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Crystal structure of lactitol (4-*O*-β-D-galactopyranosyl-D-glucitol)

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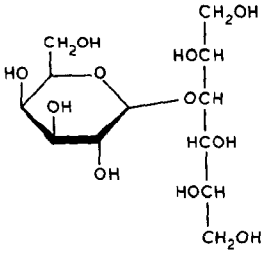
ABSTRACT

Lactitol, $C_{12}H_{24}O_{11}$, is monoclinic, space group $P2_1$ with cell dimensions a = 7.614(1), b = 10.757(1), c = 9.370(1) Å, β = 108.19(1)°, and V = 729.0(1) Å^3; Z = 2, D_x = 1.57 Mg.m^{-3}, λ(Cu-K_α) = 1.54056 Å, μ = 1.166 mm^{-1}, F(000) = 368, and T = 23°. The structure was solved by direct methods and refined by least-squares calculations to R = 0.048 for 1510 unique observed reflections. There are one intra- and eight inter-molecular hydrogen bonds in the structure. Bond lengths and angles accord well with the mean values of related structures. The galactopyranosyl ring has a chair conformation.

INTRODUCTION

Lactitol (1, 4-*O*-β-D-galactopyranosyl-D-glucitol) is not found in Nature[1], but is obtained usually by hydrogenation of lactose[2].



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Lactitol is chemically more stable than lactose, and it withstands high temperature and alkaline conditions[3]. Because of its similar properties, lactitol can replace sucrose and other sugars in many commercial applications. It can be used as a sweetener in low-calorie and diet foods and it is less cariogenic than sucrose. Depending on the application, it can be used in solution or crystalline form. The relative sweetness of lactitol is 36%, compared to that of sucrose. It is less than the relative sweetness of

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glucitol and xylitol (55% and 96%, respectively). Lactitol is soluble in water, dimethyl sulfoxide, and *N,N*-dimethylformamide, and slightly soluble in ethanol and ether. Lactitol is more hygroscopic than its mono- and di-hydrates[4]. Wijnman *et al.*[4] have patented a method to produce lactitol monohydrate and dihydrate. There are patent applications on pure crystalline lactitol monohydrate[6] and trihydrate[7], and on methods for their production.

An article on the crystal structure of lactitol monohydrate has been published[8], but only five crystal structures of carbohydrate derivatives consisting of cyclic pyranosides and acyclic polyalcohols have been reported (see ref. 8). We now report on the crystal structure of lactitol (**1**) and, in the following paper, on that of its dihydrate.

EXPERIMENTAL

Single crystals of lactitol, m.p. 146–148° (measured by d.s.c.), were obtained from aqueous solution. Intensity data were measured on an Enraf–Nonius CAD-4 diffractometer, using graphite-monochromated Cu-K_α (λ = 1.54056) radiation and the ω–2θ method. Cell parameters and the orientation matrix were determined from a least-squares fit of 25 reflections ($13 < \theta < 28°$). Two standard reflections were measured every hour; no systematic variation was detected. The crystal size was 0.25 × 0.25 × 0.40 mm. Including Friedel pairs, 3135 reflections with $\theta < 75°$ were measured. After merging, there were 1596 unique reflections, 1510 of which had $I > 3\sigma(I)$. The intensity data were corrected for Lorentz and polarisation effects but not for extinction. Empirical absorption correction was done using a ψ-scan[9], with correction factors max. = 0.997 and min. = 0.964. The structure was solved by direct methods using the MULTAN-11/82 program[10] and was refined by full-matrix least-squares, with all non-H atoms anisotropic, using the SDP-plus program package[11]. The hydrogen atoms were located in a $\Delta\rho$ map and treated as riding atoms with a fixed temperature factor (B_{eq} = 5.0 Å^2). The H atoms in hydroxyl groups were shifted along the direction of the O–H bond in order to normalise the bond length[12] to the value of 0.97 Å. The atomic scattering and dispersion correction factors for neutral atoms were taken from International Tables[13]. Altogether, 207 parameters were refined. The results were R = 0.048 and R_w = 0.047, $w = 1/[(\sigma F_o)^2 + (S \cdot F_o)^2]$($\sigma F$ from counting statistics, S = 0), max. shift/σ = 0.00 in final cycle, S = 0.981, max. and min. peaks 0.38(7), and −0.39(7) eÅ^{-3} in the final $\Delta\rho$ map. Figures were drawn using the PLUTO program[14].

