

The Crystal and Molecular Structure of Methyl β -D-Glucopyranoside Hemihydrate*

BY G. A. JEFFREY AND SHOZO TAKAGI

Chemistry Department, Brookhaven National Laboratory, Upton, New York 11973, USA

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Methyl β -D-glucopyranoside hemihydrate, $C_7H_{14}O_6 \cdot \frac{1}{2}H_2O$, crystallizes in space group $P4_12_12$ with $a = b = 7.433$ (1), $c = 34.154$ (2) Å, $Z = 8$. The structure was solved by *MULTAN* and refined to $R(F^2) = 0.035$ for 1269 symmetry-independent reflections. The molecular dimensions differ significantly from those of methyl α -D-glucopyranoside in that the glycosidic bond C(1)—O(1) is shorter (1.380 Å), the two ring C—O distances are more nearly equal (1.440 and 1.432 Å), and the ring-oxygen valence angle is smaller (111.5°). The conformation of the primary alcohol group is the same, *gauche-trans*, but the pyranose ring is more puckered. The hydrogen bonding consists of finite chains which intersect at the water molecules, and is more extensive than in methyl α -D-glucopyranoside.

Introduction

The objective of this study was to compare the molecular structure of methyl β -D-glucopyranoside with that of the corresponding α compound, which has been examined by both X-ray and neutron diffraction (Berman & Kim, 1968; Jeffrey, McMullan & Takagi, 1977). Although the configuration of the molecules differs only in the equatorial *versus* axial position of the methoxy group on C(1), small but significant differences in the molecular dimensions are anticipated; these can be measured with the present accuracy of X-ray diffractometry. These differences will arise because of the different conformation of the C—O—C—O—C acetal bond sequence in these two molecules. This is an intrinsic property of the molecules that has been studied theoretically in smaller model compounds by Jeffrey, Pople & Radom (1972, 1974). Differences in molecular dimensions may also result from the small, but significant, distortions of the pyranose rings in response to the different intermolecular hydrogen bonding in the crystals.

Experimental

Methyl β -D-glucopyranoside was obtained from Pfanstiehl Laboratories, Inc. Transparent crystals of the hemihydrate, suitable for single-crystal X-ray analysis, were grown by extremely slow evaporation of a solution of the compound in a 95% ethanol–water mixture at room temperature. The systematic absences ($00l$: $4n \pm 1$ and $4n + 2$; and $h00$: $2n + 1$) and the dif-

fraction symmetry determined the space group, $P4_12_12$ (or $P4_32_12$).

The cell constants and intensities were determined with graphite-monochromated Cu $K\alpha$ radiation on a CAD-4 diffractometer. The cell constants given in Table 1 were obtained by least-squares refinement of the setting angles of 25 reflections with $80^\circ < 2\theta < 90^\circ$. $\theta-2\theta$ scans were used to measure 4877 intensities in the hkl and $\bar{h}\bar{k}l$ octants out to $2\theta = 150^\circ$. The symmetry-related measurements were averaged to give 1269 independent reflections, of which five have $F_o^2 < 0$. The three reflections used as standards did not show any intensity decrease after 42 h of X-ray exposure. Absorption corrections were calculated with the program *ABSOR* (Templeton & Templeton, 1973),

Table 1. *Crystal and structure-determination data for methyl β -D-glucopyranoside hemihydrate*

$C_7H_{14}O_6 \cdot 0.5 H_2O$, $M_r = 203.2$, m.p. $109 \sim 111^\circ C$			
Space group	$P4_12_12$ (or $P4_32_12$)	λ (Cu $K\alpha_1$)	1.5405 Å
$a = b$	7.433 (1) Å	Z	8
c	34.154 (2)	D_x	1.430 g cm $^{-3}$
V	1886.99 Å 3	D_m	1.431
Crystal dimensions	0.18 × 0.29 × 0.29 mm		
Crystal faces	14 faces {001}{110}{014}{104}		
Number of intensities measured	4877 to $2\theta = 150^\circ$		
Number of reflections in refinement, m	1269		
Number of variables, n	184		
$R = \Sigma F_o^2 - k^2 F_c^2 / \Sigma F_o^2 $ (all reflections)	0.035		
$R_w = (\Sigma w F_o^2 - k^2 F_c^2 ^2 / \Sigma w F_o^2 ^2)^{1/2}$ (all reflections)	0.071		
$S = [\Sigma w F_o^2 - k^2 F_c^2 ^2 / (m - n)]^{1/2}$	1.92		
Average shift/error†	0.05		
Maximum shift/error†	0.19		
Extinction parameter	$0.49 (7) \times 10^4$		

