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Crystal Structure Analysis of 2,3,4-Tri-*O*-acetyl-α-methyl-D-glucopyranoside

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2,3,4-Tri-*O*-acetyl-α-methyl-D-glucopyranoside (F.W. 319.28) was synthesized, characterized by ^{1}H NMR, confirmed by X-ray crystal structure analysis. This compound crystallizes in monoclinic class under the space group orthorhombic P2(1)2(1)2(1) with cell parameters a = 9.0312(18) Å, b = 11.731(2) Å, c = 15.139(3) Å; Z = 4. The structure exhibits inter-molecular hydrogen bonds of the type O-H---O, C-H---O.

Keywords: α-Methyl-D-glucopyranoside, Protection, Synthesis, Crystal structure, Hydrogen bond.

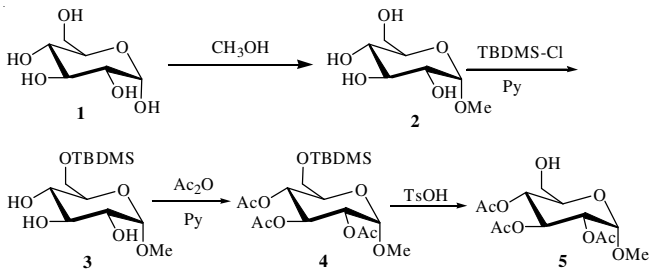
INTRODUCTION

Carbohydrates perform numerous roles in living things. Especially, their derivatives include many other important biomolecules that play key roles in the immune system, fertilization, preventing pathogenesis, blood clotting and development[1-4]. Therefore, the stereoselective introduction of glycosidic linkages presents the principal challenge to the chemical synthesis of complex oligosaccharides of biological importance[5-7]. Generally, chemical syntheses of oligosaccharides and glycoderivatives usually require multistep reaction sequences and sophisticated protecting group strategies[8,9]. For the synthesis of bioactive complex molecules, the regioselective protection and deprotection of hydroxyl groups were very important[10]. Protected monosacharides with only one free hydroxyl group are useful building blocks for the synthesis of a large number of glycoderivatives[11,12], for example, the synthesis of influenza virus trisaccarides[13], neo-oligosaccarides mimic Tn epitopes[14] and antitumoral aryl-glycoside[15] *etc*. Recently, Palomo *et al.*[16] reviewed the different methods for regioselective protection, deprotection of monosacharides and application of the mono-derivation in glycoconjugate synthesis and the various glycoconjugates have been achieved by using these techniques. The biological activity of many natural products derives from the sugar moieties, including glucose linked *via* position C-6. Therefore, selective *O*-acetylation of α-D-methyl glucopyranoside is important for modification of free hydroxyl groups on secondary or primary hydroxyl groups. 2,3,4-Tri-*O*-acetyl-α-methyl glucopyranoside was prepared according to reported procedure in the literature[17]. Its synthetic route is as **Scheme-I**. In this paper, we reported, the structure and ^{1}H NMR analysis of 2,3,4-tri-*O*-acetyl-α-methyl glucopyranoside.

EXPERIMENTAL

All analytical grade chemicals and solvents were purchased commercially and used without further purification. 2,3,4-Tri-*O*-acetyl-α-methyl glucopyranoside was prepared according to the literature procedures[18].

Melting points, measured with an XT-4 apparatus, are uncorrected. ^{1}H NMR spectra were recorded on a Bruker AVANCE 500 instrument in $CDCl_3$ solution, using tetramethylsilane as an internal reference.



Scheme-I: Preparation processes of compound **5**

Structure determination: Determination of the unit cell and data collection were performed on a Bruker SMART using graphite-monochromated MoK_α radiation (λ = 0.71073 Å) at 293(2) K with crystal size 0.30 mm × 0.20 mm × 0.10 mm for compound **5**. Semiempirical absorption corrections were applied

using the SADABS program. The structure of compound was solved by direct methods and successive fourier difference syntheses (SHELXS-97) and refined by full-matrix least-squares procedure on F2 with anisotropic thermal parameters for all on-hydrogen atoms (SHELXL-97)[19]. Hydrogen atoms were generated geometrically and initially located in a difference Fourier map. The H(-C) atoms were then constrained to an ideal geometry with C-H distances in the range of 0.96-0.98 Å and Uiso(H) = 1.5 Ueq (C). The final agreement factor values are R1 = 0.0342, wR2 = 0.0867 (I > 2σ) for complex **5**, R1 = (||F0|-|Fc||)/_|F0|,wR2 = (_(|F0|2-|Fc|2)2/_w|F0|2)2. Further details of the structure analysis for compounds **5** is given in Table-1. CCDC reference number of compounds **5** was 885842.