DISCUSSION

The atomic co-ordinates and isotropic temperature factors are given in Table I, bond distances and bond angles in Table II, torsional angles in Table III, and the geometry of the hydrogen bonds in Table IV*. A view of the compound and the

* Lists of structure factors, anisotropic thermal parameters of non-H atoms, and torsion angles including H-atoms have been 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/478/ *Carbohydr. Res.*, 223 (1992) 45–51.

TABLE I

Fractional co-ordinates and equivalent isotropic temperature factors with e.s.d.'s in parentheses

Atom	x	y	z	B_{eq} ($Å^2$)[a]
O-1′	0.6863(2)	0.035	0.3337(2)	1.84(3)
O-1	0.8053(4)	−0.4533(2)	0.3545(3)	4.80(6)
O-2′	0.6038(3)	0.2970(1)	0.2832(2)	2.40(4)
O-2	0.9720(3)	−0.1493(2)	0.2936(2)	2.81(3)
O-3	0.8419(3)	−0.1508(2)	0.5440(2)	2.67(4)
O-3′	0.7669(3)	0.4065(2)	0.0824(2)	2.49(4)
O-4′	0.9748(3)	0.1912(2)	0.0374(2)	2.46(3)
O-5′	0.7385(2)	0.0235(1)	0.1090(2)	1.74(3)
O-5	0.3479(2)	−0.1717(2)	0.4146(2)	2.24(3)
O-6′	0.7456(3)	−0.1423(2)	−0.1084(2)	2.49(4)
O-6	0.2193(3)	0.0161(2)	0.1828(2)	2.31(3)
C-1′	0.6471(3)	0.0924(2)	0.1942(2)	1.61(4)
C-1	0.9295(4)	−0.3554(2)	0.3535(3)	2.76(5)
C-2′	0.7137(3)	0.2271(2)	0.2169(2)	1.73(4)
C-2	0.8292(3)	−0.2331(2)	0.2992(3)	1.99(4)
C-3	0.7217(3)	−0.1859(2)	0.3999(2)	1.81(4)
C-3′	0.6914(3)	0.2833(2)	0.0618(2)	1.78(4)
C-4	0.5848(3)	−0.0797(2)	0.3299(2)	1.40(3)
C-4′	0.7801(3)	0.2032(2)	−0.0297(2)	1.63(4)
C-5′	0.7010(3)	0.0718(2)	−0.0410(2)	1.56(3)
C-5	0.4419(3)	−0.0569(2)	0.4098(2)	1.72(4)
C-6′	0.7864(4)	−0.0147(2)	−0.1259(3)	2.24(4)
C-6	0.3077(3)	0.0463(2)	0.3375(2)	2.10(4)
H-1′	0.508	0.096	0.139	5.0
HO-1	0.773	−0.489	0.255	5.0
H-11	1.016	−0.345	0.461	5.0
H-12	1.004	−0.378	0.273	5.0
HO-2	0.931	−0.094	0.208	5.0
HO-2′	0.651	0.287	0.391	5.0
H-2′	0.849	0.229	0.283	5.0
H-2	0.730	−0.244	0.197	5.0
HO-3	0.942	−0.095	0.543	5.0
HO-3′	0.741	0.423	−0.024	5.0
H-3	0.609	−0.229	0.407	5.0
H-3′	0.562	0.307	0.022	5.0
H-4	0.528	−0.117	0.223	5.0
HO-4′	1.021	0.275	0.037	5.0
H-4′	0.754	0.244	−0.133	5.0
H-5	0.492	−0.044	0.523	5.0
HO-5	0.221	−0.197	0.398	5.0
H-5′	0.562	0.078	−0.096	5.0
HO-6′	0.637	−0.173	−0.185	5.0
HO-6	0.107	0.061	0.132	5.0
H-61	0.199	0.060	0.384	5.0
H-61′	0.916	−0.017	−0.093	5.0
H-62	0.370	0.130	0.342	5.0
H-62′	0.733	0.020	−0.232	5.0

[a] $B_{eq} = (4/3)[a^2B(1,1) + b^2B(2,2) + c^2B(3,3) + ab(\cos\gamma)B(1,2) + ac(\cos\beta)B(1,3) + bc(\cos\alpha)B(2,3)]$.

