organic compounds

Methyl 4-O-β-L-fucopyranosyl α-D-glucopyranoside hemihydrate

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The crystal structure of methyl 4-O-β-L-fucopyranosyl α-D-glucopyranoside hemihydrate $C_{13}H_{24}O_{10} \cdot 0.5H_2O$ is organized in sheets with antiparallel strands, where hydrophobic interaction accounts for partial stabilization. Infinite hydrogen-bonding networks are observed within each layer as well as between layers; some of these hydrogen bonds are mediated by water molecules. The conformation of the disaccharide is described by the glycosidic torsion angles: $\varphi_H = -6.1°$ and $\psi_H = 34.3°$. The global energy minimum conformation as calculated by molecular mechanics *in vacuo* has $\varphi_H = -58°$ and $\psi_H = -20°$. Thus, quite substantial changes are observed between the *in vacuo* structure and the crystal structure with its infinite hydrogen-bonding networks.

Comment

The crystal structure of a compound reveals information on intermolecular interactions such as hydrophobic packing and hydrogen bonding (Taylor & Kennard, 1984; Aakeröy & Seddon, 1993). These weak forces in the crystal structure are important for a thorough understanding of molecular interactions in general. In the field of carbohydrates a number of crystal structures have been solved, but the process of obtaining crystal structure information is still hampered by difficulties in obtaining crystals of sufficient size and quality. The structure of cellulose has been investigated by analysis of methyl β-cellotrioside (Raymond *et al.*, 1995) and β-cellotetraose (Gessler *et al.*, 1995). Beyond a given degree of polymerization it is reasonable to assume that the inner residues should adopt the conformation and crystalline packing that occur in the crystalline polymer. Another example of a small oligosaccharide whose crystal structure has been solved is α-L-Fucp-(1→2)-α-D-Galp-OMe (Watt *et al.*, 1996), the disaccharide structure of which is a component of a xyloglucan. In previous studies we have determined the structures of 6-O-[(R)-1-carboxyethyl]-α-D-Galp-OMe (Eriksson *et al.*, 1996) and α-D-Manp-(1→2)-β-D-Glcp-OMe (Eriksson *et al.*, 1997). We report here the crystal structure of the title compound, β-

L-Fucp-(1→4)-α-D-Glcp-OMe (I) as the hemihydrate

(I)
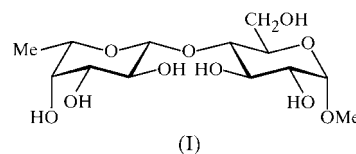
Four molecules of (I) (Fig. 1) and two water molecules are found in the unit cell. The monosaccharide units in (I), *i.e.* L-fucose and D-glucose, show their expected chair conformations, with $^1C_4$ and $^4C_1$ for fucose and glucose, respectively.

The conformation of the disaccharide, (I), is described by the torsion angles at the glycosidic linkage (Table 1). In the crystal, $\varphi_H = -6.1°$ and $\psi_H = 34.3°$. The accessible conformation space for a disaccharide can be investigated by evaluation of the potential energy for different combinations of φ_H and ψ_H. This can be represented as a Ramachandran map (Fig. 2). Each grid point was extensively energy minimized, resulting in a relaxed energy. The global energy minimum identified from energy minimization *in vacuo* has $\varphi_H = -58°$ and $\psi_H = -20°$, in which the conformation at the φ_H torsion angle is determined by the contribution from the *exo*-anomeric effect. In contrast, a significant change has occurred for the crystal structure, in which φ_H is almost eclipsed. This conformation is approximately 15 kJ mol^{-1}
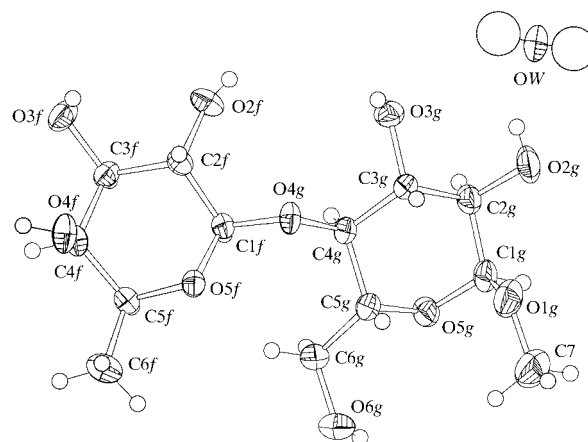

