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

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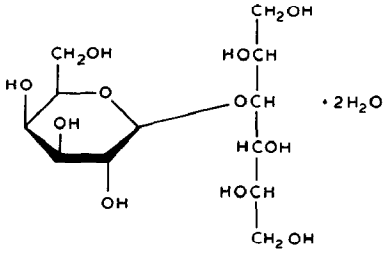
ABSTRACT

Lactitol dihydrate, $C_{12}H_{24}O_{11}\cdot 2H_2O$, is tetragonal, space group $P4_32_12$ with cell dimensions a and b = 8.762(1), c = 45.500(3) Å, and V = 3493.2(3) Å^3; Z = 8, D_x = 1.45 Mg.m^{-3}, λ(Cu-K_α) = 1.54056 Å, μ = 1.108 mm^{-1}, F(000) = 1632, and T = 23°. The structure was solved by direct methods and refined by least-squares calculations to R = 0.054 for 2037 unique observed reflections. There are three intra- and twelve inter-molecular hydrogen bonds in the structure. Bond lengths and angles accord quite well with the mean values of related structures. The galactopyranosyl ring has a chair conformation.

INTRODUCTION

The background to this study has been described in the preceding paper[1]. An article on the crystal structure of lactitol monohydrate has been also published[2] and now we report on the dihydrate (**1**).



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EXPERIMENTAL

Single crystals of lactitol dihydrate, m.p. 70–72° (measured by d.s.c.), were crystallised from water. Intensity data were measured on an Enraf–Nonius CAD-4 diffractometer using graphite-monochromated Cu-K_α (λ = 1.54056) radiation and the

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ω–2θ method. Cell parameters and the orientation matrix were determined from a least-squares fit of 25 reflections ($10 < \theta < 23°$). Two standard reflections were measured every hour; no systematic variation was detected. The crystal size was 0.40 × 0.40 × 0.25 mm. Including Friedel pairs, 7984 reflections with $\theta < 75°$ were measured. After merging, there were 2256 unique reflections, 2037 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 by applying both the ψ-scan[3] and the Fourier method[4], with correction factors max. = 0.9996, 1.347 and min. = 0.9797, 0.873, respectively. The structure was solved by direct methods using the MULTAN-11/82 program[5], and refined by full-matrix least-squares, with all non-H atoms anisotropic, using the SDP-plus program package[6]. The positions of the H atoms bonded to C atoms were calculated using known geometry (C–H distance, 1.025 Å), whereas the H atoms bonded to O atoms were located in a $\Delta\rho$ map. All H atoms were treated as riding atoms with 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[7] to the value 0.97 Å. The atomic scattering and dispersion correction factors for neutral atoms were taken from International Tables[8]. Altogether, 226 parameters were refined. The results were R = 0.054 and R_w = 0.053, w = $1/[(\sigma F_o)^2 + (S \cdot F_o)^2]$ (σF from counting statistics, S = 0), max. shift/σ = 0.00 in final cycle, S = 4.942, max. and min. peaks 0.44(9), and −0.34(9) eÅ^{-3} in the final $\Delta\rho$ map. Figures were drawn using the PLUTO program[9].

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

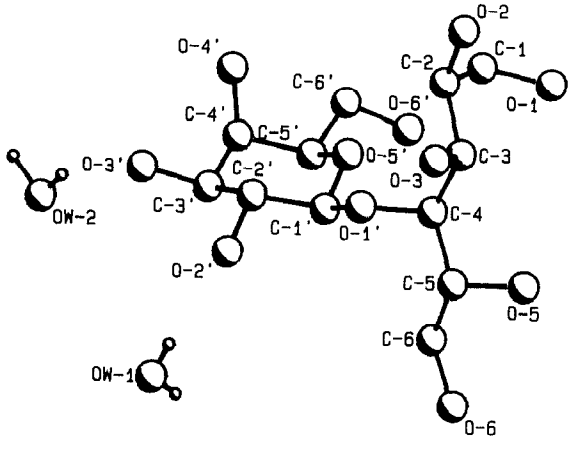

Fig. 1. PLUTO plot and numbering scheme for lactitol dihydrate.

