Synthesis and Crystal Structure of *p*-Methoxyphenyl 2-acetamido-3,4,6-tri-*O*-acetyl-2-deoxy- β -D-glucopyranoside

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p-Methoxyphenyl 2-acetamido-3,4,6-tri-*O*-acetyl-2-deoxy- β -D-glucopyranoside (**1**) was prepared by the reaction of pentaacetyl- β -D-glucosamine, *p*-methoxyphenol, and boron trifluoride etherate in dry methylene chloride. The crystal structure was determined by X-ray diffraction analysis. The title compound **1** crystallizes in the hexagonal space group $P6_5$ with $a = b = 12.5772(5)\text{\AA}$, $V = 3427.0(3)\text{\AA}^3$, and $Z = 6$. The crystal structure was solved by direct methods and refined by full-matrix least-squares. An intermolecular hydrogen bond of the amido hydrogen to the carbonyl oxygen of the acetamido group in another molecule was found.

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p-Methoxyphenyl ethers are important protecting groups for the anomeric center of glycosides and stable under most conditions used in oligosaccharide synthesis. The block synthesis of chitooligosaccharides is possible because the *p*-methoxyphenyl glycosides can be readily converted to the corresponding thioglycosides, bromides or chlorides.¹ Some chitooligomers have several important biological functions. For example, they have been used as lysozyme substrates, as antitumor and also as immunopotentiating agents.² Moreover, possible correlations between the structure and the reactivity in carbohydrate chemistry are quite interesting.

The preparation of the title compound **1** is well-known,³ but another procedure was developed. Boron trifluoride etherate (5.4 mL, 43 mmol) was added to an ice-cold solution of 2-acetamido-1,3,4,6-tetra-*O*-acetyl-2-deoxy- β -D-glucopyranose (10.00 g, 25.7 mmol) and *p*-methoxyphenol (9.50 g, 76.7 mmol) in dry methylene chloride (180 mL) under an argon atmosphere. After 72 h, the mixture was diluted with methylene chloride (100 mL), washed with water (2×100 mL), saturated aq. NaHCO_3 (100 mL) and water (3×100 mL), dried over MgSO_4 , filtered and evaporated. The residue was recrystallized from a mixture of ethyl acetate and hexane to obtain colorless needles of **1** in 87% yield.

A single crystal was used to determine the stereochemical structure by X-ray analysis. Reflections were collected using a STOE Imaging Plate Diffraction System (IPDS-II) at 210 K. The structure was solved by direct methods as implemented in the program SHELXS-97.⁴ The refinement was carried out

using SHELXL-97.⁵ All the non-hydrogen atoms were refined anisotropically. The hydrogen atoms were located from the difference Fourier map and refined isotropically. The oxygen atom O32 is disordered over two sides in the ratio of 1:1. The absolute structure arises from the known absolute structure of the D-glucopyranose moiety. Consistently with D-glucose, the title compound **1** possesses the five chiral centers C(1) (*S*), C(2) (*R*), C(3) (*R*), C(4) (*S*) and C(5) (*R*). Crystal and experimental data are summarized in Table 1. The molecular structure with the atom labeling scheme is given in Fig. 2. Selected bond lengths ($\text{\AA}$), bond angles ($^\circ$) as well as torsion angles ($^\circ$) are presented in Table 2.

Corresponding to the β -D-glucopyranoside (β -D-Glc_p)

Table 1 Crystal and experimental data

Formula: $\text{C}_{21}\text{H}_{27}\text{NO}_{10}$
Formula weight: 453.44
Crystal system: hexagonal
Space group: $P6_5$ $Z = 6$
$a = b = 12.5772(5)\text{\AA}$
$c = 25.0158(12)\text{\AA}$
$V = 3427.0(3)\text{\AA}^3$
$T = 210\text{ K}$
$D_{\text{calc}} = 1.318\text{ g/cm}^3$
No. of reflections used = 44777
No. of independent reflections used = 3955
$2\theta_{\text{max}} = 50.0^\circ$ with Mo K_α
$R, R_w = 0.0243, 0.0485$ for 3320 refs. [$I > 2\sigma(I)$]
$(\Delta/\sigma)_{\text{max}} = 0.001$
$(\Delta\rho)_{\text{max}} = 0.125\text{ e\AA}^{-3}$
$(\Delta\rho)_{\text{min}} = -0.125\text{ e\AA}^{-3}$
Measurements: Stoe IPDS-II
Program: X-AREA (Stoe)
Structure determination: SHELXS ⁵
Refinement: full-matrix least-squares

Details of the crystal structure determination can be obtained free of charge via www.ccdc.cam.ac.uk/data_request/cif or by e-mail via deposit@ccdc.cam.ac.uk on quoting the deposition number CCDC 297188.

Fig. 1 Chemical structure of the title compound **1**.

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Fig. 2 Molecular structure of the title compound **1** with atom labeling. The thermal ellipsoids were drawn at the 50% probability level.