Figure 1
The molecular structure of the title compound and the atomic numbering scheme, with 50% probability ellipsoids. H atoms are drawn as small circles of arbitrary radii.

higher in energy as deduced from the Ramachandran map. The ψ_H torsion angle is also substantially changed. In a previous study of α-D-Manp-(1→2)-β-D-Glcp-OMe, the crystal structure was found to be only 6 kJ mol^{-1} higher in energy on the Ramachandran map (Eriksson *et al.*, 1997). The torsion angle of the hydroxymethyl group of the glucose residue has $\omega = 67.8°$, *i.e.* it has a *gauche-trans* conformation with respect to O5 and C4, respectively. This is one of the two torsional states significantly populated for glucose in solution. The φ_H torsion angle of the glucose residue has the commonly observed C2g—C1g to O1g—C7 in an antiperiplanar conformation with $\varphi_H = -55.9°$ (*exo*-anomeric conformation).

There are seven distinct hydrogen bonds in the crystal structure of the title compound, which has one water molecule per two molecules of disaccharide (Table 2). The water molecule is involved in hydrogen bonding as a donor to O3f and as an acceptor from HO2g (Fig. 3). Hydrogen bonding is observed for O4f—HO4f···O2g in a 'head-to-tail' geometry for a given strand. Adjacent to the water molecule, hydrogen bonding can be identified for O3f—HO3f···O3g and O3g—HO3g···O3f, between different strands. Furthermore, a hydrogen-bond chain is found from O2f—HO2f to O2f of another chain. Together with the water hydrogen bonds, this pattern of hydrogen bonding leads to an infinite zipper of hydrogen bonds between antiparallel strands. The remaining hydrogen bond is present between the primary hydroxyl groups, i.e. O6g in one strand to O6g in another. The structure is further stabilized by additional hydrophobic interactions between the O-methyl groups of the glucose residue and the methyl group of the fucose (6-deoxygalactose) residue, leading to another antiparallel zipper. Hydrophobic packing between sugar rings and infinite hydrogen-bond chains lead to stabilization orthogonal to the previous hydrogen-bond patterns.