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† Excluding $WO(1)$, for which the average and maximum shift/error are 1.22 and 2.92 respectively.

with a linear absorption coefficient for Cu $K\alpha$ of 10.61 cm^{-1} . The minimum and maximum corrections to F_o^2 were 1.177 and 1.300 respectively.

The crystal structure was solved with *MULTAN* (Germain, Main & Woolfson, 1971) and refined by full-matrix least squares, minimizing $\sum w|F_o^2 - k^2|F_c|^2|^2$ with $w^{-1} = \sigma_c^2(F_o^2) + (0.025F^2)^2$, where σ_c is from the counting statistics. The H atoms were located from a difference synthesis. The non-H and H atoms were refined anisotropically and isotropically respectively, with a Zachariasen isotropic extinction parameter (Coppens & Hamilton, 1970). The details of the final refinement parameters are given in Table 1.

Atomic scattering factors for O and C were those tabulated by Doyle & Turner (1968), and those for H were given by Stewart, Davidson & Simpson (1965). The final positional and thermal parameters are given in Tables 2 and 3.*

The absolute configuration was not determined. The atomic coordinates were selected to comply with the D configuration of the molecule in space group $P4_12_12$. The conformation, atom numbering and thermal ellipsoids for the molecule are shown in Figs. 1 and 2.

* A list of structure factors has been deposited with the British Library Lending Division as Supplementary Publication No. SUP 32094 (9 pp.). Copies may be obtained through The Executive Secretary, International Union of Crystallography, 13 White Friars, Chester CH1 1NZ, England.

Table 3. Fractional coordinates, isotropic thermal parameters (\AA^2) and bond distances (\AA) for the H atoms

	<i>x</i>	<i>y</i>	<i>z</i>	B_{iso}	C, O—H
H(C1)	0.860 (2)	0.322 (2)	0.200 (1)	2.5 (3)	1.02 (2)
H(C2)	0.863 (3)	0.443 (2)	0.119 (1)	3.2 (4)	1.00 (2)
H(C3)	1.166 (3)	0.414 (2)	0.174 (1)	3.0 (4)	1.02 (2)
H(C4)	1.004 (2)	0.743 (2)	0.148 (1)	1.9 (3)	0.98 (1)
H(C5)	0.957 (2)	0.592 (2)	0.223 (1)	2.3 (3)	0.96 (2)
H(C61)	0.776 (3)	0.897 (3)	0.191 (1)	3.5 (4)	1.00 (2)
H(C62)	0.935 (3)	0.912 (3)	0.222 (1)	4.5 (5)	0.95 (2)
H(C71)	0.424 (3)	0.179 (3)	0.188 (1)	5.7 (5)	1.01 (2)
H(C72)	0.598 (3)	0.181 (4)	0.217 (1)	6.5 (6)	0.94 (3)
H(C73)	0.489 (3)	0.356 (3)	0.210 (1)	5.1 (5)	0.97 (3)
H(O2)	0.902 (3)	0.169 (3)	0.112 (1)	5.3 (6)	0.84 (2)
H(O3)	1.301 (3)	0.569 (3)	0.123 (1)	4.7 (5)	0.85 (2)
H(O4)	1.246 (3)	0.825 (3)	0.169 (1)	4.0 (4)	0.84 (2)
H(O6)	0.631 (4)	0.762 (3)	0.243 (1)	5.8 (6)	0.86 (3)
H(WO1)	0.173 (3)	0.174 (3)	0.019 (1)	5.2 (5)	0.87 (2)

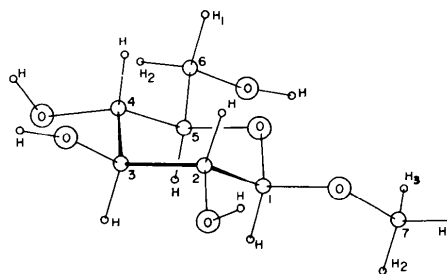


Fig. 1. Conformation and atom notation for methyl β -D-glucopyranoside in the crystal structure of the hemihydrate.

