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Crystal and molecular structure of methyl 4-*O*-methyl-β-D-*ribo*-hex-3-ulopyranoside

Immanuel Adorjan,[a] Thomas Rosenau,[a] Antje Potthast,[a] Paul Kosma,[a,*] Kurt Mereiter,[b] Jutta Pauli[c] and Christian Jäger[c]

[a]*Institute of Chemistry, Christian Doppler-Laboratory, University of Natural Resources and Applied Life Sciences, Muthgasse 18, A-1190 Vienna, Austria*
[b]*Department of Chemistry, Vienna University of Technology, Getreidemarkt 9, A-1060 Vienna, Austria*
[c]*Federal Institute of Materials Research and Testing, Project Group I.3903, Richard-Willstaetter-Str. 11, D-12489 Berlin, Germany*

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Abstract—Methyl 4-*O*-methyl-β-D-*ribo*-hex-3-ulopyranoside (**2**), a model compound for partially oxidized anhydroglucose units in cellulose, was crystallized from $CHCl_3$/*n*-hexane by vapor diffusion to give colorless plates. Crystal structure determination revealed the monoclinic space group $P2_1$ with $Z = 2C_8H_{14}O_6$ and unit cell parameters of $a = 8.404(2)$, $b = 4.5716(10)$, $c = 13.916(3)$ Å, and $\beta = 107.467(4)°$. The structure was solved by direct methods and refined to $R = 0.0476$ for 1655 reflections and 135 parameters. The hexulopyranoside occurs in a distorted chair conformation. Both hydroxyls are involved in hydrogen bonding and form zigzag bond chains along the *b*-axis. One of the two hydrogen bonds is bifurcated. The solid-state ^{13}C NMR spectrum of **2** exhibits eight carbon resonances, with well-separated signals for the two methoxyls (1-OMe: 55.72 ppm, 4-OMe: 61.25 ppm) and a keto resonance with relatively large downfield shift (206.90 ppm). Differences in the C-4 and the methoxyls' chemical shifts in the solid and liquid states were found.

Keywords: Crystal structure; Solid-state NMR; Cellulose; Carbonyl groups

1. Introduction

Cellulose is in theory an 'ideal' homopolymer built up of anhydroglucose units linked by β-(1 → 4)-glycosidic bonds. In reality, the polysaccharide present in pulp contains small amounts of various 'irregular' structures, mainly oxidized groups, such as carbonyls and carboxyls. This applies especially to material, which has undergone a number of process steps in the pulp and paper industries, and—albeit to a lesser extent—also to genuine, untreated cellulose.[1]

The generation of these functionalities along the cellulose chain is a highly undesired process, since these positions constitute 'hot spots' along the carbohydrate chain, where a pronounced chemical instability is introduced and where subsequent cleavage will primarily occur. Oxidized positions in cellulose are a main reason for strength loss and decreased performance parameters in textiles, paper, and other cellulosic materials. They are mainly responsible for general aging processes of cellulosics,[2] and are furthermore assumed to be the cause and promoter of thermal and light-induced yellowing processes.[3]

Our current research efforts are aimed at reliable methods to detect and quantify those oxidized functionalities in cellulose,[4] which requires the use of low-molecular weight model compounds to optimize derivatization and labeling reactions. For ongoing studies on oxidative damage of cellulosic substrates, methyl 4-*O*-methyl-β-D-*ribo*-hex-3-ulopyranoside (**2**) was needed as a model compound, which represents such an oxidized 'point' in a cellulose chain. This compound will serve in

* Corresponding author. Tel.: + 43-1-36006-6055; fax: +43-1-36006-6059; e-mail: pkosma@edv2.boku.ac.at

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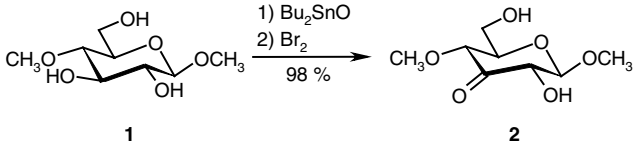
model studies of oxidatively damaged cellulosic substrates. In this report, we wish to communicate the synthesis of **2** along with the determination of its crystal and molecular structure.

