Carbohydrate Research, 232 (1992) 189–195
Elsevier Science Publishers B.V., Amsterdam

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

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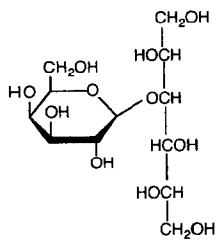
(Received August 28th, 1991; accepted January 27th, 1992)

ABSTRACT

Lactitol trihydrate, $C_{12}H_{24}O_{11} \cdot 3H_2O$, crystallises in the orthorhombic space group, $P2_12_12_1$ with cell dimensions $a = 8.306(2)$, $b = 10.163(1)$, $c = 21.321(1)$ Å, and $V = 1799.8(5)$ Å^3; $Z = 4$, $D_x = 1.47$ Mg m^{-3}, λ(Cu-K_α) = 1.54178 Å, $\mu = 1.14$ mm^{-1}, $F(000) = 856$, and $T = 23°$. There are one intra- and thirteen inter-molecular hydrogen bonds in the structure. The bond lengths and angles agree well with the mean values of related structures. The galactopyranosyl ring has a chair conformation.

INTRODUCTION

We have reported the crystal structure of lactitol (**1**) and lactitol dihydrate [1,2], and Kanters et al. [3] have reported on lactitol monohydrate. We now report on the trihydrate. The crystalline monohydrate [4,5], dihydrate [4], and trihydrate [6] have been the subject of patents.



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EXPERIMENTAL

Single crystals of the trihydrate, mp 38–40° (measured by DSC from onset), were obtained from an aq 80% solution of lactitol at 4°. Intensity data were obtained from a crystal (0.10 × 0.25 × 0.25 mm) with an Enraf–Nonius CAD-4

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diffractometer and graphite-monochromated Cu-K_α($\lambda = 1.54178$) radiation, using the ω–2θ method. The cell parameters and orientation matrix were determined from a least-squares fit of 25 reflections ($10 < \theta < 22°$). Including Friedel pairs, 4285 reflections with $\theta < 75°$ were measured. After merging, there were 2163 unique reflections, 1899 of which had $I > 3\sigma(I)$. Two standard reflections were measured every hour. Linear-decay correction, with correction factors max = 0.999 and min = 0.861, was applied to correct for changes in X-ray intensity. The intensity data were also corrected for Lorentz and polarisation effects, but not for extinction. Empirical absorption correction was done by the Fourier method [7], with correction factors max = 1.722 and min = 0.836. The structure was solved by direct methods using the MULTAN 11/82 program [8], and refined by full-matrix least squares, with all non-H atoms anisotropic, using the MolEN program package [9]. The positions of the H atoms bonded to C atoms were calculated on the basis of known geometry (C–H distance 1.000 Å), whereas the H atoms bonded to O atoms were located in a $\Delta\rho$ map. Each H atom was treated as a riding atom 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 [10] to the value 0.97 Å. The atomic scattering and dispersion correction factors for neutral atoms were taken from International Tables [11]. Altogether, 235 parameters were refined. The results were $R = 0.045$ and $R_W = 0.060$, $w = 1/[(\sigma F_0)^2 + (S \cdot F_0)^2]$ (σF from counting statistics, $S = 0.02$), max shift/$\sigma = 0.02$ in the final cycle, $S = 1.659$, $R_{int} = 1.7\%$, and max and min peaks 0.24(7) and $-0.26(7)$ eÅ^{-3} in the final $\Delta\rho$ map. Fig. 1 was drawn with the PLUTO program [12].

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

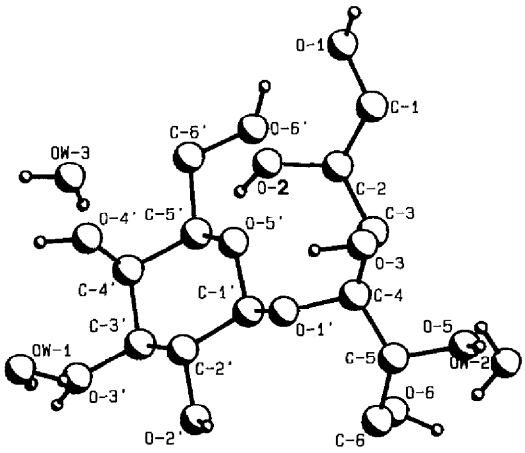

Fig. 1. PLUTO plot and numbering scheme for lactitol trihydrate.

