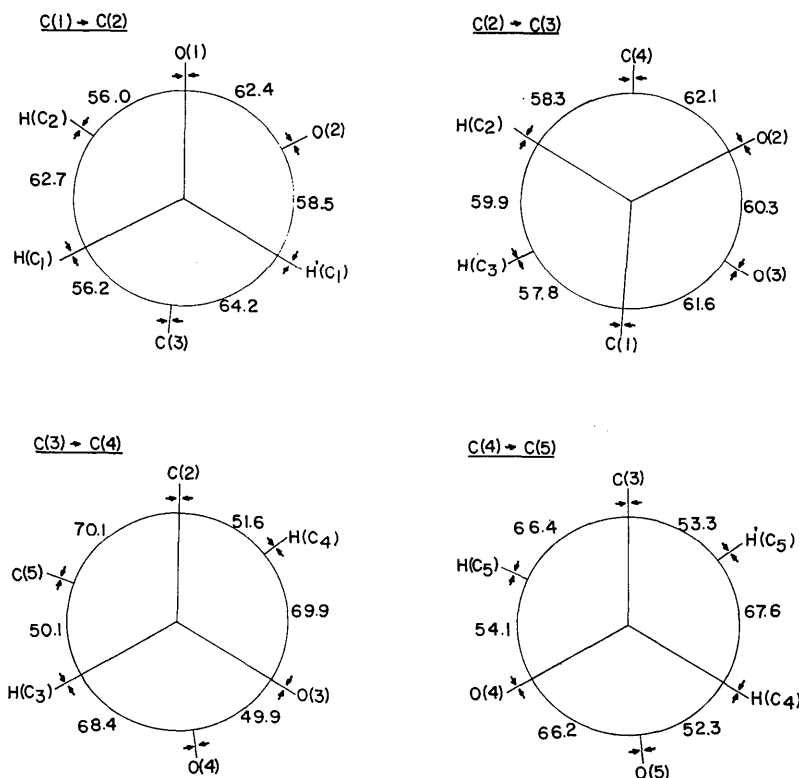


Fig. 2. Newman projections down the C-C bonds in xylitol, showing the conformation angles in degrees.

Table 3. *Least squares planes in xylitol*Equation for plane: $AX + BY + CZ = D$, where X, Y, Z are in Å.

Atoms in plane	Atoms not in plane	Distance from best plane	Given constant
C(1)		0.024	$A = 0.092$
C(2)		-0.023	$B = 0.967$
C(3)		-0.025	$C = 0.239$
C(4)		0.024	$D = 4.058$
	C(5)	1.371	
	O(1)	0.142	
	O(4)	-0.182	
C(3)		-0.086	$A = -0.293$
C(4)		-0.041	$B = 0.212$
C(5)		0.087	$C = 0.932$
O(3)		0.065	$D = 5.655$
O(5)		-0.025	
	C(1)	-1.316	
	C(2)	-1.377	
C(1)		-0.003	$A = 0.077$
C(2)		0.075	$B = 0.943$
C(3)		-0.035	$C = -0.324$
C(4)		-0.058	$D = 3.316$
O(1)		-0.018	
O(4)		0.039	
	C(5)	-1.352	

The conformation is the same as that of ribitol, except for the interchange of O(3) and H(C3), as required by the difference in configuration, and for the orientation of O(1). In xylitol, O(1) lies in the segment of the

Newman diagram, shown in Fig. 2, between O(2) and H(C2), and therefore forms a planar zigzag chain with C(1), C(2), C(3) and O(4), see Table 4. In ribitol, O(1) lies in the segment between O(2) and C(3). It is clear why xylitol does not have the same conformation about C(1)-C(2) as ribitol, since this would incur a fourth neighbour interaction between O(1) and O(3) similar to that invoked between O(2) and O(4) to explain the non-planar carbon chain. It is not apparent, however, why the C(1)-C(2) conformation of ribitol is not the same as in xylitol. In the 'free' molecule of ribitol, the conformer with O(1) staggered between O(2) and H(C2) leading to a planar O(1)-C(1)-C(2)-C(3)-C(4)-O(4) zigzag chain should have a lower energy than that observed in the crystal structure. This energy difference is presumably smaller than that incurred by an O(1)···O(3) or O(2)···O(4) interaction and can be more easily surpassed by differences in the hydrogen-bond crystal field forces. In xylitol, the conformer observed in the crystal is that which might be expected to have the lowest energy and the highest population in solution. The evidence from nuclear magnetic resonance studies of certain acyclic sugar derivatives supports this view (El Khadem, Horton & Page, 1968; Horton & Wander, 1969).

The bond lengths and angles are given in Table 4. As with ribitol, the C-C bonds at the ends of the molecule are about 0.02 Å shorter than those within.