2. Results and discussion

Methyl 4-*O*-methyl-β-D-*ribo*-hex-3-ulopyranoside (**2**) was synthesized by selective oxidation of methyl 4-*O*-methyl-β-D-glucopyranoside (**1**) with *n*-$(Bu_3Sn)_2O/Br_2$ in chloroform in the presence of molecular sieves in 98% yield as described (Scheme 1).[5] HMBC measurements allowed for an unambiguous assignment of the ^{13}C NMR resonances of **2** recorded in $CDCl_3$, especially the differentiation between the two methoxyl groups. The ^1H NMR spectrum, recorded in the same solvent, proved the absence of H-3. The 6-OH proton interestingly appeared as double–doublet ($^3J = 9.1/4.7$ Hz), while 2-OH gave the expected singlet. As reported previously,[5] compound **2** forms a keto hydrate in aqueous solution, which at room temperature exists in an equilibrium with the keto form in an approximate hydrate/keto ratio of 3:5.

Crystals of **2** were obtained from a concentrated solution in $CHCl_3$/*n*-hexane by vapor diffusion as thin plates. A comparatively thick colorless crystal ($0.8\times0.2\times0.1$ mm) was available for the X-ray diffraction measurements at 293 K with a CCD diffractometer. Crystal data and details of the data collection are given in Table 1, the conformation of the molecule and the numbering of atoms is shown in Figure 1. The structure was solved by direct methods and refined to a final $R = 0.0476$ for 1655 reflections (Table 2). The absolute structure of the chiral compound could not be determined from diffraction data (anomalous dispersion effects too small for Mo-Kα radiation), and was therefore adopted by analogy with the underlying glucose.

The hexulopyranoside unit occurs in distorted $^4C_1$ chair conformation, due to the effect of the carbonyl sp^2-hybrid at C-3. All bond lengths assume expected values (Table 3). The effect of methyl substitution at O-4 caused a slight increase in the exocyclic C-4–C-3–O-3 bond angle (112.8°) compared to the values found for cellobiose (108.1°) and methyl β-cellobioside (110.2°). The C-2–C-3–C-4 angle (115.7°) showed a slight strain imposed on the trigonal planar carbonyl moiety by the incorporation into the six-membered ring. Comparable



1 2

Scheme 1.

Table 1. Crystal data and structure refinement for hexulopyranoside **2**

Empirical formula	$C_8H_{14}O_6$
Formula weight ($g\,mol^{-1}$)	206.19
Temperature (K)	293
Crystal size (mm)	$0.8\times0.2\times0.1$
Wavelength (Å)	0.71073 (Mo-Kα radiation)
Crystal system, space group	Monoclinic, $P2_1$
Unit cell dimensions (Å, °) *a*, *b*, *c*, *β*	8.404(2), 4.572(1), 13.916(3), 107.467(4)
Unit cell volume (Å^3)	510.0(2)
Z	2
Calculated density ($Mg\,m^{-3}$)	1.343
Absorption coefficient (mm^{-1})	0.116
F(000)	220
θ range for data collection (°)	2.54–24.98
Index ranges	$-9\leqslant h\leqslant 9$, $-5\leqslant k\leqslant 5$, $-16\leqslant l\leqslant 16$
Reflections collected/independent	4519/1712 ($R_{int} = 0.0171$)
Refinement method	Full-matrix least squares on F^2
Data/restraints/parameters	1712/1/135
Goodness-of-fit on F^2	1.167
Final *R* indices [$I > 2\sigma(I)$]	$R_1 = 0.0476$, $wR_2 = 0.1126$ (1655 data)
R indices (all data)	$R_1 = 0.0491$, $wR_2 = 0.1136$ (1712 data)
Largest diff. peak and hole	0.16 and $-0.24\,e\,Å^{-3}$