Table 2. Positional and thermal parameters ($\times 10^4$) of methyl β -D-glucopyranoside hemihydrate, for the non-H atoms

The anisotropic thermal parameters are in the form $T = \exp[-(h^2\beta_{11} + k^2\beta_{22} + l^2\beta_{33} + 2hk\beta_{12} + 2hl\beta_{13} + 2kl\beta_{23})]$. No standard deviations are given for parameters fixed by crystal symmetry.

	<i>x</i>	<i>y</i>	<i>z</i>	β_{11}	β_{22}	β_{33}	β_{12}	β_{13}	β_{23}
C(1)	0.8029 (2)	0.3765 (2)	0.1758 (1)	96 (2)	105 (2)	5 (1)	-1 (2)	1 (1)	-1 (1)
C(2)	0.9300 (2)	0.3821 (2)	0.1409 (1)	94 (2)	101 (2)	6 (1)	4 (2)	1 (1)	-3 (1)
C(3)	1.0979 (2)	0.4838 (2)	0.1528 (1)	92 (2)	115 (2)	5 (1)	2 (2)	2 (1)	-1 (1)
C(4)	1.0499 (2)	0.6692 (2)	0.1691 (1)	108 (2)	105 (2)	4 (1)	-5 (2)	-1 (1)	1 (1)
C(5)	0.9076 (2)	0.6550 (2)	0.2012 (1)	115 (2)	114 (2)	4 (1)	-5 (2)	1 (1)	-1 (1)
C(6)	0.8380 (2)	0.8376 (2)	0.2139 (1)	171 (3)	122 (3)	6 (1)	4 (2)	4 (1)	-5 (1)
C(7)	0.5342 (2)	0.2459 (3)	0.1979 (1)	134 (3)	172 (3)	9 (1)	-36 (3)	12 (1)	-7 (1)
O(1)	0.6477 (1)	0.2870 (2)	0.1653 (1)	104 (2)	158 (2)	6 (1)	-31 (2)	3 (1)	-6 (1)
O(2)	0.9781 (1)	0.2051 (1)	0.1287 (1)	109 (2)	119 (2)	9 (1)	7 (2)	1 (1)	-10 (1)
O(3)	1.2102 (1)	0.5013 (2)	0.1192 (1)	117 (2)	150 (2)	7 (1)	-28 (2)	9 (1)	-8 (1)
O(4)	1.2066 (1)	0.7514 (2)	0.1852 (1)	133 (2)	146 (2)	5 (1)	-47 (2)	-3 (1)	3 (1)
O(5)	0.7556 (1)	0.5575 (1)	0.1859 (1)	97 (2)	111 (2)	6 (1)	7 (1)	1 (1)	-4 (1)
O(6)	0.7228 (2)	0.8295 (2)	0.2469 (1)	218 (3)	186 (3)	8 (1)	12 (2)	14 (1)	-10 (1)
WO(1)	0.1188 (4)	0.1188 (4)	0.0000	247 (6)	247 (6)	7 (1)	-100 (4)	-6 (1)	6 (1)

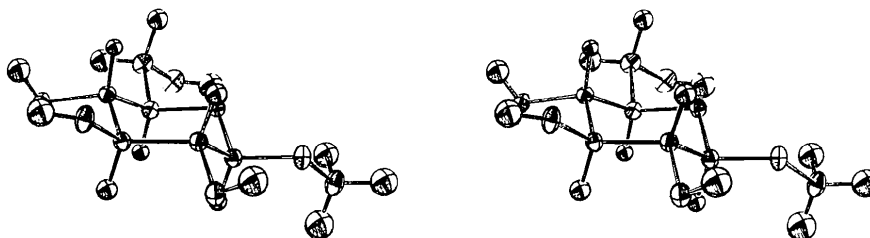


Fig. 2. Stereo ORTEP II diagram (Johnson, 1976) at 20% probability for methyl β -D-glucopyranoside. $\frac{1}{2}\text{H}_2\text{O}$.

