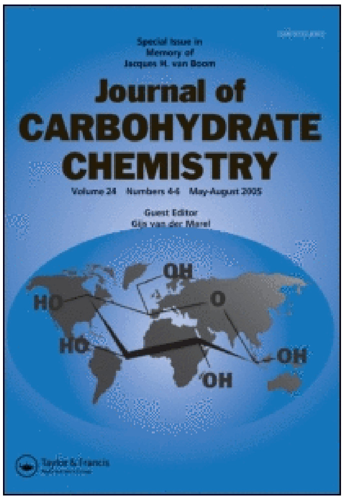

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Crystal Structure and Solid-State ^{13}C NMR of Methyl α-D-Mannofuranoside[†]

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ABSTRACT

The crystal structure of methyl α-D-mannofuranoside was determined by X-ray crystallography. The C-1–C-2, C-2–C-3, C-3–C-4, C-4–O and O-4–C-1 distances within the furanoside ring are 1.513(2), 1.523(2), 1.516(2), 1.445(2) and 1.422(2) Å, respectively. The hydrogen bonding consists of O–H···O interactions which include the anomeric oxygen but exclude the ring oxygen atom. The two hydroxyls OH-6 and OH-2 are H-bond acceptors and donors with H···O distances of 1.92–1.93 Å, whereas the OH-3 and OH-5 are only H-bond donor [H···O distance of 2.04(2) Å]. Additionally, OH-6 participates in a weak hydrogen bond to the anomeric oxygen [H···O distance of 2.19(3) Å]. The crystalline methyl α-D-mannofuranoside adopts an ^{3}E ring conformation. The analysis of ^{13}C CPMAS NMR chemical shifts for solid methyl α-D-mannofuranoside confirm such H-bonding pattern.

Key Words: Mannofuranoside; ^{13}C CP MAS solid-state analysis; X-ray diffraction analysis.

[†] This paper is dedicated to Professor Gérard Descotes on the occasion of his 70th birthday.

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INTRODUCTION

Furanosides are of great importance in biological systems. For example, D-ribose and 2-deoxy-D-ribose are each found in a furanose form in ribo- and deoxyribonucleic acids, respectively. Fructofuranose is present in sucrose, inulin and glycoconjugates, for example the lipopolysaccharides from *Vibrio cholerae*,[1] while galactofuranosyl residues have been characterized in oligosaccharides present in fungi[2] and bacteria.[3] However, structural studies have mainly focused on saccharides in their pyranose forms. Indeed there is a large number of X-ray structures of pyranosides,[4] but few X-ray structures reported for furanosides. In addition to published data on the structure of methyl α-D-lyxofuranoside[5] and methyl β-D-ribofuranoside,[6] crystal structures of five methyl D-pentofuranosides were determined recently by means of low-temperature X-ray and neutron crystallography, thus providing a set of highly accurate geometrical and conformational data.[7] In addition recent literature has reported on the measurement of ^{13}C NMR chemical shift tensors in single crystals of six methyl pyranosides, including methyl α-D-mannopyranoside,[8] and correlation of the experimental shifts with results from the gauge-invariant atomic orbital (GIAO) method. As illustrated with the study of lactulose,[9] valuable information on the configuration and the conformation of saccharides can be obtained by combining single crystal structure analysis (XRD) and solid state NMR data. According to the Cambridge Structural Database X-blackboard version 2.3.8. copyright 1994–2002 CCDC and to our knowledge, no XRD data are yet available for methyl α-D-mannofuranoside. Thus the aim of the present investigation was to collect structural data for the latter based on a combination of XRD and solid state NMR.

RESULTS AND DISCUSSION

The ORTEP views of the studied compound with the numbering of atoms and crystal packing are illustrated in Figures 1 and 2, respectively. The crystal data and structure refinement parameters are collected in Table 1 and the selected bond lengths, bond angles and torsion angles are given in Table 2.

