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X-RAY CRYSTAL STRUCTURE OF MALTITOL (4-*O*-α-D-GLUCOPYRANOSYL-D-GLUCITOL)

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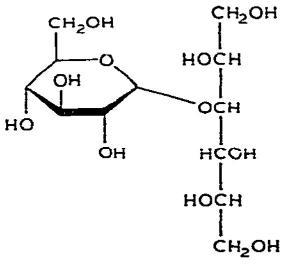
ABSTRACT

Maltitol, crystallised from aqueous solution, has m.p. 146.5–147°, $[\alpha]_D$ +106.5° (water), and is orthorhombic with the space group $P2_12_12_1$ and $Z = 4$, and with cell dimensions $a = 8.166(5)$, $b = 12.721(9)$, and $c = 13.629(6)$ Å. The molecule shows a fully extended conformation with no intramolecular hydrogen-bonds. All nine hydroxyl groups are involved in intermolecular hydrogen-bond networks and in bifurcated, finite chains. The D-glucopyranosyl moiety has the $^4C_1$ conformation, and the conformation about the C-5–C-6 bond is *gauche–gauche*. The D-glucitol residue has the bent [ap, Psc, Psc (APP)] conformation. The empirical formula for the solubility in water is $C = 119.1 + 1.204\ T + 4.137 \times 10^{-2}\ T^2 - 7.137 \times 10^{-4}\ T^3 + 7.978 \times 10^{-6}\ T^4$. The thermal properties are as follows: $\Delta H_f = 13.5$ kcal.mol^{-1}, and $Q = -5.57$ kcal.mol^{-1}.

INTRODUCTION

Maltitol (**1**, 4-*O*-α-D-glucopyranosyl-D-glucitol), usually obtained by hydrogenation[1,2] of maltose, has been widely used as a sweetener in low-calory and dietary foods[3-7].



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Many crystallographic studies have been carried out on alditols[8-13], including D-glucitol[12] and cellobiitol[13], but the only study on maltitol involved the hygroscopic, ethanol complex[14]. Hitherto, maltitol was known only as an amorphous, hygroscopic solid, but we recently obtained anhydrous crystals from a supersaturated, aqueous solution and were able to investigate some physical properties and undertake X-ray crystallography.

EXPERIMENTAL

Properties of maltitol. — After recrystallisation from water, maltitol had m.p. 146.5–147° (uncorrected), $[\alpha]_D$ +106.5° (*c* 10, water).

The solubilities of maltitol shown in Table I were obtained by measuring the moisture contents of saturated solutions using the routine quartz-sand method[15].

The heat of fusion (ΔH_f = 13.5 kcal.mol^{-1}) was determined with a Perkin–Elmer DSC-IB differential-scanning calorimeter, and a temperature programme of 5°/min, after calibration of the apparatus against the heat of indium (6.79 mcal.mg^{-1} at 156.4°). The heat of dissolution (Q = −5.57 kcal.mol^{-1}) was determined with a Tokyo Riko twin microcalorimeter at 25°.

X-Ray crystallographic analysis. — Colorless, prism-like crystals of maltitol were grown at 40° from a supersaturated, aqueous solution. A crystal with dimensions of 0.3 × 0.3 × 0.3 mm was used in the X-ray study. Refinement of the cell dimensions was carried out by the least-squares method with reference to 21 reflections that were obtained using a Syntex R3 four-circle diffractometer and graphite-monochromated MoKα radiation. The crystal data are as follows: $C_{12}H_{24}O_{11}$ (mol. wt., 344.32); orthorhombic, a = 8.166(5), b = 12.721(9), c = 13.629(6) Å; Z = 4; D_c = 1.62 g.cm^{-3}, D_m = 1.602 g.cm^{-3}; space group $P2_12_12_1$; μ(MoKα) =

TABLE I

SOLUBILITY OF MALTITOL IN WATER

Temp. (degrees)	*Solubility[a] (g/100 g of water)*	*(g/100 g of solution)*
8.5	132.5	57.0
19.6	152.5	60.4
30.0	181.1	64.4
40.3	210.8	67.8
50.3	241.2	70.7
59.5	297.6	74.8
71.0	360.8	78.3
79.0	431.6	81.2
90.0	565.3	85.0

[a] These data fit the fourth-degree equation: c = 119.1 + 1.204 T + 4.137 × 10^{-2} T^2 − 7.137 × 10^{-4} T^3 + 7.978 × 10^{-6} T^4, where c is the saturation concentration and T is the temperature.

