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Note

X-Ray diffraction and high resolution NMR analysis of methyl D-glucopyranuronate derivatives

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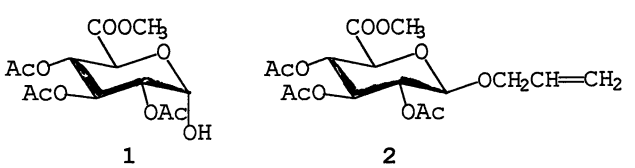
Abstract

X-Ray diffraction and high resolution ^{1}H and ^{13}C NMR spectral data for methyl 2,3,4,-tri-*O*-acetyl-α-D-glucopyranuronate and methyl (allyl 2,3,4-tri-*O*-acetyl-β-D-glucopyranosid)uronate are presented. Both compounds adopt the $^{4}C_{1}$ conformation. © 2000 Elsevier Science Ltd. All rights reserved.

Keywords: D-Glucuronic acid derivatives; X-ray diffraction; ^{1}H NMR; ^{13}C NMR

Glycosides of D-glucuronic acid are widely known as components of oligo- and polysaccharides of biological significance [1–3]. The chemical synthesis of disaccharide fragments containing uronic acid and their coupling with appropriate proteins is then needed to extend our knowledge on the mode of action of this type of glycoconjugate, which is part of our programme. In this report we present the NMR spectra and crystal structures of two methyl D-glucopyranuronate derivatives **1** and **2**, which are precursors in such disaccharide synthesis.



1 2

Selective O-deacetylation of methyl 1,2,3,4-tetra-*O*-acetyl-β-D-glucopyranuronate [4] with hydrazine acetate according to the procedure of Dullenkopf et al. [5] gave methyl 2,3,4-tri-*O*-acetyl-α-D-glucopyranuronate (**1**). High resolution ^{1}H and ^{13}C NMR spectroscopy and X-ray diffraction confirmed its structure. In the crystal lattice, the heterocyclic six-membered ring adopts the $^{4}C_{1}$ chair conformation (see Fig. 1).

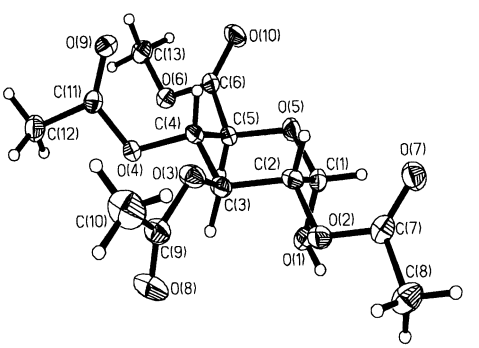


Fig. 1. ORTEP III® [7] drawing of methyl 2,3,4-tri-*O*-acetyl-α-D-glucopyranuronate (**1**) showing 50% probability displacement for ellipsoids.

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Table 1
Crystal data and summary of intensity and structure refinement for methyl 2,3,4-tri-*O*-acetyl-α-D-glucopyranuronate (**1**) and methyl (allyl 2,3,4-tri-*O*-acetyl-β-D-glucopyranosid)uronate (**2**)

Compound	**1**	**2**
Crystal system	monoclinic	orthorhombic
Empirical formula	$C_{13}H_{15}O_{10}$	$C_{16}H_{22}O_{10}$
Formula weight	334.27	374.34
Melting points (°C)	98–100	130–132
$F(000)$	352	792
Space group	$P2_1$	$P2_12_12_1$
Cell constants		
a (Å)	9.759(2)	7.508
b (Å)	9.683(2)	14.777
c (Å)	9.871(2)	17.153
α (°)	90	90
β (°)	118.12(3)	90
γ (°)	90	90
Cell volume (Å^3)	822.7(3)	1903.1(9)
Formula units/unit cell	2	4
μ_{calc} (mm^{-1})	0.118	0.110
D_{calc} (Mg m^{-3})	1.349	1.307
Decay of standard reflections (%)	0.9	8.6
Reflections collected	2419	3010
Independent reflections	2280	2217
Reflections observed ($F>2\sigma(I)$)	1444	507
2θ Range (°)	2.34–60.12	1.82–54.00
Index ranges	$-12\le h\le 12$; $0\le k\le 13$; $-12\le l\le 0$	$-9\le h\le 0$; $0\le k\le 18$; $0\le l\le 21$
No. of parameters varied	212	235
Goodness of fit	1.021	1.091
R_1	0.0379	0.0858
ωR_2	0.0945	0.1998
$\Delta\rho_{max}$ (e Å^{-3})	0.159	0.299
$\Delta\rho_{min}$ (e Å^{-3})	−0.187	−0.282

Crystallographic data, data collection and structure refinements are summarized in Table 1, and selected torsion angles taken from X-ray data and puckering parameters of this compound are shown in Table 2.