TABLE II

Bond distances and bond angles with e.s.d.'s in parentheses

Bond distances (Å)					
O-1′–C-1′	1.392(2)	O-5′–C-1′	1.420(3)	C-2–C-3	1.517(4)
O-1′–C-4	1.448(2)	O-5′–C-5′	1.441(3)	C-3–C-4	1.547(3)
O-1–C-1	1.418(4)	O-5–C-5	1.435(3)	C-3′–C-4′	1.514(3)
O-2′–C-2′	1.405(3)	O-6′–C-6′	1.428(3)	C-4–C-5	1.520(3)
O-2–C-2	1.426(3)	O-6–C-6	1.432(3)	C-4′–C-5′	1.528(3)
O-3–C-3	1.425(2)	C-1′–C-2′	1.528(3)	C-5′–C-6′	1.497(4)
O-3′–C-3′	1.433(3)	C-1–C-2	1.527(4)	C-5–C-6	1.518(3)
O-4′–C-4′	1.424(3)	C-2′–C-3′	1.534(3)		
Bond angles (°)					
C-1′–O-1′–C-4	113.5(1)	C-1–C-2–C-3	113.1(2)	O-4′–C-4′–C-5′	106.2(2)
C-1′–O-5′–C-5′	112.2(2)	O-3–C-3–C-2	111.5(2)	C-3′–C-4′–C-5′	109.3(2)
O-1′–C-1′–O-5′	107.3(2)	O-3–C-3–C-4	110.8(2)	O-5′–C-5′–C-4′	108.2(2)
O-1′–C-1′–C-2′	109.1(2)	C-2–C-3–C-4	114.0(2)	O-5′–C-5′–C-6′	107.9(2)
O-5′–C-1′–C-2′	112.0(2)	O-3′–C-3′–C-2′	108.4(2)	C-4′–C-5′–C-6′	112.6(2)
O-1–C-1–C-2	112.1(2)	O-3′–C-3′–C-4′	111.8(2)	O-5–C-5–C-4	108.5(2)
O-2′–C-2′–C-1′	110.6(2)	C-2′–C-3′–C-4′	112.1(2)	O-5–C-5–C-6	111.7(2)
O-2′–C-2′–C-3′	107.6(2)	O-1′–C-4–C-3	109.5(2)	C-4–C-5–C-6	112.6(2)
C-1′–C-2′–C-3′	107.9(2)	O-1′–C-4–C-5	108.0(2)	O-6′–C-6′–C-5′	113.0(2)
O-2–C-2–C-1	104.4(2)	C-3–C-4–C-5	113.6(2)	O-6–C-6–C-5	108.9(2)
O-2–C-2–C-3	112.1(2)	O-4′–C-4′–C-3′	112.8(2)		

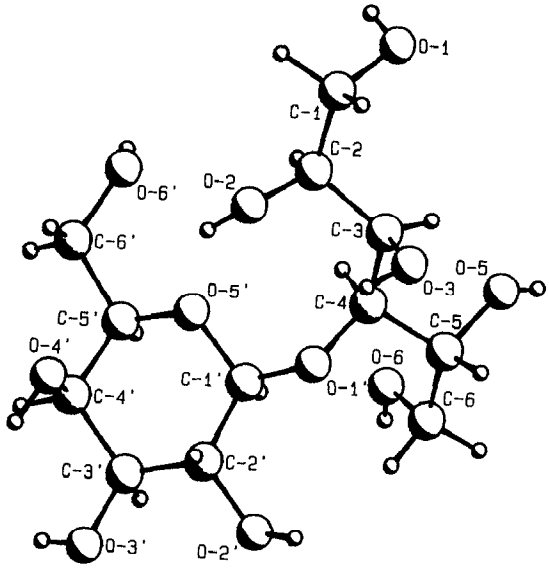

Fig. 1. PLUTO plot and numbering scheme for lactitol.