TABLE II

ATOMIC COORDINATES FOR NON-HYDROGEN ATOMS ($\times 10^4$) AND HYDROGEN ATOMS ($\times 10^3$)[a]

Atom	x	y	z	*Atom*	x	y	z
C-1	8580(3)	4775(2)	3884(2)	H-1	931(3)	538(2)	391(2)
C-2	9054(4)	4040(2)	3050(2)	H-2	1038(3)	392(2)	311(2)
C-3	8257(2)	2959(2)	3148(2)	H-3	703(3)	302(2)	299(2)
C-4	8424(3)	2532(2)	4177(2)	H-4	964(3)	234(2)	432(2)
C-5	7804(3)	3334(2)	4913(2)	H-5	664(3)	349(2)	482(2)
C-6	7918(4)	2995(2)	5967(2)	H-6A	746(4)	361(2)	641(2)
				H-6B	716(3)	235(2)	607(2)
O-1	6954(2)	5080(2)	3747(1)	H(O-2)	764(4)	456(2)	205(2)
O-2	8680(3)	4512(2)	2127(2)	H(O-3)	827(5)	177(3)	227(3)
O-3	9043(3)	2268(2)	2463(2)	H(O-4)	819(4)	108(3)	445(2)
O-4	7476(3)	1589(2)	4262(2)	H(O-6)	1022(4)	311(2)	421(2)
O-5	8802(2)	4271(1)	4806(1)				
O-6	9506(3)	2660(2)	6255(2)				
C-1′	5932(4)	8832(2)	3347(2)	H-1′A	702(3)	910(2)	348(2)
C-2′	5553(3)	7906(2)	3997(2)	H-1′B	576(3)	863(2)	267(2)
C-3′	6584(3)	6965(2)	3686(2)	H-2′	433(3)	773(2)	391(2)
C-4′	6386(3)	5970(2)	4316(2)	H-3′	636(3)	683(2)	299(2)
C-5′	4652(3)	5721(2)	4666(2)	H-4′	712(3)	606(2)	492(2)
C-6′	3552(3)	5222(2)	3897(2)	H-5′	410(3)	635(2)	492(2)
				H-6′A	253(3)	517(2)	416(2)
				H-6′B	394(4)	452(2)	372(2)
O-1′	4749(3)	9665(2)	3429(2)	H(O-1′)	461(4)	982(3)	389(3)
O-2′	5863(3)	8213(2)	4986(2)	H(O-2′)	507(4)	803(2)	527(2)
O-3′	8296(2)	7265(2)	3745(1)	H(O-3′)	870(3)	727(2)	324(2)
O-5′	4713(3)	4956(2)	5433(1)	H(O-5′)	499(4)	518(3)	589(3)
O-6′	3395(3)	5853(2)	3051(1)	H(O-6′)	394(4)	571(2)	267(2)

[a] Estimated standard deviations in parentheses.

1.6 cm^{-1}. Intensity data were collected on the diffractometer, using the ω-scan mode within $2\theta < 50°$. Periodic monitoring of the reflections revealed no significant fluctuation of the intensities. Thus, 1,446 independent reflections $[I > 1.960\sigma(I)]$ were stored as observed. These intensity data were corrected for Lorenz and polarisation effects, but not for absorption.

The molecular structure was solved by the direct method using the MULTAN program. All of the atoms, except hydrogen atoms, were revealed on the first E-map. After several cycles of refinement, all hydrogen atoms were found on the difference-Fourier map. The R value finally obtained by the block-diagonal, least-squares refinement was 0.030. The positional parameters are shown in Table II*.

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*Tables of supplemental data are deposited with, and may be obtained from: Elsevier Scientific Publishing Company, BBA Data Deposition, P.O. Box 1527, Amsterdam, The Netherlands. Reference should be made to No. BBA/DD/228/*Carbohydr. Res.*, 108 (1982) 163–171.