Methyl (allyl 2,3,4-tri-*O*-acetyl-β-D-glucopyranosid)uronate (**2**) was prepared from the corresponding glucuronosyl bromide [4]. ^{1}H and ^{13}C NMR data, and crystallographic analysis confirmed its structure. In the crystal lattice, the heterocyclic six-membered ring adopts the $^4C_1$ chair conformation (see Fig. 2). Crystallographic data, data collection and structure refinements are summarized in Table 1, and selected torsion angles and puckering parameters of this compound are shown in Table 2. Table 3 shows bond lengths and angles for hydrogen bonds of compound **1**.

1. Experimental

General procedures.—All crystallographic measurements were carried out on a KUMA KM-4 diffractometer with graphite monochromated Mo K_α radiation, and $\theta/2\theta$ scan mode. The unit cell parameters were determined from least-squares refinement based on the setting angles of 25 reflections. The stability of conditions was controlled by

Table 2
Selected torsion angles obtained from X-ray diffraction analysis and Cremer–Pople [6] parameters Q and Φ for compounds **1** and **2**

Torsion angle	Compound **1**	Compound **2**
C-5–O-5–C-1–O-1	56.3(3)	177.3(12)
C-5–O-5–C-1–C-2	−64.5(3)	−62.6(17)
C-7–O-1–C-1–O-5	–	−69.1(18)
C-7–O-1–C-1–C-2	–	168.4(14)
O-1–C-1–C-2–C-3	−60.9(3)	176.8(12)
C-1–O-5–C-5–C-6	−177.7(2)	−174.5(12)
C-3–C-4–C-5–C-6	−171.9(2)	−176.1(13)
C-1–O-1–C-7–C-8	–	−173.1(14)
O-1–C-7–C-8–C-9	–	−130(2)
Q (Å)	0.5861	0.5990
Φ (°)	−47.59°	−75.01

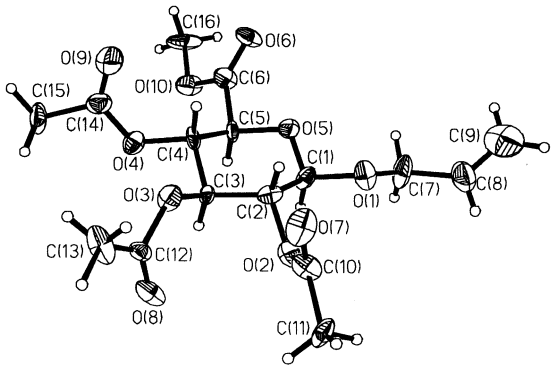

Fig. 2. ORTEP III® drawing of the X-ray structure of methyl (allyl 2,3,4-tri-*O*-acetyl-β-D-glucopyranosid)uronate (**2**) showing 50% probability displacement for ellipsoids.

Table 3
Hydrogen bonds for **1** (H···A < r(A) + 2.000 Å and angle DHA > 110°)

D–H	D(D–H)	d(H···A)	Angle DHA	d(D···A)	A
O-1···H-1B	0.820	2.115	149.14	2.850	O10 [$-x+1$, $y-1/2$, $-z+1$]
O-1···H-1B	0.820	2.474	140.47	3.150	O5 [$-x+1$, $y-1/2$, $-z+1$]

three control measurements every hundred reflections. The structures were solved by direct methods using the SHELXS (1990) program [8] from the SHELX-97 package [9]. Anisotropic displacement coefficients were applied to all non-hydrogen atoms. All non-methyl hydrogen atoms were found in difference maps for both structures. An idealized methyl group with tetrahedral angles was set with torsion angles that maximizes the sum of electron density at all three calculated hydrogen positions (SHELXL-97-AFIX 137 option). Refinement of all hydrogen atoms was done with idealized positions using isotropic temperature factors set to 1.2 times of the equivalent isotropic temperature factor of the neighboring C or O atoms. The structure refinements were performed using the SHELXL program. ^{1}H 400 MHz and ^{13}C 100 MHz NMR spectra were recorded on a VARIAN MERCURY 400 spectrometer with chloroform-*d* as a solvent and $(CH_3)_4Si$ as an internal standard.