TABLE I

Fractional co-ordinates and equivalent isotropic temperature factors with esd's in parentheses

Atoms	x	y	z	B_{eq} (Å^2) [a]
O-1′	−0.2630(2)	−0.3822(2)	0.08963(7)	2.30(3)
O-1	−0.8945(2)	−0.3436(2)	0.03443(9)	3.20(4)
OW-1	0.0211(4)	0.0753(2)	0.14198(9)	4.33(5)
O-2′	0.0196(2)	−0.2988(2)	0.15612(8)	3.45(4)
O-2	−0.5823(2)	−0.2631(2)	0.05710(8)	2.67(3)
OW-2	−0.2135(3)	−0.7352(2)	−0.0985(1)	4.42(5)
O-3′	−0.0342(3)	−0.0959(2)	0.24314(8)	3.14(4)
O-3	−0.4208(2)	−0.4378(2)	−0.03159(7)	2.73(3)
OW-3	−0.4394(3)	0.0919(3)	0.0997(1)	5.61(6)
O-4′	−0.3525(3)	−0.0333(2)	0.21102(9)	3.40(4)
O-5′	−0.4195(2)	−0.2956(2)	0.16584(7)	2.45(3)
O-5	−0.2763(3)	−0.7161(2)	0.02776(8)	3.06(3)
O-6	−0.1229(3)	−0.6757(2)	0.14844(9)	3.34(4)
O-6′	−0.7188(3)	−0.3145(2)	0.2295(1)	3.64(4)
C-1	−0.7604(3)	−0.4140(3)	0.0092(1)	2.86(5)
C-1′	−0.2641(3)	−0.3482(2)	0.1533(1)	2.23(4)
C-2	−0.6182(3)	−0.4005(2)	0.0524(1)	2.32(4)
C-2′	−0.1360(3)	−0.2454(3)	0.1648(1)	2.39(4)
C-3′	−0.1483(3)	−0.1977(2)	0.2326(1)	2.35(4)
C-3	−0.4781(3)	−0.4844(2)	0.0277(1)	2.29(4)
C-4	−0.3388(3)	−0.5057(2)	0.0739(1)	2.14(4)
C-4′	−0.3183(3)	−0.1481(2)	0.2461(1)	2.49(4)
C-5′	−0.4405(3)	−0.2536(2)	0.2298(1)	2.37(4)
C-5	−0.2071(3)	−0.5937(2)	0.0463(1)	2.43(4)
C-6′	−0.6130(3)	−0.2060(3)	0.2351(1)	2.83(5)
C-6	−0.0690(3)	−0.6187(3)	0.0914(1)	2.94(5)
H-1′	−0.241	−0.426	0.181	5.0
H-2	−0.641	−0.433	0.096	5.0
H-2′	−0.154	−0.171	0.135	5.0
H-3	−0.524	−0.574	0.020	5.0
H-3′	−0.126	−0.273	0.261	5.0
H-4′	−0.326	−0.124	0.291	5.0
H-4	−0.387	−0.547	0.112	5.0
H-5	−0.162	−0.545	0.009	5.0
H-5′	−0.421	−0.328	0.260	5.0
H-11	−0.790	−0.509	0.005	5.0
H-12	−0.731	−0.378	−0.033	5.0
H-61′	−0.630	−0.163	0.277	5.0
H-61	0.010	−0.679	0.071	5.0
H-62′	−0.635	−0.141	0.201	5.0
H-62	−0.015	−0.533	0.101	5.0
HO-1	−0.963	−0.331	−0.002	5.0
HW-11	0.030	0.001	0.114	5.0
HW-12	0.034	0.025	0.180	5.0
HO-2	−0.513	−0.243	0.092	5.0
HO-2′	0.046	−0.300	0.112	5.0
HW-21	−0.117	−0.688	−0.111	5.0
HW-22	−0.272	−0.660	−0.115	5.0
HO-3	−0.378	−0.349	−0.027	5.0
HO-3′	0.027	−0.092	0.282	5.0
HW-31	−0.423	0.161	0.130	5.0
HW-32	−0.398	0.035	0.132	5.0