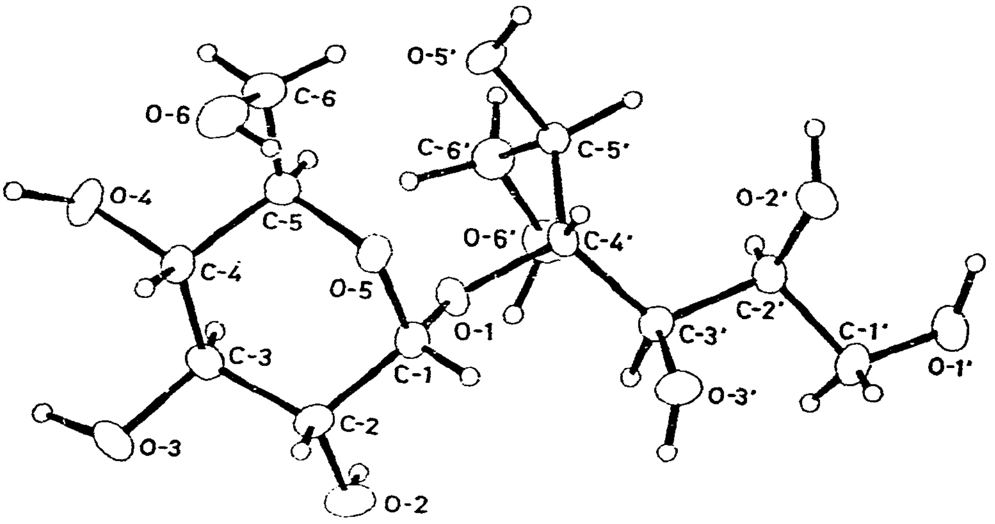

Fig. 1. Molecular structure of maltitol.

TABLE III

BOND DISTANCES (Å) AND ANGLES (DEGREES) INVOLVING NON-HYDROGEN ATOMS[a]

C-1–C-2	1.522(4)	C-1′–C-2′	1.507(4)
C-2–C-3	1.527(4)	C-2′–C-3′	1.523(4)
C-3–C-4	1.511(4)	C-3′–C-4′	1.537(4)
C-4–C-5	1.518(4)	C-4′–C-5′	1.527(4)
C-5–C-6	1.503(4)	C-5′–C-6′	1.519(4)
C-1–O-1	1.395(3)	C-1′–O-1′	1.439(4)
C-1–O-5	1.422(3)	C-2′–O-2′	1.426(3)
C-2–O-2	1.427(3)	C-3′–O-3′	1.451(3)
C-3–O-3	1.433(3)	C-4′–O-1	1.449(3)
C-4–O-4	1.432(3)	C-5′–O-5′	1.429(3)
C-5–O-5	1.452(3)	C-6′–O-6′	1.411(3)
C-6–O-6	1.420(4)		
C-1–C-2–C-3	112.3(2)	O-1′–C-1′–C-2′	113.1(2)
C-2–C-3–C-4	111.5(2)	C-1′–C-2′–C-3′	109.7(2)
C-3–C-4–C-5	110.0(2)	C-1′–C-2′–O-2′	107.7(2)
C-4–C-5–O-5	107.4(2)	C-3′–C-2′–O-2′	112.3(2)
C-5–O-5–C-1	112.8(2)	C-2′–C-3′–C-4′	115.7(2)
O-5–C-1–C-2	110.5(2)	C-2′–C-3′–O-3′	108.1(2)
O-5–C-1–O-1	111.4(2)	C-4′–C-3′–O-3′	106.7(2)
C-2–C-1–O-1	108.2(2)	C-3′–C-4′–C-5′	116.3(2)
C-1–C-2–O-2	110.2(2)	C-3′–C-4′–O-1	108.2(2)
C-3–C-2–O-2	111.4(2)	C-5′–C-4′–O-1	107.5(2)
C-2–C-3–O-3	107.7(2)	C-4′–C-5′–C-6′	114.8(2)
C-4–C-3–O-3	110.1(2)	C-4′–C-5′–O-5′	109.8(2)
C-3–C-4–O-4	109.1(2)	C-6′–C-5′–O-5′	104.0(2)
C-5–C-4–O-4	109.3(2)	C-5′–C-6′–O-6′	112.4(2)
C-4–C-5–C-6	114.7(2)		
O-5–C-5–C-6	107.3(2)	C-1–O-1–C-4′	116.8(2)
C-5–C-6–O-6	114.0(2)		

[a] Estimated standard deviations in parentheses.

DISCUSSION

The molecular structure of maltitol and the numbering of atoms are shown in Fig. 1.

