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α-Lactose monohydrate: a redetermination at 150 K

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Key indicators

Single-crystal X-ray study
T = 150 K
Mean σ(C–C) = 0.003 Å
R factor = 0.033
wR factor = 0.079
Data-to-parameter ratio = 8.1

For details of how these key indicators were automatically derived from the article, see http://journals.iucr.org/e.

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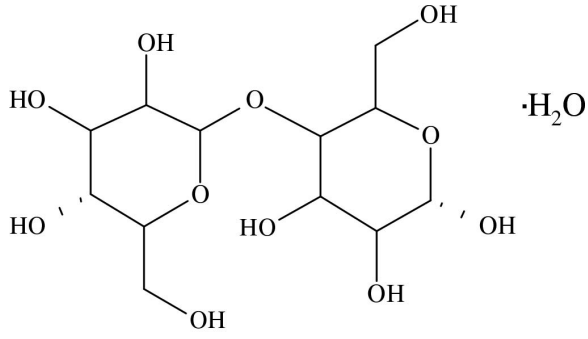
The structure of the monohydrate of α-4-(β-D-galactopyranosido)-D-glucopyranose, more commonly known as α-lactose monohydrate, $C_{12}H_{22}O_{11}\cdot H_2O$, has been previously studied by single-crystal diffraction at *ca* 296 K [Beevers & Hansen (1971). *Acta Cryst*. B**27**, 1323–1325; Fries *et al.* (1971). *Acta Cryst.* B**27**, 994–1005; Noordik *et al.* (1984). *Z. Kristallogr*. **168**, 59–65]. This redetermination at low temperature [150 (2) K] shows improved precision of geometry. Graph-set analysis of the hydrogen-bonding motifs is presented for the first time.

Comment

α-Lactose monohydrate, (I), is the most common form of lactose and may be used as the parent material for at least four different (pseudo)polymorphs of this disaccharide (Garnier *et al.*, 2002; Figura & Epple, 1995). This reducing sugar is built from a moiety of β-D-galactose and a moiety of α-D-glucose, joined by a 1,4 glycosidic bond between C1′ of the galactose and C4 of the glucose unit (Fig. 1).



(I)

A search of the Cambridge Structural Database (Allen, 2002; Fletcher *et al.*, 1996; Version 5.26, November 2004 update) highlighted previous research on this hydrate with data collections performed at *ca* 296 K (Beevers & Hansen, 1971; Fries *et al.*, 1971; Noordik *et al.*, 1984). The redetermination of (I) presented here, obtained from low temperature [150 (2) K] single-crystal diffraction data, has resulted in improved precision compared to the previously determined room-temperature structures. Standard uncertainties on C—O and C—C bond lengths are improved to *ca* 0.003 compared to *ca* 0.004 at room temperature, with an improvement to *ca* 0.0017 compared to *ca* 0.002 for standard uncertainties on C–O–C angles. The unit cell volume measured at 150 K [768.85 (14) Å^3] is *ca* 0.88% smaller than that determined at room temperature [775.7 (5) Å^3; Noordik

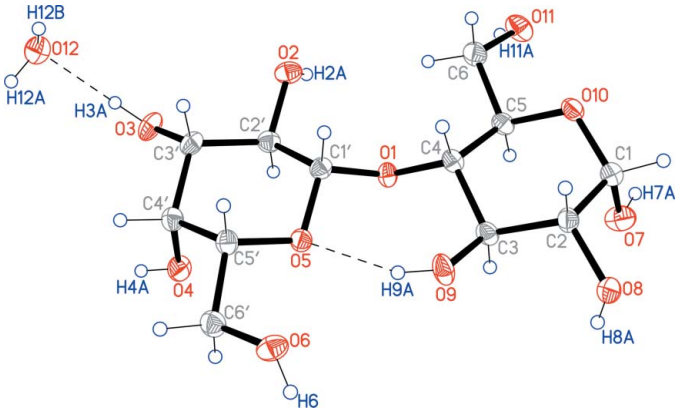


Figure 1
View of (I), showing the atom-labelling scheme. Displacement ellipsoids are drawn at the 50% probability level. Only hydroxyl H atoms involved in hydrogen bonding are labelled. Dashed lines indicate hydrogen bonds. One intramolecular hydrogen bond is present, *viz*. O9–H9*A*···O5.