The average bond lengths in pyranosides and furanosides are essentially the same,[7] although the comparison may be obscured by the fact that the geometrical data were obtained at different temperatures. According to the X-ray and neutron structures of pentofuranosides (measured at low-temperatures[7]) the furanoside C–C bond lengths are 1.522–1.534 Å and the C–O bond lengths are 1.425(2)–1.435(2) Å. In methyl α-D-mannofuranoside, the lengths of two C–C bonds extra-ring are C-4–C-5 1.507(2) Å and C-5–C-6 1503(2) Å, and those of the corresponding C–O bonds are 1.413(2)–1.425(2) Å, respectively. The five bonds within the furanoside ring are longer than their counterparts: C–C 1.513(2)–1.523(2) Å, C–O 1.422(2) Å and 1.445(2) Å, which may be attributed to the strain intrinsic to the five membered ring. The glycosidic C-1–O-1 bond is short [1.399(2) Å] and the glycosidic torsion-angle, O-4–C-1–O-1–C-7 is 104.5(2)° and C-2–C-1–O-1–C-7 is −139.4(2)°.

The characteristic feature of the crystal structure of methyl α-D-mannofuranoside is the location of five-membered rings which stack in a column, i.e., one ring above (and

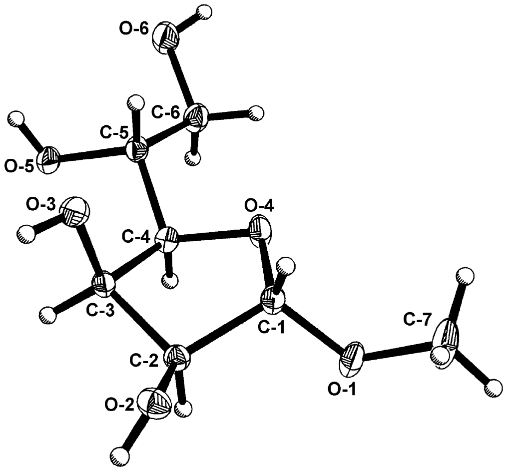

Figure 1. Molecular structure and atomic numbering of methyl α-D-mannofuranoside.

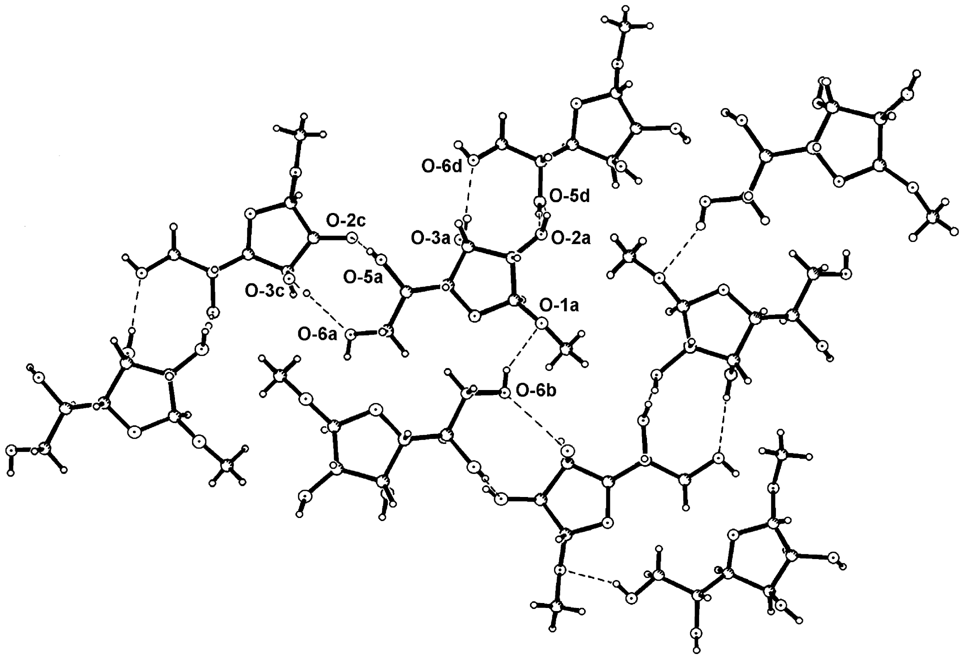

Figure 2. The crystal structure of methyl α-D-mannofuranoside. The intermolecular O–H···O hydrogen bonds are indicated by broken lines.

Table 1. Crystal data and structure refinement for methyl α-D-mannofuranoside.