Table 4. *Intramolecular distances and angles in xylitol*

The estimated standard deviations given in parentheses refer to the last decimal positions of the respective values.

i	j	D_{ij}	D_{ij}^*	i	j	k	$\angle (ijk)$
C(1)	C(2)	1.517 (4) Å	1.517 Å	C(1)	C(2)	C(3)	110.8 (2)°
C(2)	C(3)	1.527 (3)	1.529	C(2)	C(3)	C(4)	113.6 (2)
C(3)	C(4)	1.536 (3)	1.537	C(3)	C(4)	C(5)	111.4 (2)
C(4)	C(5)	1.510 (3)	1.513	O(1)	C(1)	C(2)	111.6 (2)
C(1)	O(1)	1.419 (3)	1.420	O(2)	C(2)	C(1)	109.5 (2)
C(2)	O(2)	1.442 (3)	1.444	O(2)	C(2)	C(3)	110.9 (2)
C(3)	O(3)	1.438 (2)	1.440	O(3)	C(3)	C(2)	108.4 (2)
C(4)	O(4)	1.431 (3)	1.433	O(3)	C(3)	C(4)	109.8 (2)
C(5)	O(5)	1.429 (3)	1.429	O(4)	C(4)	C(3)	110.2 (2)
C(1)	H(C1)	1.00		O(4)	C(4)	C(5)	106.9 (2)
C(1)	H'(C1)	0.99		O(5)	C(5)	C(4)	112.2 (2)
C(2)	H(C2)	0.99					
C(3)	H(C3)	1.00					
C(4)	H(C4)	0.99					
C(5)	H(C5)	1.00					
C(5)	H'(C5)	1.00					
O(1)	H(O1)	0.94					
O(2)	H(O2)	0.86					
O(3)	H(O3)	0.81					
O(4)	H(O4)	0.95					
O(5)	H(O5)	0.92					

Mean values calculated from $l = \frac{\sum (l_i)}{\sum (1/\sigma_i^2)} / \sum (1/\sigma_i^2)$.

$$\sigma_{\text{mean}} = [\sum (l - l_i)^2 / N - 1]^{1/2}$$

C-C	1.523 (11) Å
C-O	1.433 (9)
C-C-C	111.9 (15)°
O-C-C	109.9 (17)

 D_{ij}^* = bond lengths corrected for libration.

This has been observed to a greater or lesser degree in all the polyol structures. This difference can be removed wholly or in part by corrections for thermal

motion assuming rigid-body libration. Therefore the chemical significance of this observation, if any, is obscured by uncertainty in the application of thermal