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′	−0.2377(2)	0.3179(3)	0.46185(4)	1.51(4)
O-1	0.1691(3)	0.6329(3)	0.47718(6)	3.25(5)
OW-1	−0.6715(3)	−0.0290(3)	0.41472(5)	2.69(5)
O-2	−0.0469(3)	0.5980(3)	0.52542(4)	2.27(5)
O-2′	−0.5297(3)	0.2107(3)	0.44749(6)	2.75(5)
OW-2	−0.9561(3)	0.4823(3)	0.38877(5)	3.39(6)
O-3	−0.0843(3)	0.2933(3)	0.51416(4)	1.96(4)
O-3′	−0.7380(2)	0.4491(3)	0.43292(5)	2.11(4)
O-4′	−0.5534(3)	0.7042(3)	0.44000(5)	2.56(5)
O-5′	−0.2749(2)	0.5328(2)	0.43398(4)	1.57(4)
O-5	0.1490(3)	0.1599(3)	0.46094(5)	2.08(4)
O-6	0.0179(3)	−0.0358(3)	0.41889(6)	3.92(6)
O-6′	−0.1373(3)	0.7416(3)	0.39211(5)	2.58(5)
C-1	0.0080(4)	0.6631(4)	0.47642(7)	2.31(6)
C-1′	−0.3168(3)	0.3776(3)	0.43757(6)	1.36(5)
C-2′	−0.4843(3)	0.3669(4)	0.44599(7)	1.62(6)
C-2	−0.0766(4)	0.5526(4)	0.49585(6)	1.73(6)
C-3	−0.0233(3)	0.3877(3)	0.49118(6)	1.38(5)
C-3′	−0.5832(3)	0.4443(4)	0.42323(6)	1.58(6)
C-4	−0.0735(3)	0.3248(4)	0.46113(6)	1.35(5)
C-4′	−0.5251(4)	0.6057(4)	0.41610(6)	1.65(6)
C-5	−0.0121(4)	0.1654(4)	0.45547(7)	1.65(6)
C-5′	−0.3535(4)	0.5995(4)	0.40936(6)	1.59(6)
C-6′	−0.2867(4)	0.7549(4)	0.40419(8)	2.15(7)
C-6	−0.0441(4)	0.1118(4)	0.42407(8)	3.01(8)
H-1′	−0.292	0.322	0.418	5.0
H-2	−0.191	0.554	0.491	5.0
H-2′	−0.500	0.418	0.466	5.0
H-3	0.094	0.386	0.492	5.0
H-3′	−0.575	0.385	0.404	5.0
H-4	−0.033	0.394	0.445	5.0
H-4′	−0.581	0.649	0.398	5.0
H-5′	−0.338	0.536	0.391	5.0
H-5	−0.068	0.093	0.470	5.0
H-11	−0.030	0.653	0.455	5.0
H-12	−0.012	0.772	0.484	5.0
H-61′	−0.355	0.814	0.390	5.0
H-61	−0.160	0.108	0.420	5.0
H-62	0.005	0.189	0.410	5.0
H-62′	−0.282	0.811	0.424	5.0
HO-1	0.231	0.706	0.488	5.0