Empirical formula	$C_7\,H_{14}O_6$
Molecular weight	194.18
Melting point (K)	491–492
$[\alpha]_D^{20}$(c 1, H_2O)	+113
Temperature (K)	293(2)
Wavelength (Å)	0.71073
Crystal system	orthorombic
Space group	P2(1)2(1)2(1)
Unit cell dimensions (Å)	a = 4.6380(10) α = 90° b = 11.818(2) β = 90° c = 15.848(3) γ = 90°
Volume (Å^3)	868.7(3)
Z (molecules/cell)	4
Density (calculated, Mg cm^{-1})	1.485
Absorption coefficient (mm^{-1})	0.131
F(000)	416
Crystal size (mm)	0.3 × 0.25 × 0.2
Θ Range for data collection (°)	3.68 to 28.70
Index ranges data for collection (°)	$-6 \leq h \leq 6$, $-15 \leq k \leq 15$, $-21 \leq l \leq 20$
Reflections collected	8049
Independent reflections	2095 [R(int) = 0.0660]
Refinement method	Full-matrix least-squares on F^2
Data (restraints) parameters	2094/0/135
Goodness-of-fit on F^2	1.081
Final R indices [$I > 2\sigma(I)$]	$R_1 = 0.0369$, $wR_2 = 0.0938$
Extinction coefficient	0.040(5)
Absolute structure parameter	0.4(11)
R indices (all data)	$R_1 = 0.0413$, $wR_2 = 0.1010$
Largest diff. peak and hole (e Å^{-3})	0.168 and −0.156

below) another, whereas the C-5(OH)–C-6(OH) fragments form side-chains linked by intermolecular H-bonds.

The molecules participate in an intermolecular hydrogen bonding network in which each hydroxyl group is involved in OH···O bonds. The O···O and OH···O distances are given in Table 2. The hydrogen bonds formed by the double donor/acceptor hydroxyls: OH-2 and OH-6 tend to be shorter [H···O distances of 1.92(2)–1.93(2) Å] than that involving at least one hydroxyl group participating in a single interaction [O-3–H···O-6, the H···O-3 distance is 2.04(2) Å], which is in agreement with the known ‘‘cooperative effect’’ interaction[10] The distance of 2.19(3) Å in O-6–H···O-1 hydrogen bond donor interaction to the anomeric oxygen is longer than other comparable bonds in this X-ray structure. The interactions O-6–H···O-1 are weak, with a large deviation from O–H···O linearity of 151.9(3)°. The ring oxygen does not accept any hydrogen bond.

An attempt was made to describe the conformation of the five-membered ring. The exact geometry was defined in terms of Φ_i parameters, i.e., five torsional angles.

Table 2. Selected bond lengths, bond angles, torsion angles and hydrogen bonding structure for methyl α-D-mannofuranoside.

Atoms	Bond length (Å)	Atoms	Bond angles (°)
C-1–C-2	1.513(2)	O-4–C-1–C-2	105.84(12)
C-2–C-3	1.523(2)	C-1–C-2–C-3	102.90(12)
C-3–C-4	1.516(2)	C-4–C-3–C-2	98.99(11)
C-4–O-4	1.445(2)	O-4–C-4–C-3	105.04(11)
C-1–O-4	1.422(2)	C-1–O-4–C-4	109.06(11)
C-1–O-1	1.399(2)		
			Torsion angles (°)
C-2–O-2	1.415(2)	O-1–C-1–C-2–C-3	−146.58(12)
C-3–O-3	1.414(2)	O-4–C-1–C-2–C-3	−28.2(2)
C-5–O-5	1.425(2)	C-1–C-2–C-3–C-4	40.43(14)
C-6–O-6	1.421(2)	C-2–C-3–C-4–O-4	−39.13(15)
		C-2–C-1–O-4–C-4	3.4(2)
	H-bonding distances (Å)		H-bonding angles (°)
O-2···O-5	2.715(2)	O-2–H-22···O-5	162.9(2)
H-22···O-5	1.92(2)	O-5–H-55···O-2	167.7(2)
O-5···O-2	2.732(2)	O-6–H-66···O-1	151.9(3)
H-55···O-2	1.93(2)	O-3–H-33···O-6	172.142(2)
O-6···O-1	2.883(2)		
H-66···O-1	2.19(3)		
O-6···O-3	2.797(2)		
O-6···H-33	2.04(2)		

Defining the plane as C-2–O-4–C-4, in this case the C-2 atom slightly deviates from this plane (−0.087 Å) and C-3 significantly (0.576 Å).