TABLE I (continued)

Atom	x	y	z	B_{eq} (Å) [a]
HO-4′	−0.322	0.043	0.236	5.0
HO-5	−0.265	−0.719	−0.017	5.0
HO-6	−0.108	−0.770	0.148	5.0
HO-6′	−0.813	−0.303	0.203	5.0

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

geometry of the hydrogen bonds in Table IV *. Crystallographically interesting bond distances and angles in β-pyranoses [13] are given in Table V for lactitol and its mono-, di-, and tri-hydrate. A view of the compound and the numbering scheme are shown in Fig. 1. The primed numbers designate the atoms of the galactose moiety.

TABLE II

Bond distances and bond angles with esd's in parentheses

Bond distance (Å)					
O-1′–C-1′	1.401(3)	O-5′–C-1′	1.422(3)	C-2–C-3	1.535(4)
O-1′–C-4	1.444(3)	O-5′–C-5′	1.440(3)	C-3–C-4	1.535(3)
O-1–C-1	1.429(3)	O-5–C-5	1.426(3)	C-3′–C-4′	1.527(4)
O-2′–C-2′	1.414(3)	O-6′–C-6′	1.415(3)	C-4–C-5	1.530(3)
O-2–C-2	1.431(3)	O-6–C-6	1.419(3)	C-4′–C-5′	1.516(4)
O-3–C-3	1.431(3)	C-1′–C-2′	1.510(4)	C-5′–C-6′	1.517(4)
O-3′–C-3′	1.421(3)	C-1–C-2	1.504(4)	C-5–C-6	1.518(4)
O-4′–C-4′	1.415(3)	C-2′–C-3′	1.530(3)		
Bond angles (°)					
C-1′–O-1′–C-4	115.9(2)	C-1–C-2–C-3	109.5(2)	O-4′–C-4′–C-5′	109.1(2)
C-1′–O-5′–C-5′	113.6(2)	O-3–C-3–C-2	111.8(2)	C-3′–C-4′–C-5′	110.0(2)
O-1′–C-1′–O-5′	106.3(2)	O-3–C-3–C-4	111.3(2)	O-5′–C-5′–C-4′	110.2(2)
O-1′–C-1′–C-2′	108.8(2)	C-2–C-3–C-4	115.4(2)	O-5′–C-5′–C-6′	106.2(2)
O-5′–C-1′–C-2′	110.4(2)	O-3′–C-3′–C-2′	109.6(2)	C-4′–C-5′–C-6′	112.9(2)
O-1–C-1–C-2	109.6(2)	O-3′–C-3′–C-4′	110.3(2)	O-5–C-5–C-4	109.2(2)
O-2′–C-2′–C-1′	110.9(2)	C-2′–C-3′–C-4′	110.2(2)	O-5–C-5–C-6	109.5(2)
O-2′–C-2′–C-3′	107.8(2)	O-1′–C-4–C-3	110.8(2)	C-4–C-5–C-6	113.2(2)
C-1′–C-2′–C-3′	109.0(2)	O-1′–C-4–C-5	106.6(2)	O-6′–C-6′–C-5′	109.4(2)
O-2–C-2–C-1	107.2(2)	C-3–C-4–C-5	112.0(2)	O-6–C-6–C-5	111.9(2)
O-2–C-2–C-3	114.1(2)	O-4′–C-4′–C-3′	111.0(2)		
HW-11–OW-1–HW-12	96.1(2)				
HW-21–OW-2–HW-22	86.2(2)				
HW-31–OW-3–HW-32	84.3(2)				

* 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/503/*Carbohydr. Res.*, 232 (1992) 189–195.