The bond lengths and angles involving carbon atoms are given in Table III. The C–C bond-lengths are in the range 1.503–1.537 Å (mean 1.519 Å). Shortening of the C–C bonds of the primary alcohol groups is observed. The C–O bond-lengths are in the range 1.395–1.452 Å (mean 1.430 Å). The lengths of the endocyclic C–O bonds are unequal, and the glycosidic bond, C-1–O-1, is much shorter. The above features have been reported for many pyranosides[16,17]. The average length of C–H bonds is 1.00 Å, and that of O–H bonds is 0.79 Å. The C–C–C angles are in the range 109.7–116.3° (mean 113.1°), and the C–C–O angles in the range 104.0–114.0° (mean 109.3°). The angle in the bridge C-1–O-1–C-4′ is 116.8°, which is in good agreement with those found in (1→4)-linked disaccharides[16,17].

The D-glucopyranosyl residue has the $^4C_1$ conformation, and the endo- and exo-cyclic torsional angles are given in Table IV. The endocyclic torsional angles about the ring bonds vary from 46.8 to 66.3° (mean 56.1°). The values deviate slightly from those of the normal chair conformation. The conformation about the C-5–C-6 bond in maltitol is *gauche–gauche*, whereas that in the α-D-glucosyl group of α-[18] and β-maltose[19] is *gauche–trans*.

TABLE IV

ENDO- AND EXO-CYCLIC TORSIONAL ANGLES (DEGREES) FOR THE D-GLUCOPYRANOSYL MOIETY OF MALTITOL

Endocyclic		*Exocyclic*	
O-5–C-1–C-2–C-3	49.6	O-5–C-1–C-2–O-2	174.4
C-1–C-2–C-3–C-4	−46.8	O-1–C-1–C-2–C-3	−72.6
C-2–C-3–C-4–C-5	52.6	O-1–C-1–C-2–O-2	52.2
C-3–C-4–C-5–O-5	−60.6	C-1–C-2–C-3–O-3	167.7
C-4–C-5–O-5–C-1	66.3	O-2–C-2–C-3–C-4	−171.0
C-5–O-5–C-1–C-2	−60.7	O-2–C-2–C-3–O-3	68.1
		C-2–C-3–C-4–O-4	−172.4
		O-3–C-3–C-4–C-5	−172.1
		O-3–C-3–C-4–O-4	−68.1
		C-3–C-4–C-5–C-6	−179.7
		O-4–C-4–C-5–O-5	−179.7
		O-4–C-4–C-5–C-6	60.5
		C-4–C-5–C-6–O-6	53.5
		O-5–C-5–C-6–O-6	−65.7
		C-5–O-5–C-1–O-1	59.6
		C-6–C-5–O-5–C-1	−169.9
		O-5–C-1–O-1–C-4′	73.0
		C-2–C-1–O-1–C-4′	−165.4

TABLE V

TORSION ANGLES (DEGREES) FOR THE D-GLUCITOL RESIDUE OF MALTITOL WITH CORRESPONDING VALUES FOR D-GLUCITOL

	Maltitol	D-*Glucitol*
O-1′–C-1′–C-2′–C-3′	165.8	−173.7
O-1′–C-1′–C-2′–O-2′	−71.7	−55.2
C-1′–C-2′–C-3′–C-4′	177.3	−51.1
C-1′–C-2′–C-3′–O-3′	57.9	−174.1
O-2′–C-2′–C-3′–C-4′	57.5	−172.6
O-2′–C-2′–C-3′–O-3′	−61.9	64.3
C-2′–C-3′–C-4′–C-5′	39.0	−178.3
C-2′–C-3′–C-4′–O-1	160.1	−55.8
O-3′–C-3′–C-4′–C-5′	159.3	−56.2
O-3′–C-3′–C-4′–O-1	−79.7	66.5
C-3′–C-4′–C-5′–C-6′	78.3	179.9
C-3′–C-4′–C-5′–O-5′	−165.1	−57.1
O-1–C-4′–C-5′–C-6′	−43.1	57.8
O-1–C-4′–C-5′–O-5′	73.6	−179.2
C-4′–C-5′–C-6′–O-6′	−57.7	−173.6
O-5′–C-5′–C-6′–O-6′	−177.6	63.6
C-3′–C-4′–O-1–C-1	94.3	
C-5′–C-4′–O-1–C-1	−139.4	