RESULTS AND DISCUSSION

^{1}H NMR spectral analysis: 2,3,4-Tri-*O*-acetyl-α-methyl glucopyranoside was characterized by ^{1}H NMR spectroscopy. The chemical shift of ^{1}H NMR spectrum, triplet peaks of δ 5.54 and 5.03 ppm with coupling constant J = 10 Hz are assigned to the proton signals at C-3, C-4, respectively. H-2 displays a strong dd signal at δ 4.86 with $J_{H_2\text{-}H_1}$ = 3.5 Hz, $J_{H_2\text{-}H_3}$ = 10 Hz. While double peaks of δ 4.97 ppm with coupling constant $J_{H_1\text{-}H_2}$ = 3.5 Hz is due to hydrogen signal at C-1, These indicate a gauche relationship between H-1 and H-2 and methyl glucopyranoside ring is α-conformation[20,21]. The crystal structure determination of **5** now confirms the assignment.

Structure description: Table-1 gives the bond lengths and bond angles of non-hydrogen atoms. In crystal **5**, the ORTEP of the molecule at 30 % probability is shown in Fig. 1. The hydroxy group was found to be disordered over two orientations. The occupancies of the disordered positions O9/O9', H9/H9' were refined to 0.70/0.30. Suitable restraints were applied to the C---O and O---H distances involving the disordered atoms. An analysis of the C-C bond lengths within the pyranose ring shows that the bond lengths are in the range between 1.507 and 1.532 Å. Amongst the bonds within the pyranose ring, exocyclic C1-O2 bond length of 1.398(2) Å is found to be the shortest. The bond lengths C5-O1 and O1-C1 are 1.433(2) and 1.416(2) Å, respectively. The shortening of C1-O2 bond compared to O1-C1 bond distance indicates a significant anomeric effect. The valence bond angles of 114° and 112.8° in the sequence C5-O1-C1-O2, respectively and the torsion angle 60.01(12)° for the sequence C5-O1-C1-O2 indicate the α-configuration at the anomeric center. The molecular conformation is a distorted $^4C_1$ with cremer-pople puckering (**5**) Q = 0.573 Å, θ = 173.10° and ϕ = 117.7°

Torsion angles O(1)-C(5)-C(6)-O(9) of -76.91(14) and C(4)-C(5)-C(6)-O(9) of 41.46(16) indicate the gauche-gauche orientation of hydroxy group with respect to the ring oxygen as well as to the C-4 substituent. On the other hand, the torsion angles of C(7)-O(2)-C(1)-O(1) of 70.33(12) and C(7)-O(2)-C(1)-C(2) of -167.57(10) show that the anomeric substituent has gauche-*trans* orientation with respect to the pyranose ring. Nearly eclipsed, 'Z' conformations are found for the ester moieties.

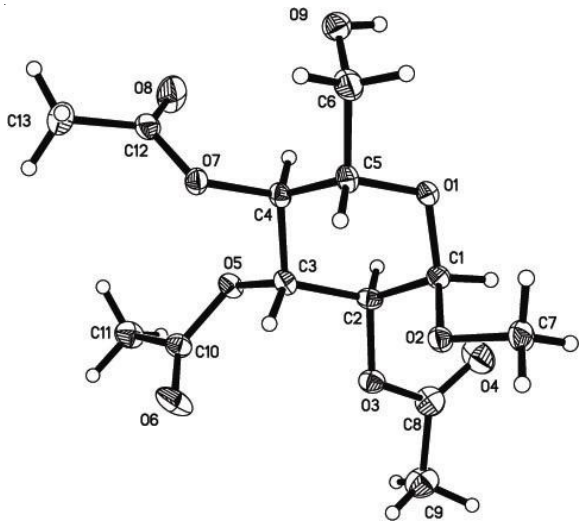


Fig. 1. Structure of compound **5**, with displacement ellipsoids for non-H atoms drawn at the 30 % probability level

An analysis of the noncovalent interactions shows that an array of O-H---O and C-H---O interactions stabilizes the molecular packing in the crystal lattice of **5** (Fig. 2). Applying

TABLE-1
SELECTED BOND LENGTHS (Å) AND BOND ANGLES (°)

Bond	Dist.	Bond	Dist.	Bond	Dist.
O(1)-C(1)	1.4158(15)	O(4)-C(8)	1.2005(18)	O(5)-C(3)	1.4470(13)
O(1)-C(5)	1.4334(14)	O(6)-C(10)	1.1957(15)	C(1)-C(2)	1.5315(17)
O(2)-C(1)	1.3981(14)	O(8)-C(12)	1.1931(16)	C(2)-C(3)	1.5109(17)
O(2)-C(7)	1.4441(14)	O(9)-C(6)	1.2925(19)	C(3)-C(4)	1.5070(17)
O(3)-C(8)	1.3553(16)	O(9)-H(9)	0.8200	C(4)-C(5)	1.5179(16)
O(3)-C(2)	1.4329(14)	O(5)-C(10)	1.3506(15)	C(5)-C(6)	1.5036(18)
O(7)-C(12)	1.3594(15)	O(7)-C(4)	1.4375(14)	-	-
Angle	(°)	Angle	(°)	Angle	(°)
C(1)-O(1)-C(5)	114.02(8)	C(3)-C(2)-C(1)	111.71(9)	-	-
C(1)-O(2)-C(7)	112.51(9)	O(5)-C(3)-C(4)	106.75(9)	O(9')-C(6)-C(5)	126.11(16)
C(8)-O(3)-C(2)	116.52(10)	C(4)-C(3)-C(2)	109.87(9)	O(9)-C(6)-C(5)	116.92(13)
C(6)-O(9)-H(9)	109.5	O(7)-C(4)-C(3)	108.59(9)	O(4)-C(8)-O(3)	122.68(13)
O(2)-C(1)-O(1)	112.78(9)	C(3)-C(4)-C(5)	110.65(9)	O(4)-C(8)-C(9)	126.40(14)
O(1)-C(1)-C(2)	110.05(9)	O(1)-C(5)-C(6)	107.61(10)	O(3)-C(8)-C(9)	110.92(12)
-	-	O(1)-C(5)-C(4)	106.85(9)	O(6)-C(10)-C(11)	125.33(12)
O(3)-C(2)-C(3)	106.76(9)	C(6)-C(5)-C(4)	114.09(10)	O(8)-C(12)-C(13)	126.27(13)