HW-11	−0.627	0.050	0.427	5.0
HW-12	−0.595	−0.028	0.399	5.0
HO-2	−0.097	0.541	0.541	5.0
HO-2′	−0.461	0.131	0.454	5.0
HW-21	−0.901	0.505	0.407	5.0
HW-22	−1.020	0.572	0.387	5.0
HO-3	0.007	0.245	0.522	5.0
HO-3′	−0.752	0.550	0.441	5.0
HO-4′	−0.615	0.788	0.433	5.0
HO-5	0.169	0.202	0.442	5.0
HO-6	0.127	−0.024	0.417	5.0
HO-6′	−0.080	0.835	0.394	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′	1.405(3)	O-5′–C-1′	1.418(4)	C-2–C-3	1.533(4)
O-1′–C-4	1.440(3)	O-5′–C-5′	1.439(4)	C-3–C-4	1.538(4)
O-1–C-1	1.437(4)	O-5–C-5	1.434(4)	C-3′–C-4′	1.538(5)
O-2′–C-2′	1.426(4)	O-6′–C-6′	1.425(4)	C-4–C-5	1.518(4)
O-2–C-2	1.427(3)	O-6–C-6	1.422(5)	C-4′–C-5′	1.536(4)
O-3–C-3	1.436(4)	C-1′–C-2′	1.521(4)	C-5′–C-6′	1.500(5)
O-3′–C-3′	1.427(4)	C-1–C-2	1.506(5)	C-5–C-6	1.530(5)
O-4′–C-4′	1.410(4)	C-2′–C-3′	1.511(4)		
Bond angles (°)					
C-1′–O-1′–C-4	117.3(2)	C-1–C-2–C-3	112.0(3)	O-4′–C-4′–C-5′	110.3(2)
C-1′–O-5′–C-5′	110.8(2)	O-3–C-3–C-2	109.2(2)	C-3′–C-4′–C-5′	109.5(3)
O-1′–C-1′–O-5′	108.6(2)	O-3–C-3–C-4	109.5(2)	O-5′–C-5′–C-4′	109.1(2)
O-1′–C-1′–C-2′	104.8(2)	C-2–C-3–C-4	111.9(2)	O-5′–C-5′–C-6′	107.7(2)
O-5′–C-1′–C-2′	109.8(2)	O-3′–C-3′–C-2′	110.3(2)	C-4′–C-5′–C-6′	112.4(3)
O-1–C-1–C-2	110.6(3)	O-3′–C-3′–C-4′	110.6(3)	O-5–C-5–C-4	110.5(2)
O-2′–C-2′–C-1′	109.9(2)	C-2′–C-3′–C-4′	111.6(2)	O-5–C-5–C-6	109.4(3)
O-2′–C-2′–C-3′	107.7(2)	O-1′–C-4–C-3	106.3(2)	C-4–C-5–C-6	112.1(3)
C-1′–C-2′–C-3′	110.7(2)	O-1′–C-4–C-5	108.6(2)	O-6′–C-6′–C-5′	110.2(3)
O-2–C-2–C-1	106.5(3)	C-3–C-4–C-5	112.3(2)	O-6–C-6–C-5	111.3(3)
O-2–C-2–C-3	109.7(2)	O-4′–C-4′–C-3′	110.0(2)		
HW-11–OW-1–HW-12		98.1(2)	HW-21–OW-2–HW-22		101.5(3)