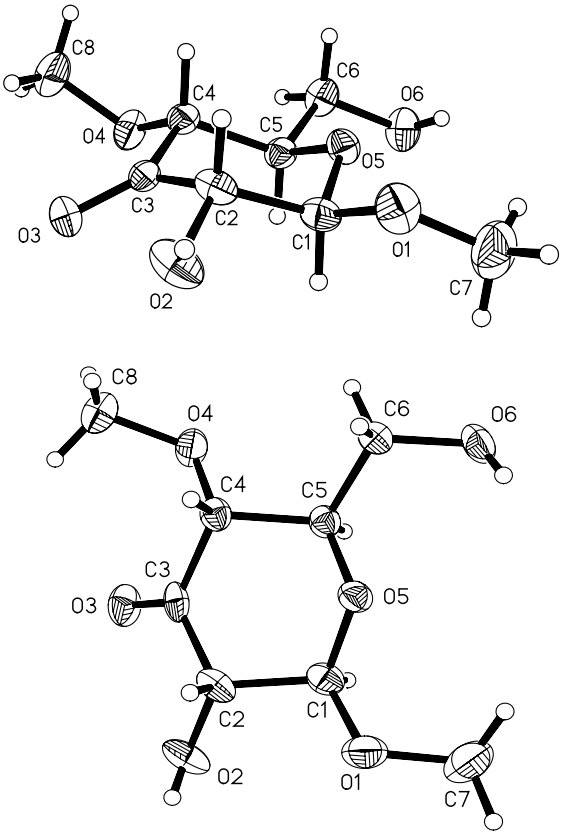


Figure 1. Perspective view and atom labeling of methyl 4-*O*-methyl-β-D-*ribo*-hex-3-ulopyranoside (**2**). Displacement ellipsoids enclose 30% probability.

Table 2. Atomic coordinates ($\times 10^4$) and equivalent isotropic displacement parameters ($Å^2 \times 10^3$) for compound **2**

Atom	*x*	*y*	*z*	U_{eq}[a]
O(1)	3207(3)	−428(5)	2591(2)	59(1)
O(2)	4732(3)	2882(5)	4394(2)	61(1)
O(3)	7506(3)	5627(5)	4378(1)	58(1)
O(4)	9068(2)	5251(5)	2925(1)	52(1)
O(5)	5343(2)	828(4)	2004(1)	39(1)
O(6)	6008(3)	1950(5)	164(1)	56(1)
C(1)	4404(3)	1669(6)	2650(2)	42(1)
C(2)	5548(4)	1791(6)	3729(2)	43(1)
C(3)	7060(3)	3683(6)	3776(2)	42(1)
C(4)	7907(3)	3075(6)	2970(2)	39(1)
C(5)	6558(3)	2939(6)	1949(2)	38(1)
C(6)	7239(3)	1952(8)	1113(2)	48(1)
C(7)	1906(4)	−385(12)	1670(3)	85(1)
C(8)	10,653(4)	4910(9)	3666(2)	69(1)

[a] $U_{eq} = 1/3$ of the trace of the orthogonalized U_{ij} tensor.

Table 3. Selected bond lengths (Å) for **2** (only nonhydrogen atoms)

Atoms	Bond lengths
O(1)–C(1)	1.374(3)
O(1)–C(7)	1.413(4)
O(2)–C(2)	1.400(3)
O(3)–C(3)	1.201(3)
O(4)–C(4)	1.408(3)
O(4)–C(8)	1.428(3)
O(5)–C(1)	1.416(3)
O(5)–C(5)	1.424(3)
O(6)–C(6)	1.412(3)
C(1)–C(2)	1.521(4)
C(2)–C(3)	1.522(4)
C(3)–C(4)	1.523(4)
C(4)–C(5)	1.530(3)
C(5)–C(6)	1.512(4)

dimensions were reported for the very few solid-state structures related to ketopyranoses, for example, compounds DUWXEY,[7] TAYXEW,[8] or YAHWEJ[9] of the Cambridge Crystallographic Database.[10]