The molecular dimensions for non-H atoms are reported in Fig. 3; the σ 's for the bond lengths and angles were 0.002 Å and 0.1° respectively. The C—H and O—H bond distances and their estimated standard deviations are given in Table 3.

A rigid-body-motion analysis for the pyranose ring and the non-H atoms attached to the ring [O(1), O(2), O(3), O(4), C(6)] was calculated by the procedure of Schomaker & Trueblood (1968), and the results are reported in Table 4.

Table 4. Results of rigid-body motion for the pyranose ring and the O(1), O(2), O(3), O(4), C(6) atoms

R.m.s. ($U_{ij} - U_{ijRBM}$)	0.0016 Å ²
Max. ($U_{ij} - U_{ijRBM}$)	0.0038
$\sigma(U_{ij})$	0.0019
Thermal motion corr. (C—C)	0.004 Å
(C—O)	0.003

Rigid-body T and ω elements and r.m.s. values for the principal axes of the T and ω tensors referred to the axes a , b and c

T	248 (7)	11 (6) 272 (7)	-13 (7) 5 (7) 265 (9)	(Å × 10 ⁴)
ω	7.5 (0.8)	5.5 (0.6) 10.1 (1.1)	0.4 (0.6) 3.4 (0.7) 9.6 (0.7)	(deg ²)

Directions relative to axes

Tensor	R.m.s. value	a	b	c
T	0.17 Å	67.5°	22.5°	91.6°
	0.16	113.3	79.1	26.0
	0.15	33.4	109.5	64.1
ω	4.0°	59.5°	41.8°	64.4°
	3.0	119.1	99.6	30.9
	1.6	44.6	130.2	73.9

Discussion

In comparison with the molecular structure of methyl α -D-glucopyranoside (Berman & Kim, 1968; Jeffrey, McMullan & Takagi, 1977), there are small, but significant, differences associated with the acetal sequence of C—O bonds. The glycosidic bond C(1)—O(1) is shorter, and the difference between the two C—O ring bonds is less in the β -pyranoside. As shown in Table 5, this is in excellent agreement with observations from the crystal structures of other methyl α - and β -pyranosides. These differences are also in good agreement with the results of quantum-mechanical calculations relating to the conformational energies and C—O bond-length variations associated with the 'anomeric effect' in carbohydrates (Jeffrey, Pople & Radom, 1972, 1974). The

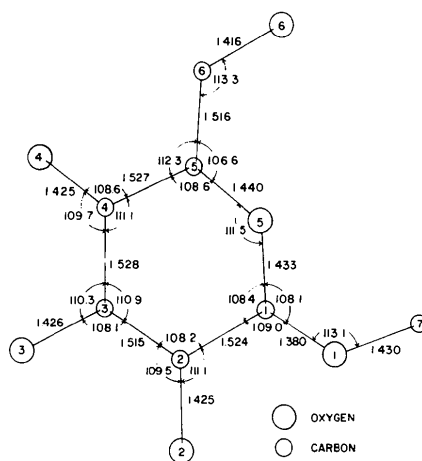


Fig. 3. Bond lengths and valence angles for non-H atoms in methyl β -D-glucopyranoside.