geometry of the hydrogen bonds in Table IV*. A view of the compound and the 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 [1.405(3) Å] and the angles in the acetal sequence [C-5′–O-5′–C-1′ 110.8(2)° and O-5′–C-1′–O-1′ 108.6(2)°] accord with the mean values of related structures (1.38 Å, 111.9°, and 107.4°)[2,10]. Likewise, the shortening of the C-5′–C-6′ distance is normal[11]. The angles in the acetal sequence of three lactitols are similar (max. deviation 1.4°). The glycosidic angle C-1′–O-1′–C-4 117.3(2)° of the dihydrate is smaller than that [118.2(3)°] of the monohydrate, but larger than that [113.5(1)°] of lactitol, and it is out of the range for six reported β-(1→4)-linked disaccharides[1,2,12]. The galactopyranosyl ring has a chair conformation: C-1′,2′,4′,5′ are coplanar, whereas C-3′ is −0.617(3) Å below, and O-5′ is 0.699(2) Å above, the plane.

* 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/479/ *Carbohydr. Res.*, 233 (1992) 53–59.

TABLE III

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

Endocyclic for D-*galactopyranosyl moiety*			
O-5′–C-1′–C-2′–C-3′	56.9(3)	C-3′–C-4′–C-5′–O-5′	−56.7(3)
C-1′–C-2′–C-3′–C-4′	−50.0(3)	C-1′–O-5′–C-5′–C-4′	66.0(3)
C-2′–C-3′–C-4′–C-5′	50.0(3)	C-5′–O-5′–C-1′–C-2′	−65.8(3)
Exocyclic for D-*galactopyranosyl moiety*			
O-1′–C-1′–C-2′–C-3′	173.4(2)	C-2′–C-3′–C-4′–O-4′	−71.4(3)
O-1′–C-1′–C-2′–O-2′	−67.8(3)	O-4′–C-4′–C-5′–O-5′	64.5(3)
O-5′–C-1′–C-2′–O-2′	175.7(2)	O-4′–C-4′–C-5′–C-6′	−54.9(3)
O-2′–C-2′–C-3′–C-4′	−170.1(2)	C-3′–C-4′–C-5′–C-6′	−176.1(3)
O-2′–C-2′–C-3′–O-3′	66.5(3)	O-5′–C-5′–C-6′–O-6′	71.9(3)
C-1′–C-2′–C-3′–O-3′	−173.4(2)	C-4′–C-5′–C-6′–O-6′	−167.8(2)
O-3′–C-3′–C-4′–O-4′	51.8(3)	C-1′–O-5′–C-5′–C-6′	−171.7(2)
O-3′–C-3′–C-4′–C-5′	173.2(2)	C-5′–O-5′–C-1′–O-1′	−179.8(2)
C-4–O-1′–C-1′–O-5′	−57.8(3)	C-4–O-1′–C-1′–C-2′	−175.1(2)
D-*Glucitol residue*			
O-1–C-1–C-2–C-3	−46.2(3)	C-2–C-3–C-4–O-1′	−65.3(3)
O-1–C-1–C-2–O-2	73.8(3)	C-2–C-3–C-4–C-5	176.1(3)
O-2–C-2–C-3–O-3	50.2(3)	O-1′–C-4–C-5–O-5	−167.3(2)
O-2–C-2–C-3–C-4	171.7(2)	O-1′–C-4–C-5–C-6	70.4(3)
C-1–C-2–C-3–O-3	168.3(2)	C-3–C-4–C-5–O-5	−50.1(3)
C-1–C-2–C-3–C-4	−70.2(3)	C-3–C-4–C-5–C-6	−172.4(3)
O-3–C-3–C-4–O-1′	56.0(3)	O-5–C-5–C-6–O-6	55.4(3)
O-3–C-3–C-4–C-5	−62.6(3)	C-4–C-5–C-6–O-6	178.3(3)
C-1′–O-1′–C-4–C-5	−106.4(3)	C-1′–O-1′–C-4–C-3	132.7(2)

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 −57.8(3)° and 132.7(2)°, respectively, whereas the corresponding angles are −75.1(2)° and 126.3(2)° in lactitol and −86.3(2)° and 116.8(2)° in lactitol monohydrate[1,2]. The endocyclic torsional angles are almost the same, as in lactitol and lactitol monohydrate. Likewise, the exocyclic torsional angles are similar (difference <8°), except about the C-5′–C-6′ bond, where the maximum difference between three lactitols is 26°. For the D-glucitol residue, the torsional angles of the dihydrate are closer to those of the monohydrate and differ considerably from some of the values for lactitol. The exocyclic torsional angles in the dihydrate vary from −71.4(3)° to 71.9(3)° (*gauche*) and from −167.8(2)° to 173.2(2)° (*trans*).