In order to test the accuracy of the ring structure, the ΔC_2 parameter was calculated $\left[\Delta C_2 = \sqrt{\sum(\Phi_1 - \Phi_2)^2/m}\right]$.[11] The found value of $\Delta C_2 = 16$ indicated that the assumption of a twist conformation was not valid. However, assuming the presence of a two-fold symmetry axis, i.e., the envelope conformation, the $\Delta C_S = 3$ was obtained $\left[\Delta C_S = \sqrt{\sum(\Phi_1 + \Phi_2)^2/m}\right]$,[11] which is in agreement with the structure shown in Figure 3 (with only C-3 significantly deviated from the plane). The analysis of ring conformation was also performed using the Cremer–Pople[12] puckering parameters and the following results were obtained: $Q = 0.4159$ Å and $\psi = 282.84°$. The pseudorotation parameters $P = 13.7°$ and $\tau = 42.5°$ were calculated as proposed by Rao, Westhof and Sundaralingam.[13] This conformation results from the location of two hydroxyls (C-2–OH and C-3–OH), and $CHOHCH_2OH$ (at C-4) on the same side of the furanoside ring, which led to unfavorable interactions. It is obvious that the C-3 hydroxyl group will not want to be eclipsed with either the two-carbon chain at C-4 or the hydroxyl group at C-2. In addition, a $^3T_2$ form is less likely because it would also tend to eclipse the hydroxyl group at C-2 with the methoxyl group at C-1. The bulky

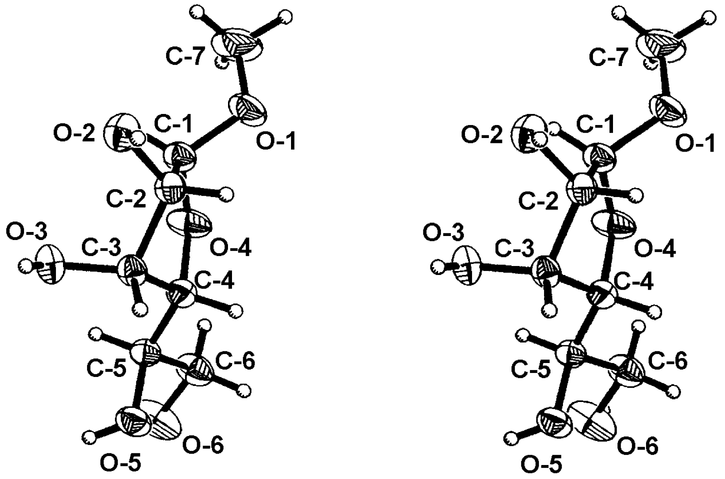

Figure 3. Stereo view of methyl α-D-mannofuranoside.

substituents prefer not to be pseudo axial and this makes the E_3 form less probable. The deviation from the plane, releasing part of the energy, avoids increased O-3···O-2 distances than stabilizing the ^3E conformation of the ring.

The solid state spectrum of methyl α-D-mannofuranoside recorded with cross polarization and magic angle spinning techniques (CPMAS) at 75.5 MHz is illustrated in Figure 4. Chemical shifts for solid phase and $CDCl_3$ solution are collected in Table 3. The differences in chemical shifts $\Delta = \delta_{liquid} - \delta_{solid}$ are significant for C-2, C-3 and OCH_3. The deshielding of 2.5 ppm which occurs for the methyl carbon is due to the participation of the anomeric oxygen in an intermolecular OH···O-1 hydrogen bond in the solid state. Such an effect was previously observed for a series of ureido glucopyranosides.[14,15] In the latter series, the downfield shift of C-1 (1.7 ppm), together with the downfield shift of OMe (2 ppm) were related to the formation of a NH···O-1 hydrogen bond. Thus, by comparison to the usually observed chemical shift of OMe (57 ppm), a value of 59 ppm may be assumed as indicative of such an arrangement of intermolecular hydrogen bonds which involve the anomeric oxygen. The chemical shifts of C-4 and C-5 carbons are