Table 2 Selected bond lengths (Å), bond angles (°) and torsion angles (°)

O1-C1	1.420(2)	O1-C5	1.4320(19)
O11-C1	1.404(2)	O12-C14	1.368(2)
O12-C17	1.430(2)	O31-C3	1.4408(19)
O61-C6	1.440(2)	N1-C2	1.455(2)
N1-H21	0.84(2)	C2-C3	1.527(2)
C1-C2	1.518(2)	C3-C4	1.511(3)
C4-C5	1.520(2)	C5-C6	1.502(3)
C1-O1-C5	111.06(13)	O11-C11-C12	122.32(14)
C1-O11-C11	118.08(12)	O11-C11-C16	117.00(15)
C14-O12-C17	117.58(16)	C3-O31-C31	120.39(16)
O12-C14-C15	125.21(15)	O12-C14-C13	115.38(17)
C4-O41-C41	116.90(14)	C6-O61-C61	117.56(14)
C2-N1-H21	123.10(17)	C2-N1-H21	115.0(12)
O11-C1-C2	105.84(13)	O1-C1-O11	108.03(15)
O1-C1-C2	110.56(13)	C1-C2-C3	112.65(13)
N1-C2-C1	110.17(13)	N1-C2-C3	110.98(15)
C3-C4-C5	109.95(13)	C4-C5-C6	114.76(14)
O1-C5-C6	107.91(15)	O1-C5-C4	106.80(12)
C5-O1-C1-O11	-178.49(11)	C5-O1-C1-C2	-63.11(17)
C1-O1-C5-C6	-166.55(13)	C1-O1-C5-C4	69.57(16)
C11-O11-C1-C2	165.98(15)	C11-O11-C1-O1	-75.57(16)
C1-O11-C11-C12	62.35(19)	C1-O11-C11-C16	-124.61(18)
C17-O12-C14-C15	-6.1(2)	C17-O12-C14-C13	172.88(19)
C3-O31-C31-C32	172.00(18)	C4-O41-C41-O42	-3.9(3)
C4-O41-C41-C42	174.71(16)	C6-O61-C61-O62	-2.7(3)
C6-O61-C61-C62	176.49(16)	C2-N1-C21-O21	6.9(3)
C2-N1-C21-C22	-172.57(15)	O1-C1-C2-N1	173.69(14)
O1-C1-C2-C3	49.2(2)	O11-C1-C2-C3	165.92(15)
N1-C2-C3-O31	73.70(17)	C1-C2-C3-C4	-44.2(2)
N1-C2-C3-C4	-168.24(13)	C1-C2-C3-O31	-162.23(15)
C2-C3-C4-O41	169.86(13)	C2-C3-C4-C5	50.80(19)
C3-C4-C5-O1	-62.38(19)	C3-C4-C5-C6	178.08(15)
O1-C5-C6-O61	-66.97(16)	C4-C5-C6-O61	51.9(2)
O11-C11-C12-C13	-172.66(17)	O11-C11-C12-C16	172.66(18)
C12-C13-C14-O12	-178.35(18)	O12-C14-C15-C16	178.63(19)

configuration, all non-hydrogen substituents are located in equatorial positions. The carbonyl bonds of the acetamido group and all of the acetyl groups are nearly coplanar with their respective ring C-H bonds and point in the same direction. The

bond lengths at the anomeric center are more different (exocyclic: C1-O11 1.404(2), endocyclic: C1-O1 1.420(2) Å) then in some other β -D-glucopyranosides (2-nitrophenyl β -D-Glc_p⁶: 1.409(4)/1.411(3) Å; 3,4-dinitrophenyl β -D-Glc_p⁷: 1.405(4)/1.405(5) Å; 3,4-dinitrophenyl 2,3,4,6-tetra-O-acetyl- β -D-Glc_p⁸: 1.400(6)/1.395(6) Å; *p*-nitrophenyl 2,3,4,6-tetra-O-acetyl- β -D-Glc_p⁹: 1.408(3)/1.417(3) Å), but less different in comparison with phenyl- β -D-Glc_p¹⁰ (1.394(6)/1.434(5) Å) or unsubstituted β -D-Glc_p¹¹ (1.394/1.431 Å). The dihedral angle between the glucopyranoside and the phenyl ring is 16.82(8)°. The corresponding torsion angles are -75.57(16)° for O1-C1-O11-C11 and 62.35(19)° for C1-O11-C11-C12. The former one agrees well with reference data from the literature (-73.62 to -82.5°).⁶⁻¹⁰ In contrast, the second one is greater (10.8 to 29.5°)⁶⁻¹⁰ indicating that in the structure reported here the phenyl ring is more torsioned around the O11-C11 bond. However, the methoxy group is almost coplanar with the phenyl ring, forming a C15-C14-O12-C17 torsion angle of -6.1(2)°.

The crystal packing of **1** shows an intermolecular hydrogen bond between N1 and O21' with the following parameters: N1-H21...O21' 0.841(18) Å, 2.8086(18) Å, 157.6(15)°; the symmetry operator for O21' is $x - y + 1, x, z - 1/6$. The molecules are linked along the *c* axis by the hydrogen bond.

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