Table 5. Bond lengths, valence angles (α, β) and torsion angles (θ) in the acetal moiety of methyl α -D- and methyl β -D-pyranosides

	Bond angles (°)		Torsion angles (°)	Bond lengths (Å)				Reference
	α	β		θ	C(5)—O(5)	C(1)—O(1)	O(1)—CH ₃	
Methyl β -D-glucopyranoside	111.5	108.1	-73.2	1.440	1.433	1.380	1.430	This work
Methyl β -D-xylopyranoside	110.6	107.0	-72.3	1.425	1.422	1.390	1.427	(1)
Methyl β -maltopyranoside	111.5	107.1	-69.2	1.430	1.427	1.375	1.425	(2)
Methyl β -cellobiopyranoside. MeOH	111.3	108.3	-76.2	1.432	1.434	1.379	1.435	(3)
Methyl 3,4-O-ethylidene- β -D-galactopyranoside	110.6	107.9	-69.7	1.442	1.423	1.393	1.421	(4)
Methyl 6-O-acetyl- β -D-glucopyranoside	110.8	106.9	-69.8	1.429	1.429	1.384	1.428	(5)
Methyl 6-O-acetyl- β -D-galactopyranoside	112.6	107.3	-82.3	1.427	1.437	1.374	1.428	(6)
Methyl α -D-glucopyranoside	114.0	112.6	63.0	1.434	1.414	1.411	1.430	(7)
Methyl α -D-galactopyranoside. H ₂ O	113.8	111.3	63.5	1.439	1.418	1.405	1.437	(8)
Methyl α -D-mannopyranoside	114.3	111.7	60.9	1.450	1.421	1.407	1.442	(9)
Methyl α -D-altropyranoside	113.9	112.1	63.8	1.440	1.416	1.405	1.428	(10)
Methyl 4-deoxy-4-fluoro- α -D-glucopyranoside	113.7	112.2	66.2	1.434	1.416	1.409	1.432	(11)

(1) Brown, Cox & Llewellyn (1966). (2) Chu & Jeffrey (1967). (3) Ham & Williams (1970). (4) Lindberg (1976a). (5) Lindberg (1976b). (6) Lindberg (1976c). (7) Berman & Kim (1968). (8) Gatehouse & Poppleton (1971a). (9) Gatehouse & Poppleton (1970). (10) Gatehouse & Poppleton (1971b). (11) Choong, Stephenson & Stevens (1975).

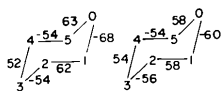
valence-bond angles in the sequence C(5)—O(5)—C(1)—O(1) are smaller in the β compound than the α , *i.e.* 108.1 and 111.5 *versus* 112.6 and 114.0°. These differences not only occur in the methyl pyranosides but also appear to be general amongst pyranose sugars, as was originally noted by Arnott & Scott (1972).

In addition to these bond-length and bond-angle differences, there is a consistent conformational preference in the methyl β -pyranosides for the glycosidic torsion angle to be closer to 70, rather than the ideal 60° staggered angle. This is also consistent with the conformational potential-energy curves calculated by Jeffrey, Pople & Radom (1974).

The C—C bond lengths and the other exocyclic C—O bond lengths agree in the two molecules within the sum

Table 6. Ring-puckering parameters (Cremer & Pople, 1975) and torsion angles (°) for methyl β -D-glucopyranoside (I) and methyl α -D-glucopyranoside (II) (X-ray data from Berman & Kim, 1968)

	I	II
q_2	0.072 Å	0.023 Å
q_3	0.593 Å	0.567 Å
θ	7.0°	2.4°
ϕ_2	38.8°	116.0°
Q	0.598 Å	0.568 Å



O(5)—C(5)—C(6)—O(6)	69°	73°
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of the standard deviations (0.006 Å), except for C(5)—C(6)—O(6), where the effects of thermal motion are significant, and the differences are greater.

There are relatively large differences in the conformation of the pyranose rings as shown in Table 6. The ring in the β anomer is significantly more puckered and less regular, with ring torsion angles varying from 52 to 70°. This is also shown in the comparison of the Cremer & Pople (1975) puckering parameters. In the β compound the direction of the distortion is more towards the twist-boat ($\phi_2 = 30^\circ$), whereas in the α compound it is in the direction of the boat conformation ($\phi_2 = 120^\circ$).