There are three intra- and twelve inter-molecular hydrogen bonds in the structure. The crystal water oxygens OW-1 and OW-2 form an intramolecular hydrogen bond to atoms O-2′ and O-3′, respectively. The intramolecular hydrogen bond O-3′···O-4′ is weak, and the intermolecular hydrogen bonds O-1···O-1′, O-2···O-4′, and O-5···O-3′ are

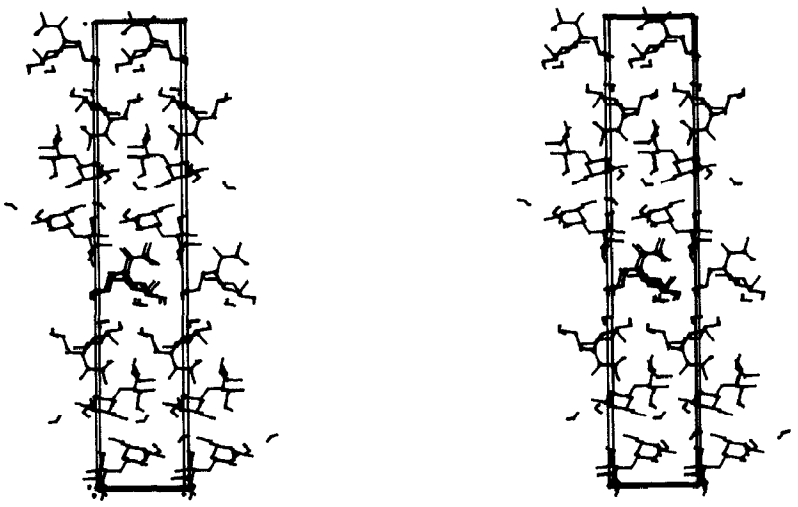

Fig. 2. A view of the packing for lactitol dihydrate. The *c*-axis is vertical and the *b*-axis horizontal.

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	OW-1–HW-11···O-2′	1.89(2)	2.860(3)	174(1)	*x, y, z*
2	OW-1–HW-12···OW-2	1.79(2)	2.680(3)	151(1)	$-3/2-x, -1/2+y, 3/4-z$
3	OW-2–HW-21···O-3′	1.92(2)	2.788(3)	147(1)	*x, y, z*
4	OW-2–HW-22···O-6′	1.82(2)	2.776(4)	167(1)	$-1+x, y, z$
5	O-1–HO-1···O-1′	2.46(2)	3.268(3)	140(1)	$y, 1+x, -1+z$
6	O-1–HO-1···O-3	1.92(2)	2.735(3)	140(1)	$y, 1+x, 1-z$
7	O-2′–HO-2′···O-2	1.89(2)	2.805(3)	156(1)	$-1+y, x, 1-z$
8	O-2–HO-2···O-4′	2.11(2)	2.998(3)	151(1)	$-1+y, 1+x, 1-z$
9	O-3′–HO-3′···O-1	1.91(2)	2.704(3)	137(1)	$1+x, y, z$
10	O-3′–HO-3′···O-4′	2.21(2)	2.778(3)	116(1)	*x, y, z*
11	O-3–HO-3···O-5	1.76(2)	2.731(3)	174(1)	$y, x, 1-z$
12	O-4′–HO-4′···OW-1	1.87(2)	2.803(3)	161(1)	$x, 1+y, z$
13	O-5–HO-5···O-3′	2.34(2)	3.004(3)	125(1)	$1+x, y, z$
14	O-6′–HO-6′···O-6	1.80(2)	2.672(4)	147(1)	$x, 1+y, z$
15	O-6–HO-6···OW-1	1.77(2)	2.730(4)	172(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.

also weak. Crystal water oxygens are bonded together by an intermolecular hydrogen bond. All hydroxyl H atoms are involved in hydrogen bonding. Oxygen atoms act as single donors and acceptors, with the exception of OW-1 and O-3′ which act as double donors and acceptors, OW-2 and O-1 which act as double donors and single acceptors, O-4′ which acts as a double acceptor and single donor, O-1′ which acts as a single donor, and O-5′ which does not accept hydrogen bonds.

The amount of water affects the packing of the molecules. Thus, from lactitol to lactitol dihydrate, the symmetry is raised from monoclinic to tetragonal. Moreover, the different packing causes some bond angles and especially the torsional angles to have different values[1,2]. Surprisingly, lactitol trihydrate crystallises in the orthorhombic space group[13].

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