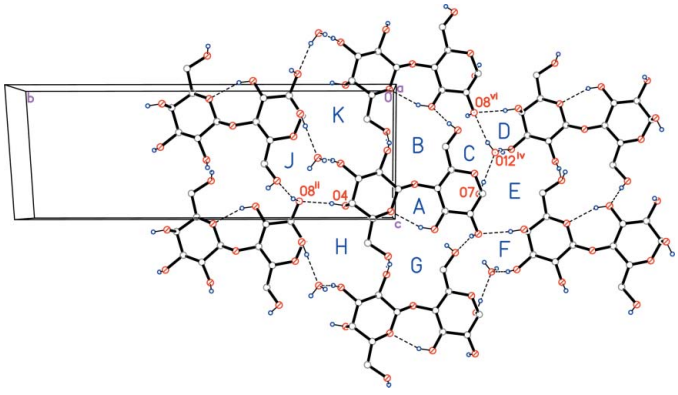


Figure 2
Packing diagram of (I) showing graph-set notation for hydrogen bonding within the crystal structure when viewed along the crystallographic *a* axis. It can be observed that each system of (I), results in motifs: (A) $S(7)$; (B) $R_3^3(16)$; (C) $R_3^3(14)$; (D) $R_3^3(9)$; (E) $R_4^4(18)$; (F) $R_4^3(16)$; (G) $R_3^3(19)$; (H) $R_4^3(18)$; (J) $R_4^3(15)$; (K) $R_5^4(21)$ approximately in the *bc* plane.

et al., 1984], this latter unit-cell volume itself being smaller than that derived from previous measurements.

The unit cell has previously been reported as 7.937 (2) Å, 21.568 (7) Å, 4.815 (1) Å and β = 109.77 (2)° (Noordik *et al.*, 1984); the unit cell reported here is related to the Noordik unit cell by a simple transformation and is currently regarded as the conventional unit cell, having the shortest possible vectors in the *ac* plane (International Tables for X-ray Crystallography, 1969, Vol. 1).

An examination of the final difference Fourier map reveals a peak of 0.27 e Å^{-3} at a distance of 1.48 Å from C1, close to the equatorial atom H1. Since the α and β anomers establish a 40:60 equilibrium in solution over time, the question arises whether there is a small component of β-lactose present, even though only the α-anomer spontaneously crystallizes below 366.5 K (Walstra & Jenness, 1984). In this present determination, the largest ten difference map features lie in the range 0.22–0.32 e Å^{-3}, so this dubious peak is, in fact, indistinguishable from the noise. This means that, if present at all,

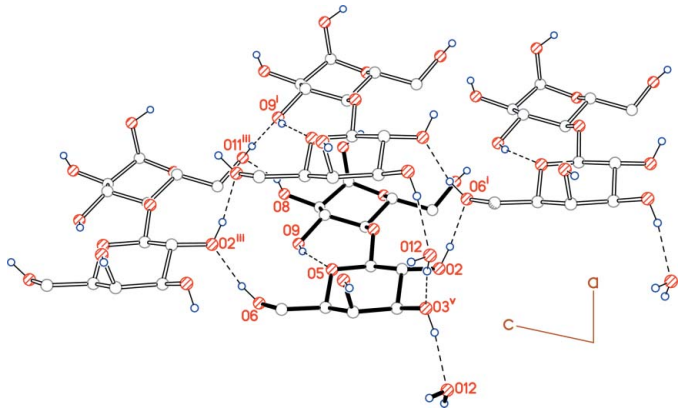


Figure 3
View of (I) along the crystallographic *b* axis, showing the remaining hydrogen bonding motifs formed between layers of (I) and water molecules; containing O2—H2*A*···O6^{i}, O3—H3*A*···O12, O6—H6···O2^{iii}, O8—H8*A*···O11^{iii}, O9—H9*A*···O5, O11—H11*A*···O9^{i} and O12—H12*B*···O3^{v} hydrogen bonds [symmetry codes: (i) $x-1, y, z-1$; (iii) $x, y, 1+z$; (v) $1+x, y, z$].