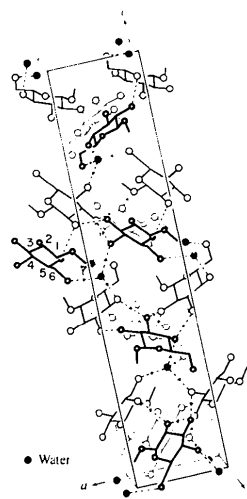


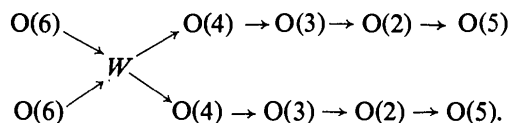
Fig. 4. Unit-cell contents of methyl β -D-glucopyranoside hemihydrate. The hydrogen bonds are shown by dotted lines.

Table 7. Hydrogen-bond distances and angles in the structure of methyl β -D-glucopyranoside hemihydrate

	H...O	H...O (corr.*)	O...O	O—H...O
Type... O—H...O—H...				
O(4)—H...O(3)	1.87 (2) Å	1.75 Å	2.700 (2) Å	170 (2)°
$[x,y,z]$ to $[\frac{3}{2}-x, \frac{1}{2}+y, \frac{1}{4}-z]$				
O(3)—H...O(2)	1.93 (2)	1.82	2.769 (2)	168 (2)
$[x,y,z]$ to $[\frac{3}{2}-x, \frac{1}{2}+y, \frac{1}{4}-z]$				
Type... O—H...O<				
O(2)—H...O(5)	2.19 (2)	2.07	3.015 (2)	169 (2)
$[x,y,z]$ to $[\frac{3}{2}-x, -\frac{1}{2}+y, \frac{1}{4}-z]$				
Type... WO—H...O—H...				
WO—H...O(4)	1.89 (2)	1.80	2.748 (2)	170 (2)
$[x,y,z]$ to $[\frac{3}{2}-x, -\frac{1}{2}+y, \frac{1}{4}-z]$				
$[-\frac{1}{2}+y, \frac{3}{2}-x, -\frac{1}{4}+z]$				
Type O—H...WO—H...				
O(6)—H...WO	2.15 (3)	2.06	2.985 (2)	162 (2)
$[x,y,z]$ to $[\frac{1}{2}-y, \frac{1}{2}+x, \frac{1}{4}+z]$				
$[\frac{1}{2}-x, \frac{1}{2}+y, \frac{1}{4}-z]$				

* Corrected by expanding the covalent O—H bond distances to the neutron diffraction value of 0.96 Å in the direction of the bond.

In the methyl β -glucopyranoside hemihydrate structure the hydrogen bonding consists of finite chains which originate at O(6)H and terminate at the ring oxygen O(5). These chains intersect in pairs at the water molecules, which lie on the twofold axes and are four-coordinated. The scheme is shown diagrammatically below (and in Fig. 4):



The hydrogen-bond distances and angles are given in Table 7. When corrected for the shortening of the O—H bond length characteristic of X-ray data, as compared with neutron diffraction O—H distances, the H...O hydrogen-bond distances show a similar distribution to that reported from neutron diffraction studies of methyl α -D-glucoside, α -D-mannoside and α -D-altropyranosides (Jeffrey, McMullan & Takagi, 1977; Poppleton, Jeffrey & Williams, 1975). The donor-acceptor ...O—H...O—H... bonds are shorter, at 1.75 and 1.82 Å, than the ...O—H...O< bond to the ring O, which is 2.07 Å. Of the two hydrogen bonds involving the water molecule, that for which the O has both donor and acceptor properties is the shorter (1.80 versus 2.06 Å). The water and O(6) oxygen atoms have substantially larger temperature factors than the other O atoms, which may be indicative of a small amount of disorder of the water molecules away from the twofold axes.

The hydrogen bonding is more extensive than in the methyl α -D-glucopyranoside structure, where only three of the hydroxyl groups are involved in strong hydrogen bonding. This and the influence of the water molecule in determining the hydrogen-bond structure are likely to be the principal reasons for the larger distortion in the pyranose ring.

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