Figure 2 shows the packing of the molecules in the unit cell. The hexulopyranoside rings align approximately perpendicular to the *b*-axis to form columns that are arranged in layers parallel to (1 0 0). The molecules thus form herringbone-patterned sheets (Fig. 2). Within one layer the molecules are mutually linked in two dimensions, that is, in the *b*–*c*-plane, by hydrogen bond zigzag chains, which extend along the *b*-axis, but contribute also to coherence along the *c*-axis. Perpendicular to the *b*–*c*-plane only van der Waals forces are effective. This main structural feature is in good accord with the platy character of the crystals parallel to the *b*–*c*-plane, their elongation parallel to *b*, and with their softness. O(6)–H(6) forms a straight hydrogen bond to O(6) of a neighboring molecule, resulting in a chain of H-bonds parallel to the *b*-axis (left and right hydrogen bond chain in Fig. 2). The O(6)–O(6) distance is 2.800(3) Å, the O–H–O angles 172(4)°. An analogous hydrogen bond chain is formed by O(2)–H(2)–O(2), but here, in addition, an asymmetric bifurcation to the keto-oxygen O(3) is

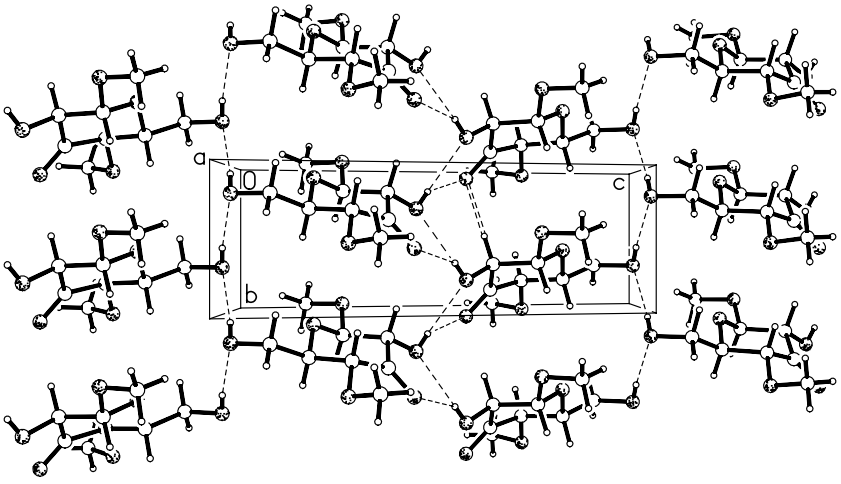


Figure 2. Packing mode and unit cell of compound **2** in a perspective view down the *a*-axis. O–H–O hydrogen bonds are indicated by dashed lines. The doubly dashed line in the center shows one C(2)–H(2)–O(3) hydrogen bond type interaction.

found, the relevant distances and angles being O(2)–O(2) = 2.795(3) Å, O(2)–O(3) = 3.074(3) Å, H(2)–O(2) = 2.16 Å, H(2)–O(3) = 2.44 Å, and both O(2)–H(2)–O angles 143°. Interestingly, a C–H–O hydrogen bond from C(2) to O(3) of a neighboring molecule [C–O = 3.251(3), H–O = 2.30 Å] is also present, as shown in Figure 2 only once as a dotted double line. No intramolecular hydrogen bonds are present.

The solid-state ^{13}C NMR spectrum was recorded using cross-polarization and rotation at the magic angle (CPMAS). The spectrum as shown in Figure 3 displays eight carbon resonances, as expected. The line width of 15–18 Hz is quite narrow. The unambiguous assignment of the signals is given in Table 4. The discrimination between C-6 and the methoxyl resonances can easily be achieved by comparing CPMAS spectra with different cross-polarization times. For the shorter cross-polarization the OCH_3 signals have a decreased intensity by about 50% as compared to C-6 due to free methyl group rotation. The chemical shifts in liquid and solid state agree quite well, larger differences (>1 ppm) between the liquid and solid-state NMR spectra were only noticed for the chemical shifts of the methoxyl carbons, C-4 and C-6. These carbons should show a high sensitivity towards conformational changes, which—in contrast to the solid state—are averaged by motion in solution.