TABLE III

Torsional angles (°) with e.s.d.'s in parentheses

Endocyclic for D-*galactopyranosyl moiety*			
O-5′–C-1′–C-2′–C-3′	54.4(3)	C-3′–C-4′–C-5′–O-5′	−58.9(2)
C-1′–C-2′–C-3′–C-4′	−51.7(3)	C-1′–O-5′–C-5′–C-4′	63.8(2)
C-2′–C-3′–C-4′–C-5′	55.3(3)	C-5′–O-5′–C-1′–C-2′	−62.9(2)
Exocyclic for D-*galactopyranosyl moiety*			
O-1′–C-1′–C-2′–C-3′	173.0(2)	C-2′–C-3′–C-4′–O-4′	−62.7(3)
O-1′–C-1′–C-2′–O-2′	−69.5(2)	O-4′–C-4′–C-5′–O-5′	63.1(2)
O-5′–C-1′–C-2′–O-2′	171.9(2)	O-4′–C-4′–C-5′–C-6′	−56.1(2)
O-2′–C-2′–C-3′–C-4′	−171.1(2)	C-3′–C-4′–C-5′–C-6′	−178.1(2)
O-2′–C-2′–C-3′–O-3′	65.1(3)	O-5′–C-5′–C-6′–O-6′	47.3(3)
C-1′–C-2′–C-3′–O-3′	−175.5(2)	C-4′–C-5′–C-6′–O-6′	166.7(2)
O-3′–C-3′–C-4′–O-4′	59.2(2)	C-1′–O-5′–C-5′–C-6′	−174.1(2)
O-3′–C-3′–C-4′–C-5′	177.2(2)	C-5′–O-5′–C-1′–O-1′	177.5(2)
C-4–O-1′–C-1′–O-5′	−75.1(2)	C-4–O-1′–C-1′–C-2′	163.4(2)
D-*Glucitol residue*			
O-1–C-1–C-2–C-3	62.4(3)	C-2–C-3–C-4–O-1′	−75.0(2)
O-1–C-1–C-2–O-2	−175.4(2)	C-2–C-3–C-4–C-5	164.2(2)
O-2–C-2–C-3–O-3	−51.0(3)	O-1′–C-4–C-5–O-5	−176.6(2)
O-2–C-2–C-3–C-4	75.3(3)	O-1′–C-4–C-5–C-6	59.2(2)
C-1–C-2–C-3–O-3	66.7(3)	C-3–C-4–C-5–O-5	−55.0(2)
C-1–C-2–C-3–C-4	−166.9(2)	C-3–C-4–C-5–C-6	−179.2(2)
O-3–C-3–C-4–O-1′	51.7(2)	O-5–C-5–C-6–O-6	−65.4(2)
O-3–C-3–C-4–C-5	−69.2(2)	C-4–C-5–C-6–O-6	57.0(3)
C-1′–O-1′–C-4–C-5	−109.5(2)	C-1′–O-1′–C-4–C-3	126.3(2)

numbering scheme are shown in Fig. 1. A stereoscopic view of the packing is presented in Fig. 2. The atoms of the galactose moiety are designated with primed numbers.

The bond distances and angles are normal. The shortening of the O-1′–C-1′ distance [1.392(2) Å] and the angles in the acetal sequence [C-5′–O-5′–C-1′ 112.2(2)° and O-5′–C-1′–O-1′ 107.3(2)°] accord well with the mean values of related structures (1.38 Å, 111.9°, and 107.4°, respectively)[8,15]. The shortening of the C-5′–C-6′ distance is also normal[16]. The glycosidic angle C-1′–O-1′–C-4 of 113.5(1)° is smaller than in lactitol monohydrate and six β-(1→4)-linked disaccharides[8,17]. The galactopyranosyl ring has a chair conformation: C-1′,2′,4′,5′ are coplanar, whereas C-3′ is −0.649(2) Å below, and O-5′ is 0.671(2) Å above, the plane.