TABLE-2
HYDROGEN BOND LENGTHS (Å) AND BOND ANGLES (°)

D–H···A	d(D–H)	d(H···A)	d(D···A)	∠DHA
O(9)-H(9)---O(2)[a]	0.82	2.23	2.9342(16)	144
O(9)-H(9)---O(3)[a]	0.82	2.49	3.1799(16)	143
C(3)-H(3)---O(1)[b]	0.98	2.36	3.3140(15)	164
C(11)-H(11B)---O(9)[c]	0.96	2.40	3.240(2)	145
C(11)-H(11C)---O(4)[d]	0.96	2.60	3.525(2)	162

Symmetry codes: (a) 0.5 + x, 1.5-y, 1-z; (b) -0.5 + x, 1.5-y, 1-z ; (c) 2-x, 0.5 + y, 1.5-z; (d) 2-x, -0.5 + y, 1.5-z

the criteria H---O < 2.7 A ° and D-H---A > 120, with analysis using the PARST PARST97 program, five intermolecular hydrogen bonds were detected (not including those involving disordered hydroxyl groups of low site occupancy), Data on intermolecular interactions arising from O-H---O and C-H---O hydrogen bonds are presented in Table-2. These two types of hydrogen bonds, specifically arising from O-H---O and C-H---O contacts, form a zig-zag chain, which runs down along the translation axis b (Fig. 3). Strong intermolecular hydrogen bonds O9-H9---O2 (2.9342(16) Å 144 º) and O9-H9---O3 (3.1799(16) Å 143 º) contacts, form an infinite chain connecting molecules, while weak non-classical hydrogen bonds C-H---O(C(3)-H(3)···O(1) (3.3140(15) Å, 164º); C(11)-H(11b)···O(9) (3.240(2) Å, 145 º); C(11)-H(11c)···O(4) (3.525(2) Å, 162 º)) lead to the formation of a three-dimensional network structure and further stabilize the crystal structure.

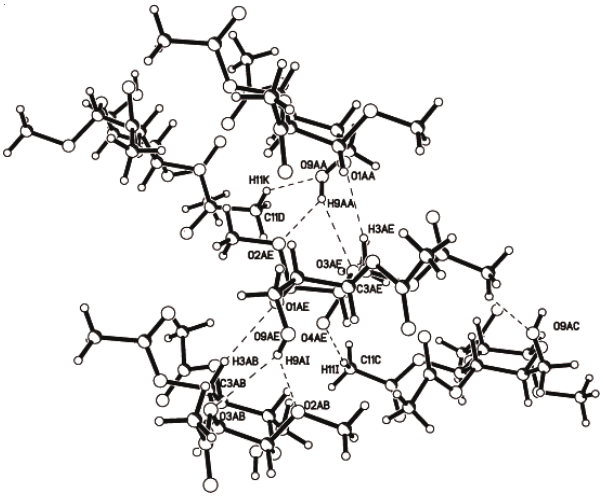


Fig. 2. Part of the crystal structure of compound **5**, showing the formation of network *via* hydrogen bonds

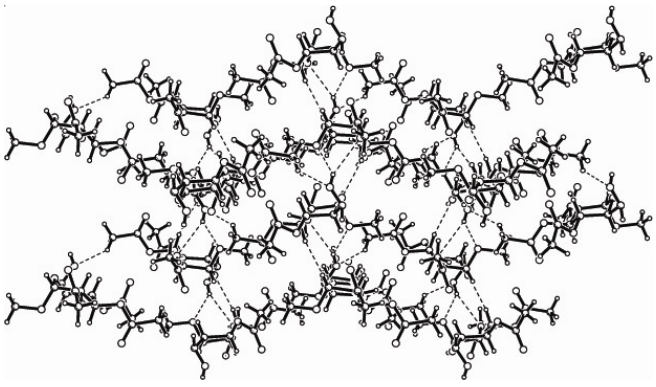


Fig. 3. Packing diagram for compound **5** along the b axis

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