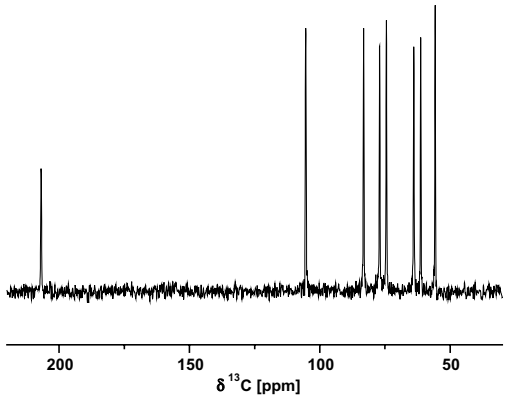


Figure 3. ^{13}C CPMAS-NMR spectrum of hexulopyranoside **2**. For assignment see Table 4.

3. Experimental

X-Ray data collection of **2**[5] was performed with a Bruker AXS Smart APEX CCD diffractometer and graphite monochromatized Mo-Kα radiation; corrections for absorption with the program SADABS, structure solution with direct methods, structure refinement on F^2 (Bruker AXS, 2001: programs SMART, version 5.626; SAINT, version 6.36A; SADABS version 2.05; XPREP, version 6.12; SHELXTL, version 6.10. Bruker AXS Inc., Madison, WI, USA).

CCDC-226797 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge at www.ccdc.cam.ac.uk/conts/retrieving.html [or from the Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK; fax: (internat.) +44-1223-336-033; deposit@ccdc.cam.ac.uk].

The solid-state NMR measurements were recorded on a Bruker DMX400 spectrometer, using a double channel CPMAS probe head. The spinning frequency of the 4 mm ZrO_2-CRAMPS-rotor was 12,500 Hz and was stabilized to ±2 Hz. The ^{13}C CPMAS spectra were acquired at a radio frequency of 100.3 MHz. The 90° proton pulse was set to 2.5 μs, a ^{13}C B_1-field of 50 kHz during the ramped (50% ramp on proton channel) CP sequence with a mixing time of 1 ms or 100 μs was used. The TPPM sequence[6] with a phase shift of 10° was applied to decouple the protons during the acquisition time.

Spectra in solution were recorded with a Bruker Avance DPX instrument operating at 300 MHz for ^1H and 75.47 MHz for ^{13}C using $CDCl_3$ or D_2O as the solvents and tetramethylsilane as internal standard. ^1H and ^{13}C NMR spectra were measured at 293 K and referenced to 1,4-dioxane (δ 67.40). Homo- and heteronuclear 2D NMR spectroscopy was performed with Bruker standard software. Chemical shifts are given in parts per million, coupling constants in Hertz.

Table 4. ^{13}C NMR data of hexulopyranoside **2**

Atom	CPMAS	$CDCl_3$ solution	D_2O solution[a]	
			Keto form	Hydrate form
C-1	105.41	105.60	105.19	103.08
C-2	77.01	77.19	77.64	74.68
C-3	206.90	204.96	206.81	95.78
C-4	83.15	80.26	81.45	80.64
C-5	74.45	75.21	75.73	75.29
C-6	63.93	61.62	61.16	61.45
1-OMe	55.72	57.60	58.20	57.86
4-OMe	61.25	59.65	60.22	62.03

[a] Data given for comparison, values are taken from Ref. 5.

3.1. Methyl 4-*O*-methyl-β-D-*ribo*-hex-3-ulopyranoside (2)

Mp 149–152 °C (MeOH).[5] NMR ($CDCl_3$): δ 4.25 (d, 1H, ^3J 7.8 Hz, H-1), 4.11 (m, 2H, H-2, H-4), 4.01 (m, 1H, H-6a), 3.86 (m, 1H, H-6b), 3.62 (s, 3H, 1-OMe, 1-OMe), 3.58 (s, 3H, 2-OMe, 4-OMe), 3.45 (dt, 1H, ^3J 9.7/3.2 Hz, H-5). ^{13}C NMR ($CDCl_3$): see Table 4.

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