As shown in Fig. 1, the D-glucitol moiety has a non-planar arrangement of the carbon chain. Alditols adopt[20] a planar, zigzag conformation in the absence of a parallel arrangement of C(*n*)–O and C(*n* +2)–O bonds, whereas, in the presence of such steric interaction, a non-planar, bent conformation formed by rotation of 120° about the C–C bond is adopted. For D-glucitol, the parallel interaction between the C-2–O-2 and C-4–O-4 bonds gives two bent-chain rotamers. One is formed by twisting about the C-2–C-3 bond and is observed in crystals of D-glucitol[13] and the D-glucitol–pyridine complex[12] (Msc-ap-ap). The other is derived by rotation about the C-3–C-4 and C-4–C-5 bonds and has not been reported hitherto. The carbon chains of the D-glucitol moiety of maltitol have 141° and 102° rotations about the C-3′–C-4′ and C-4′–C-5′ bonds, respectively, and are almost identical to the latter rotamer (ap-Psc-Psc). Cellobiitol[14] (4-*O*-β-D-glucopyranosyl-D-glucitol) also has the bent (Msc-ap-Psc) carbon-chain conformation, and two intramolecular hydrogen-bonds seem to be responsible for the hydrogen-bond geometry. From the fact that no intramolecular hydrogen-bond is observed in the crystal of maltitol, the lower steric hindrance should contribute to the ideal conformation in the D-glucitol moiety. The orientation of the terminal hydroxyl group appears to depend upon the intermolecular environment in the crystal (Table V).

The torsional angles about the bridge bonds are ϕ_1(C-5–C-1–O-1–C-4′) 73.0° and ϕ_2(C-1–O-1–C-4′–C-3′) 94.3°, respectively: ϕ_1 deviates from the value of 63° found in methyl α-D-glucopyranoside[21], but is within the range of ϕ_1 which the