In the crystal structure of α-D-Manp-(1→2)-β-D-Glcp-OMe, a local hydrogen-bonding network with a limited extension was observed (Eriksson et al., 1997). No water molecule was involved in this crystal structure. The conformational difference between the in vacuo and crystal structures at the glycosidic linkage between the two sugar residues was substantially smaller than in the present investigation. Using energetic criteria a similar observation can be identified, in particular since in the previous study a procedure was used in which bond lengths and angles were not relaxed. Thus, the
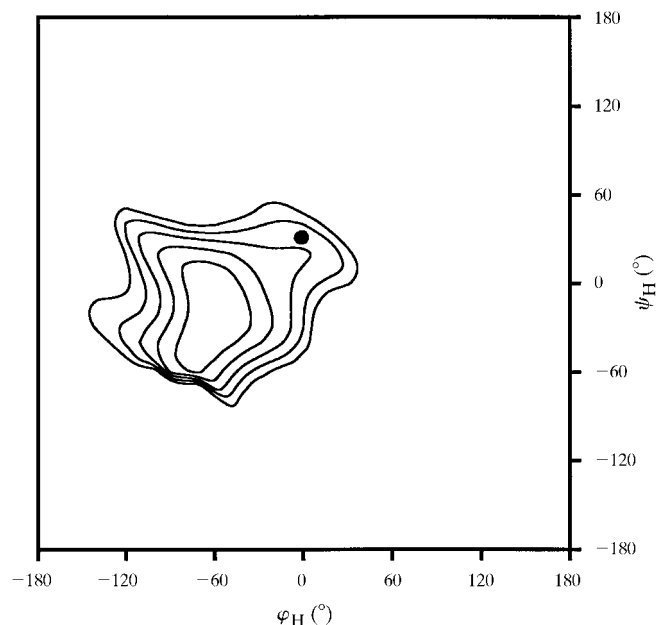
crystal structure of α-D-Manp-(1→2)-β-D-Glcp-OMe shows a rather small difference from the in vacuo structure, whereas for (I), the differences using the same criteria are quite large. The most conspicuous difference is the extended hydrogen-bonding networks, mediated not only by water molecules but also by other hydrogen bonds, that in effect lead to the zippers being observed. The extent to which conformational changes between in vacuo and crystal structures occur as a consequence of extended hydrogen-bonding networks is particularly intriguing and will be analyzed in future studies.
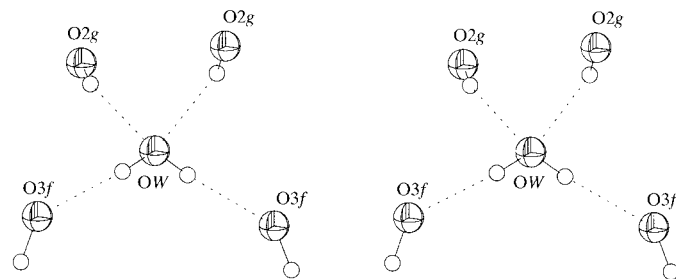

Figure 3
A stereoview of the water bridging molecules in the title compound with the acceptor and donor atoms from the sugar residues.

Experimental

The synthesis of compound (I) by glycosylation of 2,3,6-tri-O-bensyl-α-D-glucopyranoside with ethyl 2,3,4-tri-O-benzoyl-1-thio-β-L-fuco-pyranoside under methyl trifluoromethanesulphonate promotion has been described previously by Backman et al. (1988). The disaccharide was crystallized from methanol/water at ambient temperature. Molecular mechanics calculations were performed with QUANTA/CHARMm, using the force field PARM22 (Molecular Simulations Inc., 1996) and a dielectric constant of 2. The Ramachandran map was generated by 10° increments on a φ_H/ψ_H grid. Each conformer was restrained by a harmonic potential with a force constant of 4184 kJ mol^{-1} followed by extensive energy minimization using steepest descent, conjugate gradient and finally Newton–Raphson algorithms.

Crystal data

$C_{13}H_{24}O_{10} \cdot 0.5H_2O$	$D_x = 1.461$ Mg m^{-3}
$M_r = 349.33$	Mo $K\alpha$ radiation
Monoclinic, $C2$	Cell parameters from 1078
$a = 23.343$ (9) Å	reflections
$b = 4.7027$ (9) Å	$\theta = 1.7–26.0°$
$c = 14.935$ (6) Å	$\mu = 0.128$ mm^{-1}
$\beta = 104.36$ (5)°	$T = 293$ (2) K
$V = 1588.2$ (9) Å^3	Prism, colourless
$Z = 4$	$0.20 \times 0.15 \times 0.10$ mm

Figure 2
A Ramachandran map of the title compound. Contour lines are drawn in 4.2 kJ mol^{-1} increments above the global energy minimum. The conformation of the crystal structure of (I)·0.5H$_2$O is marked.

Table 1
Selected torsion angles (°).