the percentage of the β-anomer must be in the low single figures and any significant β component can definitely be ruled out.

Graph-set analysis of the hydrogen-bonding patterns (Bernstein *et al.*, 1995; Etter *et al.*, 1990) within the structure shows the complicated nature of the linking together of the lactose and water molecules. There are 15 different ring motifs involving one molecule of hydrated α-lactose (Figs. 2 and 3). The motifs use either two or three molecules of (I), hydrogen bonding with zero, one or two water molecules. Fig. 4 shows a stacking formation of the lactose molecules when viewed, as a packing plot, along the crystallographic *c* axis. The molecules are held rigidly by a chain, $C_2^2(4)$, of hydrogen bonds between O6–H6*A*···O2^{iii} and O2–H2*A*···O6^{i} [symmetry codes: (i) $x-1, y, z-1$; (iii) $x, y, 1+z$] propagating along the crystallographic *a* axis and are also linked through hydrogen bonding to water molecules.

As well as those motifs present along the crystallographic *a* axis (Fig. 2), higher order motifs $R_6^6(21)$, $R_4^4(20)$, $R_5^5(20)$, $R_6^6(23)$ and $R_4^4(18)$ can be found between layers of (I) and interconnecting water molecules (Figs. 3 and 4).

Experimental

Colourless X-ray quality crystals of (I) were produced using powdered D-(+)-α-lactose monohydrate (supplied by Fluka Biochemica, Stenheim). A 10% aqueous solution of (I) was prepared as in methods previously studied by Larhrib *et al.* (2003). This solution was then diluted through addition of acetone, resulting in a 35:65 mixture of 10% lactose solution–acetone. Crystallization occurred upon standing at room temperature over a period of 48 h. A second crystalline sample of (I) was produced by a similar method except that acetone was substituted with a 10% potassium methoxide aqueous solution. Diffraction data from this sample were recorded by the EPSRC National Crystallographic Service, affording very similar unit-cell dimensions.

Crystal data

$C_{12}H_{22}O_{11}\cdot H_2O$
M_r = 360.31
Monoclinic, $P2_1$
a = 4.7830 (5) Å
b = 21.540 (2) Å
c = 7.7599 (8) Å
β = 105.911 (2)°
V = 768.85 (14) Å^3
Z = 2
D_x = 1.556 Mg m^{-3}
Mo $K\alpha$ radiation
Cell parameters from 3523 reflections
θ = 2.7–28.2°
μ = 0.14 mm^{-1}
T = 150 (2) K
Block, colourless
0.53 × 0.27 × 0.21 mm

Data collection

Bruker SMART 1000 CCD diffractometer
Narrow-frame ω scans
Absorption correction: multi-scan (*SADABS*; Sheldrick, 2003)
T_{min} = 0.878, T_{max} = 0.971
6697 measured reflections
1864 independent reflections
1692 reflections with $I > 2\sigma(I)$
R_{int} = 0.022
θ_{max} = 28.9°
$h = -6 \rightarrow 6$
$k = -27 \rightarrow 27$
$l = -9 \rightarrow 9$

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)]$ = 0.033
$wR(F^2)$ = 0.079
S = 1.10
1864 reflections
231 parameters
H atoms treated by a mixture of independent and constrained refinement
$w = 1/[\sigma^2(F_o^2) + (0.0394P)^2 + 0.1957P]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max} < 0.001$
$\Delta\rho_{max}$ = 0.32 e Å^{-3}
$\Delta\rho_{min}$ = −0.17 e Å^{-3}

Table 1
Selected geometric parameters (Å, °).