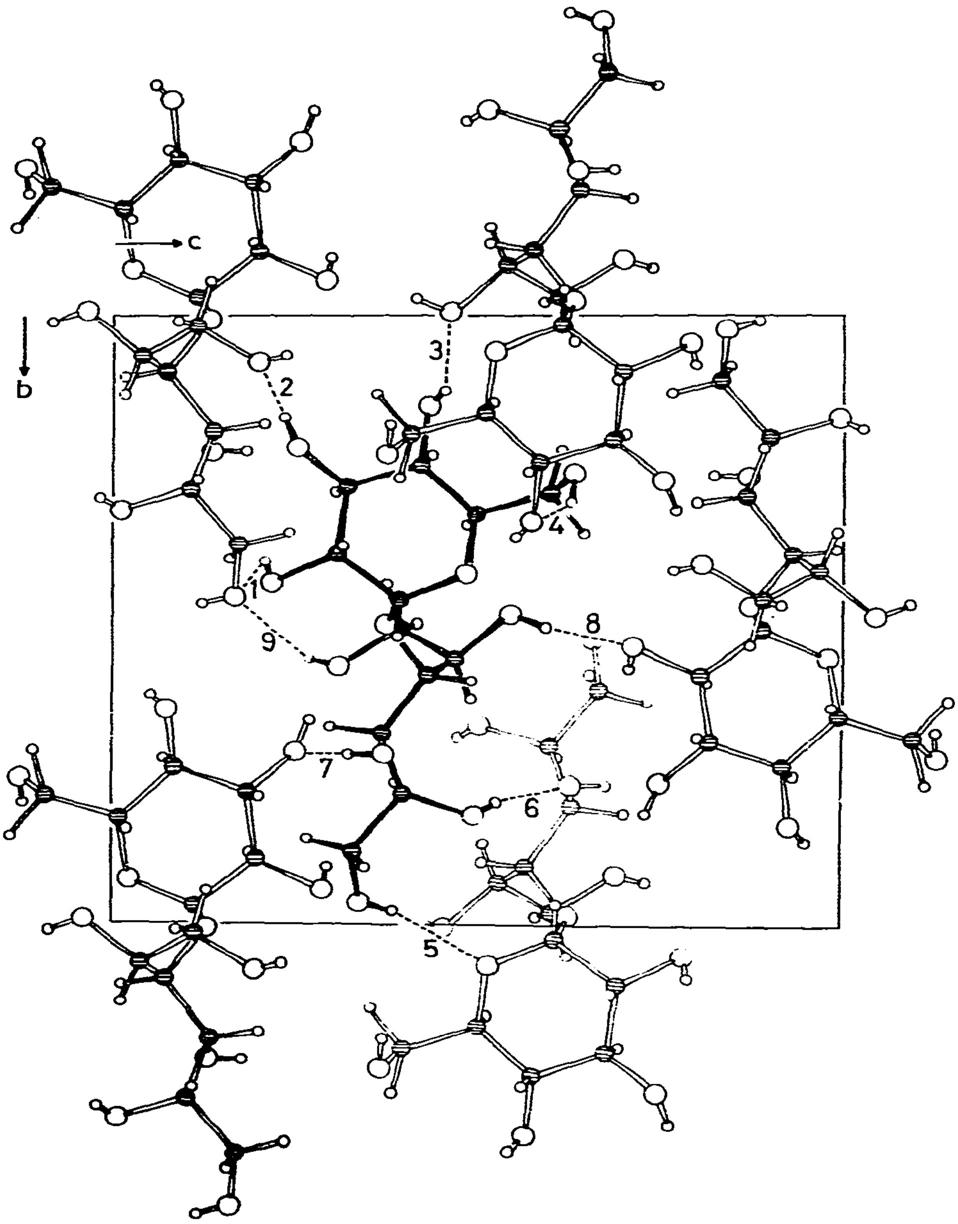

Fig. 2. Molecular packing viewed along the *a* axis. Hydrogen bonds, numbered according to Table VI, are shown by broken lines.

TABLE VI

GEOMETRY OF THE HYDROGEN BONDS IN MALTITOL

Number		*O-H (Å)*	*H···O (Å)*	*O···O (Å)*	*O-H···O (deg)*	*Symmetry operation*[a]
1	O-2–H(O-2)···O-1′	0.82	2.10	2.907	169	645.3
2	O-3–H(O-3)···O-6′	0.93	1.84	2.774	174	645.3
3	O-4–H(O-4)···O-5′	0.91	1.82	2.715	168	556.2
4	O-6–H(O-6)···O-4	0.82	1.99	2.701	145	556.2
5	O-1′–H(O-1′)···O-5	0.67	2.22	2.867	163	466.2
6	O-2′–H(O-2′)···O-3′	0.79	2.01	2.786	166	466.2
7	O-3′–H(O-3′)···O-3	0.77	2.08	2.727	143	755.3
8	O-5′–H(O-5′)···O-2	0.73	2.04	2.740	162	665.4
9	O-6′–H(O-6′)···O-1′	0.71	2.27	2.940	159	645.3

[a] The symmetry operation is performed on the acceptor O atoms. The first set of numbers specifies the lattice translation, *e.g.*, 645.4 is +a−b from 555.4. The last digit indicates one of the following symmetry operations: (*1*) x,y,z; (*2*) 0.5 + x,0.5−y,−z; (*3*) −x,0.5 + y,0.5−z; (*4*) 0.5−x,−y,0.5 + z.

$^4C_1$(α-D) conformation[22] seems to adopt. The rotation about the C-1–C-4′ bond may be much restricted by intermolecular forces due to the absence of intramolecular hydrogen-bonds.

The molecular packing is shown in Fig. 2, and the distances and angles are listed in Table VI. A notable feature is the absence of intramolecular hydrogen-bonds. The molecules are oriented approximately perpendicularly to the *a* axis, and parallel to the *b* axis. All nine hydroxyl groups are involved in hydrogen-bond networks, and act as donors; O-1′ is a double acceptor, but the bridge-oxygen atoms, O-1, O-6, and O-2′, do not accept a hydrogen bond. The bonding sequence consists of bifurcated, finite chains, and suggests the following termination of the ring-oxygen atom, O-5:

$$\begin{tikzcd}
\text{O-6} \arrow[r] & \text{O-4} \arrow[r] & \text{O-5}' \arrow[r] & \text{O-2} \arrow[dr] & & \\
 & & & & \text{O-1}' \arrow[r] & \text{O-5.} \\
\text{O-2}' \arrow[r] & \text{O-3}' \arrow[r] & \text{O-3} \arrow[r] & \text{O-6} \arrow[ur] & &
\end{tikzcd}$$

In the intermolecular hydrogen-bondings, the O···O distances are in the range 2.701–2.940 Å (mean 2.795 Å).

For many disaccharides, it has been reported[23] that intermolecular hydrogen-bonding is not negligible, and that, in trisaccharide crystals, hydrogen bonding between the saccharide molecule and water plays an important role in place of intramolecular hydrogen-bonding. It was reported[14] that, for the ethanol-complex, the presence of the partner molecule seems to accelerate the crystallisation of maltitol.

Our study suggests that the crystallisation of maltitol without a partner molecule is difficult and that only intermolecular interactions play a predominant role in its symmetrical packing.

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