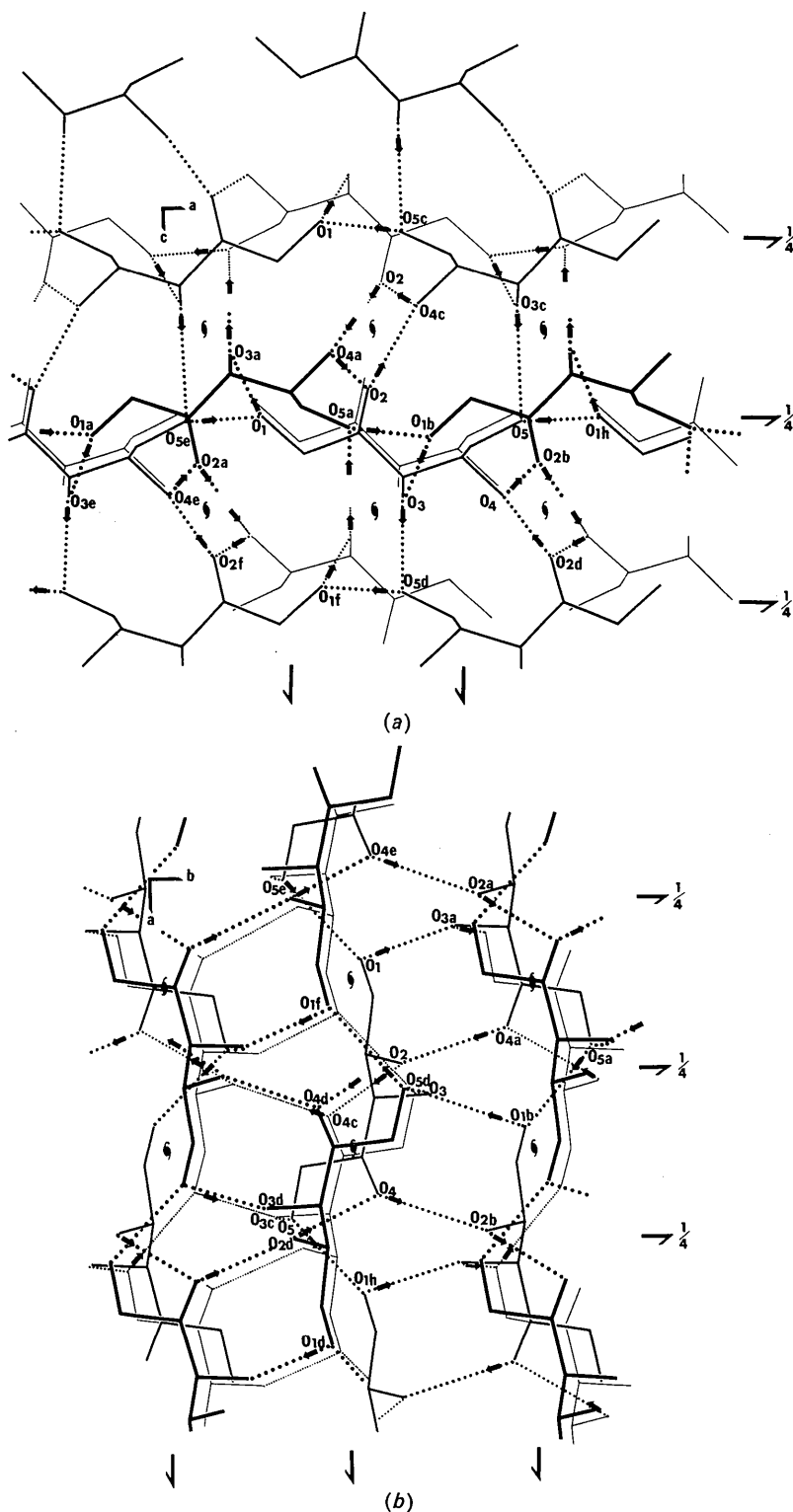


Fig. 3. The crystal structure of xylitol. Solid lines indicate primary C-C and C-O bonds. Dotted lines represent hydrogen bonds, with arrows pointing in the donor direction, (a) viewed down the *b* axis, (b) viewed down the *c* axis.

Table 5. Intermolecular hydrogen bond distances and angles

<i>i</i>	<i>j</i>	<i>k</i>	<i>l</i>	D_{jk}	$\angle(ijk)$	$\angle(jkl)$
C(1)	O(1)	O(3A)	C(3A)	2.718 Å	110.4°	128.7°
C(2)	O(2)	O(4C)	C(4C)	2.873	97.2	124.0
C(3)	O(3)	O(5D)	C(5D)	2.700	102.7	116.1
C(4)	O(4)	O(2B)	C(2B)	2.849	108.2	133.3
C(5)	O(5)	O(1H)	C(1H)	2.690	122.7	126.0

Symmetry code

<i>A</i>	$-\frac{1}{2} + x$	$1\frac{1}{2} - y$	$1 - z$
<i>B</i>	$\frac{1}{2} + x$	$1\frac{1}{2} - y$	$1 - z$
<i>C</i>	$1\frac{1}{2} - x$	$1 - y$	$-\frac{1}{2} + z$
<i>D</i>	$1\frac{1}{2} - x$	$1 - y$	$\frac{1}{2} + z$
<i>E</i>	$-1 + x$	y	z
<i>H</i>	$1 + x$	y	z

motion corrections. The same applies to the apparent systematic shortening of the C–O bonds attached to the terminal carbon atoms. The angles are similar to those observed in ribitol, with a less systematic tendency for those in the carbon chain to be about 2° greater.

The molecular packing and hydrogen-bonding is shown in Fig. 3(a) and (b); the hydrogen bond distances and angles are given in Table 5. As is general in polyol structures, all hydroxyl groups are involved in the hydrogen-bonding and each forms one donor and one acceptor bond. The range of O–(H)···O distances is 2.690 to 2.873 Å, and the hydrogen atoms deviate from the line of centers by less than 0.18 Å, except for H(O5) which is 0.31 Å away from the line of O(5)···O(1). Xylitol is 4 per cent denser than ribitol, but there is no obvious correlation with the intermolecular distances; in fact, the hydrogen-bond distances in xylitol vary over a wider range with a mean separation which is greater than that in ribitol.

The hydrogen bond scheme consists of four-link infinite spirals, *i.e.* O(2) → O(4) → O(2) → O(4) and six-link infinite spirals, *i.e.* O(5) → O(1) → O(3) → O(5) → O(1) → O(3) →, both about the screw axes parallel to **b**. As in ribitol, the molecules tend to align parallel when viewed down two of the principal axes, as shown in Fig. 3.

Since the space group is enantiomorphic, all the molecules have the same sense and resolution of the different handed conformers takes place on crystallization. This is in contrast to the other *meso* polyols, ribitol and galactitol, which crystallize as racemates. It is tempting to speculate that the elusive monoclinic form may be the conformational racemate.

If the differences in conformational energy are large enough they should become recognizable factors in determining the course of chemical reactions. Most discussions of the favored ring structures in the polyol acetals, for example, are based on configurational differences only, rather than both configurational and conformational (Barker & Bourne, 1952). It is noteworthy that the sterically most favored conformations of the preferred di-*O*-isopropylene derivatives of ribitol, xylitol and arabinitol have the pentitol residue in the

same conformation as observed in the crystal structures of the pentitol itself; *i.e.* a non-planar carbon chain conformation in ribitol and xylitol and planar carbon chain conformation in arabinitol. These preferred derivatives are 1,2;4,5-di-*O*-isopropylidene ribitol, 2,3;4,5-di-*O*-isopropylidene xylitol and 2,3;4,5-di-*O*-isopropylidene arabinitol (Nakagawa, Tokuoka, Shinoto, Yoshimura & Sato, 1967).

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