TABLE III

Torsional angles (°) with esd's in parentheses

Endocyclic for galactopyranosyl moiety			
O-5′–C-1′–C-2′–C-3′	57.9(2)	C-3′–C-4′–C-5′–O-5′	−54.9(3)
C-1′–C-2′–C-3′–C-4′	−55.4(3)	C-1′–O-5′–C-5′–C-4′	59.5(2)
C-2′–C-3′–C-4′–C-5′	54.3(3)	C-5′–O-5′–C-1′–C-2′	−61.3(2)
Exocyclic for galactopyranosyl moiety			
O-1′–C-1′–C-2′–C-3′	174.2(2)	C-2′–C-3′–C-4′–O-4′	−66.6(3)
O-1′–C-1′–C-2′–O-2′	−67.2(2)	O-4′–C-4′–C-5′–O-5′	67.0(3)
O-5′–C-1′–C-2′–O-2′	176.4(2)	O-4′–C-4′–C-5′–C-6′	−51.6(3)
O-2′–C-2′–C-3′–C-4′	−175.9(2)	C-3′–C-4′–C-5′–C-6′	−173.5(2)
O-2′–C-2′–C-3′–O-3′	62.6(3)	O-5′–C-5′–C-6′–O-6′	68.7(3)
C-1′–C-2′–C-3′–O-3′	−176.9(2)	C-4′–C-5′–C-6′–O-6′	−170.4(2)
O-3′–C-3′–C-4′–O-4′	54.6(2)	C-1′–O-5′–C-5′–C-6′	−177.8(2)
O-3′–C-3′–C-4′–C-5′	175.5(2)	C-5′–O-5′–C-1′–O-1′	−179.2(2)
C-4–O-1′–C-1′–O-5′	−80.1(2)	C-4-O-1′-C-1′-C-2′	161.0(2)
D-*Glucitol residue*			
O-1–C-1–C-2–C-3	175.9(2)	C-2–C-3–C-4–O-1′	−62.9(3)
O-1–C-1–C-2–O-2	−59.9(3)	C-2–C-3–C-4–C-5	178.2(2)
O-2–C-2–C-3–O-3	−55.4(3)	O-1′–C-4–C-5–O-5	−178.0(2)
O-2–C-2–C-3–C-4	73.1(3)	O-1′–C-4–C-5–C-6	59.8(2)
C-1–C-2–C-3–O-3	64.7(3)	C-3–C-4–C-5–O-5	−56.7(2)
C-1–C-2–C-3–C-4	−166.8(2)	C-3–C-4–C-5–C-6	−178.9(2)
O-3–C-3–C-4–O-1′	65.9(2)	O-5–C-5–C-6–O-6	−65.0(3)
O-3–C-3–C-4–C-5	−53.0(3)	C-4–C-5–C-6–O-6	57.1(3)
C-1′–O-1′–C-4–C-5	−117.4(2)	C-1′–O-1′–C-4–C-3	120.5(2)

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-3	1.91(2)	2.78(3)	148(1)	$1/2-x, -1/2-y, -z$
2	OW-1–HW-12 ··· O-3′	1.90(2)	2.81(3)	154(1)	x, y, z
3	OW-2–HW-21 ··· OW-3	1.78(3)	2.70(4)	157(1)	$1/2+x, -1/2-y, -z$
4	OW-2–HW-22 ··· OW-1	2.01(3)	2.89(4)	151(1)	$-1/2-x, -1/2-y, -z$
5	OW-3–HW-32 ··· O-4′	1.85(2)	2.79(3)	161(1)	x, y, z
6	O-1–HO-1 ··· O-2	1.81(2)	2.72(3)	156(1)	$1/2+x, 1/2+y, -z$
7	O-2–HO-2 ··· O-5′	1.83(2)	2.70(2)	149(1)	x, y, z
8	O-2′–HO-2′ ··· O-1	1.78(2)	2.73(3)	166(1)	$1+x, y, z$
9	O-3–HO-3 ··· O-1	1.97(2)	2.87(3)	153(1)	$1/2+x, 1/2+y, -z$
10	O-3′–HO-3′ ··· O-6	1.89(2)	2.78(3)	151(1)	$-x, 1/2+y, 1/2-z$
11	O-4′–HO-4′ ··· O-6′	1.66(2)	2.63(3)	172(1)	$-1-x, 1/2+y, 1/2-z$
12	O-5–HO-5 ··· OW-2	1.79(2)	2.75(3)	171(1)	x, y, z
13	O-6–HO-6 ··· OW-1	1.79(2)	2.80(3)	153(1)	$x, -1+y, z$
14	O-6′–HO-6′ ··· O-2′	1.71(2)	2.68(3)	175(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.