O5f—C1f—O4g—C4g	113.8 (2)	O5g—C1g—O1g—C7	64.8 (3)
H1f—C1f—O4g—C4g	−6.1	H1g—C1g—O1g—C7	−55.9
C1f—O4g—C4g—C3g	152.6 (2)	C1f—O4g—C4g—C5g	−88.3 (3)
C1f—O4g—C4g—H4g	34.3	C2f—C1f—O4g—C4g	−127.9 (2)
O5g—C5g—C6g—O6g	67.8 (3)	C2g—C1g—O1g—C7	−173.8 (3)

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Data collection

Stoe IPDS area-detector diffractometer	$R_{int} = 0.054$
	$\theta_{max} = 25.98°$
Area-detector scans	$h = -28 \rightarrow 28$
6288 measured reflections	$k = -5 \rightarrow 5$
1751 independent reflections	$l = -18 \rightarrow 18$
1358 reflections with $I > 2\sigma(I)$	

Refinement

Refinement on F^2	H atoms treated by a mixture of independent and constrained refinement
$R[F^2 > 2\sigma(F^2)] = 0.035$	
$wR(F^2) = 0.090$	
$S = 1.041$	$w = 1/[\sigma^2(F_o^2) + (0.0521P)^2]$
1751 reflections	where $P = (F_o^2 + 2F_c^2)/3$
223 parameters	$(\Delta/\sigma)_{max} = 0.001$
	$\Delta\rho_{max} = 0.17$ e Å^{-3}
	$\Delta\rho_{min} = -0.17$ e Å^{-3}

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

$D-H\cdots A$	$D-H$	$H\cdots A$	$D\cdots A$	$D-H\cdots A$
$OW-HW\cdots O3f^i$	0.83 (4)	1.92 (4)	2.749 (3)	172 (5)
$O6g-HO6g\cdots O6g^{ii}$	0.82	1.95	2.738 (2)	162
$O3g-HO3g\cdots O3f^{iii}$	0.82	2.17	2.844 (3)	140
$O2g-HO2g\cdots OW$	0.82	1.95	2.702 (3)	152
$O4f-HO4f\cdots O2g^{iv}$	0.82	1.91	2.730 (3)	177
$O3f-HO3f\cdots O3g^{iii}$	0.82	1.98	2.755 (3)	158
$O2f-HO2f\cdots O2f^{iii}$	0.82	1.97	2.759 (2)	162

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

The reflection conditions give $C2$, Cm and $C2/m$ as possible space groups. Of these, $C2/m$ could be disregarded as it is centrosymmetric and we are convinced that the sample is enantiomorphically pure. With the short b axis (4.7 Å) and the mirror planes in Cm we must also disregard that space group as an impossible choice. The only remaining space group is $C2$, in which the structure model also refines nicely. The number of Friedel pairs measured was 1101. The Friedel equivalents were merged as no significant information can be extracted from equivalents when oxygen is the heaviest atom using Mo radiation. All non-H atoms were refined with anisotropic displacement parameters using a 'rigid-bond' restraint to U_{ij} of two bonded atoms (Rollett, 1970), implemented as the *DELU* instruction in *SHELXL*97 (Sheldrick, 1997). All H atoms except the water H were positioned geometrically and allowed to ride during the least-squares refinements. The water-H-atom parameters were refined independently. The torsion angles containing H atoms were calculated with geometrically placed H atoms; therefore, the s.u.'s of these angles are of minor significance since the s.u.'s of the H-atom positions will be related to those of the atom to which the H atoms are connected. The absolute configuration of (I) is determined by its constituent monosaccharides, which have the L- and D-configurations.

Data collection: *EXPOSE* (Stoe, 1997); cell refinement: *CELL* (Stoe, 1997); data reduction: *INTEGRATE* (Stoe, 1997); program(s) used to solve structure: *SHELXS*97 (Sheldrick, 1990); program(s) used to refine structure: *SHELXL*97; molecular graphics: *DIAMOND* (Bergerhoff, 1996); software used to prepare material for publication: *PLATON*98 (Spek, 1998).

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