Methyl 2,3,4-tri-O-*acetyl*-α-D-*glucopyranuronate* (**1**).—Methyl 1,2,3,4-tetra-*O*-acetyl-β-D-glucopyranuronate [3] (1.00 g; 2.7 mM) was dissolved in EtOAc (14 mL), and hydrazine acetate (0.3 g; 3.3 mM) was added. The suspension was stirred for 90 h at rt. After addition of EtOAc (55 mL), the insoluble salts were filtered off and the solution was washed twice with 10% sodium chloride in water (25 mL). The organic layer was dried with $MgSO_4$ and concentrated under reduced pressure. The resulting thick oil was dissolved in diethyl ether resulting in crystalline methyl 2,3,4-tri-*O* - acetyl - α - D - glucopyranuronate (0.28 g; 32%); mp 98–100 °C; $[\alpha]_D^{20} + 81.17°$ (c 0.105, $CHCl_3$). ^{1}H NMR ($CDCl_3$): δ 5.58 (dd, 1 H, $J_{3,4}$ 9.2 Hz, H-3), 5.54 (d, 1 H, $J_{1,2}$ 3.6 Hz, H-1), 5.17 (dd, 1 H, $J_{4,5}$ 10.0 Hz, H-4), 4.90 (dd, 1 H, $J_{2,3}$ 10.0 Hz, H-2), 4.59 (d, 1 H, H-5), 3.75 (s, 3 H, OCH_3), 2.09–2.03 (9 H, $3 \times OCOCH_3$); ^{13}C NMR ($CDCl_3$): δ 169.73–168.01 (4 C, $3 \times OCOCH_3$, $1 \times COOCH_3$), 90.04 (C-1), 70.50 (C-3), 69.28 (C-4), 68.84 (C-5), 67.86 (C-2), 52.84 ($COOCH_3$), 20.65–20.51 (3 C, $3 \times OCOCH_3$). Anal. Calcd for $C_{13}H_{18}O_{10}$: C, 46.71; H, 5.39. Found: C, 47.15; H, 5.52.

Methyl (allyl 2,3,4-tri-O-*acetyl*-β-D-*glucopyranosid)uronate* (**2**).—A mixture of methyl 2,3,4-tri-*O*-acetyl-α-D-glucopyranosyluronate bromide [4] (2.65 g; 6.7 mM), mercuric cyanide (1.82 g) and allyl alcohol (21.0 mL; 310 mM) was stirred for 24 h at rt. Volatile compounds were removed under reduced pressure and the residue was dissolved in $CHCl_3$ (80 mL). The solution was washed with water, dried with Na_2SO_4 and concentrated. The resulting crude syrup was dissolved in EtOH yielding crystalline methyl (allyl 2,3,4-tri-*O*-acetyl-β-D-glucopyranosid)uronate (1.10 g; 44%,): mp 130–132 °C, $[\alpha]_D^{20} + 191.67°$ (c 0.12, $CHCl_3$); ^{1}H NMR ($CDCl_3$): δ 5.83 (m, 1 H, –CH=), 5.29 (m, 1 H, OCH_2), 5.24 (m, 2 H, $J_{3,4}$ 9.2, $J_{4,5}$ 9.6 Hz, H-3, H-4), 5.04 (m, 1 H, $J_{2,3}$ 8.0 Hz, H-2), 4.60 (d, 1 H, $J_{1,2}$ 7.6 Hz, H-1), 4.36 (m, 1 H, $=CH_2$), 4.10 (m, 1 H, $=CH_2$), 4.03 (q, 1 H, H-5), 3.76 (s, 3 H, OCH_3), 2.02–2.05 (9 H, $3 \times OCOCH_3$); ^{13}C NMR ($CDCl_3$): δ 169.76–166.87 (4 C, $3 \times OCOCH_3$, $1 \times COOCH_3$), 132.75 (–CH=), 117.60 (OCH_2), 99.27 (C-1), 72.44 ($=CH_2$), 71.89 (C-3), 71.02 (C-4), 69.96 (C-5), 69.26 (C-2), 52.80 ($COOCH_3$), 20.61–20.47 (3 C, $3 \times OCOCH_3$). Anal. Calcd for $C_{16}H_{22}O_{10}$: C, 51.34; H, 5.88. Found: C, 50.68; H, 5.90.

2. Supplementary material

Tables of atomic coordinates, bond lengths and bond angles for both reported compounds have been deposited with the Cambridge Crystallographic Data Center. These tables may be obtained, on request, from the Director, Cambridge Crystallographic Data Center, 12

Union Road, Cambridge, CB2 1EZ, UK (Fax: +44-1223336033; e-mail: deposit@ccdc.cam.ac.uk); deposit numbers: CCDC 143703/CCDC 143704.

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