The torsional angles characterising the glycosidic link [C-4–O-1′–C-1′–O-5′ and C-1′–O-1′–C-4–C-3] are −75.1(2)° and 126.3(2)°, respectively. Comparison with lactitol monohydrate shows the torsional angles in the galactopyranosyl moiety to be about the same. The biggest differences are about the C-5′–C-6′ bond. In the D-glucitol residue, there are more and bigger differences. The exocyclic torsional angles vary from 65.1(3)° to −69.5(2)° (*gauche*) and from −166.7(2)° to 171.9(2)° (*trans*).

TABLE IV

Geometry of the hydrogen bonds[a]

Number	*O–H···O*	*H···O (Å)*	*O···O (Å)*	*O–H···O (°)*	*Symmetry operation for ···O atom*
1	O-1–HO-1···O-3′	1.95(2)	2.897(3)	164(1)	$x, -1+y, z$
2	O-2′–HO-2′···O-5	1.87(2)	2.760(2)	151(1)	$1-x, 1/2+y, 1-z$
3	O-2–HO-2···O-5′	1.94(2)	2.773(2)	143(1)	x, y, z
4	O-3′–HO-3′···O-6	1.89(2)	2.782(3)	151(1)	$1-x, 1/2+y, -z$
5	O-3–HO-3···O-1	2.41(2)	3.323(3)	157(1)	$2-x, 1/2+y, 1-z$
6	O-4′–HO-4′···O-6′	1.91(2)	2.702(3)	137(1)	$2-x, 1/2+y, -z$
7	O-5–HO-5···O-2	1.91(2)	2.740(3)	142(1)	$-1+x, y, z$
8	O-6′–HO-6′···O-2′	1.80(2)	2.732(3)	159(1)	$1-x, -1/2+y, -z$
9	O-6–HO-6···O-4′	1.79(2)	2.699(2)	156(1)	$-1+x, y, z$

[a] O–H bond distances are corrected for the neutron diffraction value of 0.97 Å in the direction of the bond.

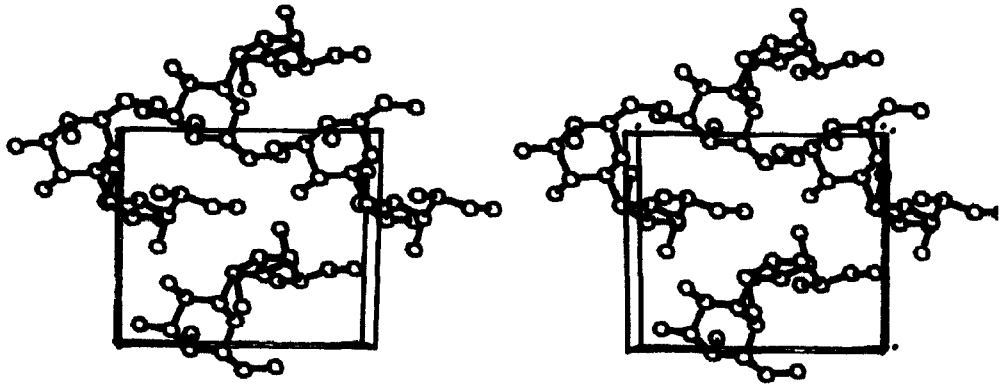

Fig. 2. A stereoscopic view of the packing for lactitol. The *c*-axis is vertical and the *b*-axis horizontal.

There are one intra- and eight inter-molecular hydrogen bonds in the structure. The intramolecular hydrogen bond O-2···O-5′ gives rise to an eight-membered ring. All hydroxyl H-atoms are involved in hydrogen bonding. The bond between O-3···O-1 is weak because of the long O···O distance [3.323(3) Å]. O-1,2,5,6 and O-2′,3′,4′,6′ act both as donors and acceptors; O-5′ acts only as an acceptor, and O-3 only as a donor.

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