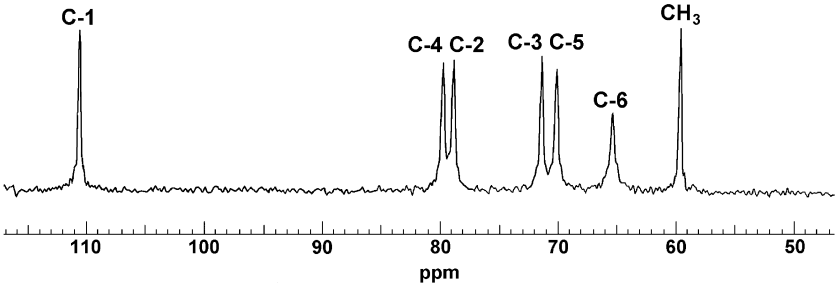

Figure 4. ^{13}C CP MAS spectrum of methyl α-D-mannofuranoside.

Table 3. ^{13}C NMR chemical shifts for methyl α-D-mannofuranoside (δ, ppm, TMS).

Atoms	C-1	C-2	C-3	C-4	C-5	C-6	OCH_3
In $CDCl_3$	109.7	77.9	72.5	80.5	70.6	64.5	57.2
Solid state	110.6	78.9	71.5	79.8	70.2	65.4	59.7
$\Delta = \delta_{solution} - \delta_{solid}$	−0.9	−1.0	1.0	0.7	0.4	−0.9	−2.5

almost the same as those in solution. Contributions to the chemical shifts from intermolecular and intramolecular sources have to be considered, if the information from solid state NMR and XRD analysis is to be correlated with the solution data. We assume that intermolecular OH···O interactions should have a dominant effect in the solid state spectra and outweigh the shift perturbations attributable to intramolecular structural changes. The formation of hydrogen bonds in the crystals was responsible for the changes of the relative order of ^{13}C chemical shifts from the solution to the solid-state spectra, as observed for α-D- and β-D-glucose.[16] The ^{13}C chemical shifts can be interpreted in detail with quantum-chemical computations of shielding constants. Unfortunately the computations are performed on isolated molecules and neglect any effects of intermolecular hydrogen bonds.

EXPERIMENTAL

Methyl α-D-mannofuranoside was synthesized according to the described procedure.[17] A single crystal was obtained by recrystallization from ethanol.

^{13}C NMR spectra were recorded on a Bruker MSL-300 instrument at 75.5 MHz for $CDCl_3$ solution and solid state. The cross polarization magic angle spinning (CP MAS) solid state spectrum was recorded with a spinning speed of 6.5 kHz. A contact time of 4 ms, a repetition time of 6 s, and a spectral width of 20 kHz were used for accumulation of 300 scans. Chemical shifts were calibrated indirectly through the glycine C═O signal recorded at 176.0 ppm relative to TMS.

The X-ray measurements of the crystal were made on a KUMA KM4CCD κ-axis diffractometer applying a graphite-monochromated MoKα radiation. The species positioned at 62.25 mm from the KM4CCD camera; 500 frames were measured at 1.2° intervals with a counting time of 10 sec. The data were also corrected for Lorentz and polarization effects, and no absorption correction was made. Data reduction and analysis were carried out using the KUMA Diffraction (Wrocław) programs. The structure was solved by the direct methods[18] and refined using SHELXL computer program.[19] The refinement was based on F^2 for all reflections. Weighted R factors, wR, and all goodness-of-fit S values are based on the F^2 parameters. Conventional R factor are based on F with F set to zero for negative F^2. The $F_o^2 > 2s(F_o^2)$ criterion was used only for calculation of the R factors and is not relevant to choice of reflections for the refinement. The R factors based on F^2 were about twice as large as those based on F. Ten hydrogen atoms were refined using riding atoms model and four hydrogen atoms (H-22, H-33, H-55 and H-60) were located from a differential map and refined isotropically. Scattering factors were taken from the literature (Tables 6.1.1.4 and 4.2.4.2 of Ref. [20]).

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Crystallographic data for the structures reported in this paper has been deposited at the Cambridge Crystallographic Data Centre (CCDC Identification Number 202844). These data may be obtained, on request, from The Directory, Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge, CB2 1EZ, UK (fax: +44-1223-336033; e-mail: deposit@ccdc.cam.ac.uk. or www: http://www.csdc.cam.ac.uk).

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