O1—C1′	1.398 (3)	C1—O7	1.399 (3)
O1—C4	1.437 (3)		
C1′—O1—C4	116.88 (17)		

Table 2
Hydrogen-bond geometry (Å, °).

D—H···A	D—H	H···A	D···A	D—H···A
O2—H2A···O6^{i}	0.84	1.85	2.665 (2)	163
O3—H3A···O12	0.84	1.89	2.722 (3)	168
O4—H4A···O8^{ii}	0.84	1.97	2.806 (3)	173
O6—H6···O2^{iii}	0.84	1.90	2.707 (2)	161
O7—H7A···O12^{iv}	0.84	1.97	2.772 (2)	161
O8—H8A···O11^{iii}	0.84	1.91	2.700 (3)	157
O9—H9A···O5	0.84	2.02	2.819 (2)	159
O11—H11A···O9^{i}	0.84	1.92	2.755 (2)	174
O12—H12B···O3^{v}	0.85 (1)	1.89 (2)	2.740 (3)	174 (4)
O12—H12A···O8^{vi}	0.84 (1)	2.23 (2)	2.920 (2)	140 (3)

Symmetry codes: (i) $x-1, y, z-1$; (ii) $-x, y+\frac{1}{2}, -z+2$; (iii) $x, y, z+1$; (iv) $-x, y-\frac{1}{2}, -z+1$; (v) $x+1, y, z$; (vi) $-x+1, y+\frac{1}{2}, -z+2$.

Non-water H atoms were placed in geometric positions using a riding model [C—H = 0.99 (methylene H) and 1.00 Å (methine H); O—H = 0.84 Å], and U_{iso}(H) = 1.2U_{eq}(C) and 1.5U_{eq}(O). The data set was truncated at 2θ = 52°, as only statistically insignificant data were present above this limit. Water H atoms were located in a difference Fourier map and refined using restraints on the O—H bond length [target value 0.840 (15) Å] and the 1,3-distance [target value 1.43 (2) Å] and U_{iso}(H) = 1.5U_{eq}(O). In the absence of significant anomalous dispersion effects, 1526 Friedel pairs were merged during the refinement of (I).

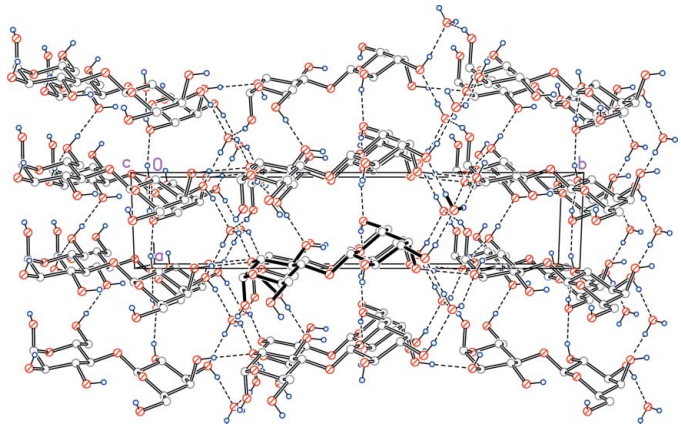


Figure 4
Packing diagram of (I), viewed along the crystallographic c axis, showing the hydrogen bonding linking molecules of (I) and water, above and below a central molecule.

Data collection: *SMART* (Bruker, 2001); cell refinement: *SAINT* (Bruker, 2001); data reduction: *SAINT*; program(s) used to solve structure: *SHELXTL* (Sheldrick, 2000); program(s) used to refine structure: *SHELXTL*; molecular graphics: *SHELXTL*; software used to prepare material for publication: *SHELXTL* and local programs.

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