TABLE V

Some bond lengths and angles of lactitol (L) and its mono-, di- and tri-hydrate

	L	L·H_2O	L·$2H_2O$	L·$3H_2O$
O-1′–C-1′ (Å)	1.392(2)	1.394(3)	1.405(3)	1.401(3)
C-5′–O-5′–C-1′(°)	112.2(2)	111.4(2)	110.8(2)	113.6(2)
O-5′–C-1′–O-1′(°)	107.3(2)	108.1(2)	108.6(2)	106.3(2)
C-1′–O-1′–C-4(°)	113.5(1)	118.2(2)	117.3(2)	115.9(2)
C-4–O-1′–C-1′–O-5′(°)	−75.1(2)	−86.3(2)	−57.8(3)	−80.1(2)
C-1′–O-1′–C-4–C-3(°)	126.3(2)	116.8(2)	132.7(2)	120.5(2)
Ref.	1	3	2	

The bond distances and angles are normal. The shortening of the O-1′–C-1′ distance [1.401(3) Å] and the angles in the acetal sequence [C-5′–O-5′–C-1′ 113.6(2)° and O-5′–C-1′–O-1′ 106.3(2)°] agree with the mean values of related structures (1.38 Å, 111.9°, and 107.4°) [3,13]. The glycosidic angle C-1′–O-1′–C-4 is 115.9(2)°. The galactopyranosyl ring has a chair conformation with C-1′,2′,4′,5′ coplanar, C-3′ − 0.675(2) Å below, and O-5′ 0.640(2) Å above, the plane.

The torsional angles of the linkage C-4–O-1′–C-1′–O-5′ and C-1′–O-1′–C-4–C-3 are −80.1(2)° and 120.5(2)°, respectively. The exocyclic torsional angles (Table III) have values close to 60° or 180°, which correspond to the ideal *gauche* or *trans* arrangements, respectively (max deviations, 8.7° and 9.6°, respectively).

There are one intra- and thirteen inter-molecular hydrogen bonds in the structure. The intramolecular hydrogen bond lies between O-2 and O-5′. All hydroxyl H atoms are involved in hydrogen bonding. The oxygen atoms act as single acceptors, except for OW-1 and O-1 which act as double acceptors and O-1′ and O-5 which are non-acceptors. The water molecules 1 and 2 (OW-1 and OW-2)

TABLE VI

Weak interactions (up to 2.87 Å) [a]

Number	O–H ··· O	H ··· O (Å)	O–H ··· O (°)	Symmetry operation for ··· O atom
1	OW-2–HW-22 ··· OW-3	2.87(2)	70(1)	$-1/2-x, -y-1/2, -z$
2	OW-3–HW-31 ··· OW-2	2.62(2)	85(1)	$x-1/2, -y-1/2, -z$
3	OW-3–HW-31 ··· O-4′	2.69(2)	86(1)	x, y, z
4	OW-3–HW-31 ··· O-5	2.79(2)	82(1)	$x, y-1, z$
5	O-1–HO-1 ··· O-3	2.84(2)	82(1)	$x+1/2, -1/2-y, -z$
6	O-2–HO-2 ··· O-1′	2.51(2)	111(1)	x, y, z
7	O-2′–HO-2′ ··· O-1′	2.74(2)	88(1)	x, y, z
8	O-3–HO-3 ··· O-1′	2.68(2)	96(1)	x, y, z
9	O-3–HO-3 ··· O-2	2.62(2)	98(1)	x, y, z
10	O-3–HO-3 ··· O-2	2.79(2)	133(1)	$x-1/2, 1/2+y, -z$
11	O-4′–HO-4′ ··· O-3′	2.78(2)	81(1)	x, y, z

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

donate two hydrogen bonds. Water molecule 3 (OW-3) donates and accepts one hydrogen bond. Altogether, they form a link between lactitol molecules.

In addition to the principal hydrogen bonds, there are several weaker interactions which are given in Table VI (H ··· O distances are calculated up to 2.90 Å) [14].

ACKNOWLEDGMENTS

The Academy of Finland and the Emil Aaltonen Foundation are acknowledged for financial support (to J.K.).

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