

Communication

The Molecular Structure of 1,2:5,6-Di-*O*-isopropylidene-3-*O*-toluenesulfonyl- α -D-glucofuranose

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Abstract: The crystal and molecular structure of 1,2:5,6-di-*O*-isopropylidene-3-*O*-toluenesulfonyl- α -D-glucofuranose is reported. This compound crystallizes from a petroleum ether/ethyl acetate mixture with the chiral orthorhombic space group $P2_12_12_1$ with four molecules in the unit cell. The unit cell parameters are: $a = 9.7945(7)$ Å, $b = 10.1945(7)$ Å, $c = 21.306(1)$ Å, and $V = 2127.4(2)$ Å³. No classical hydrogen bonds were found. Bond lengths and angles of this tosylated glucofuranose derivative are typical.

Keywords: carbohydrates; glucose; tosylation

1. Introduction

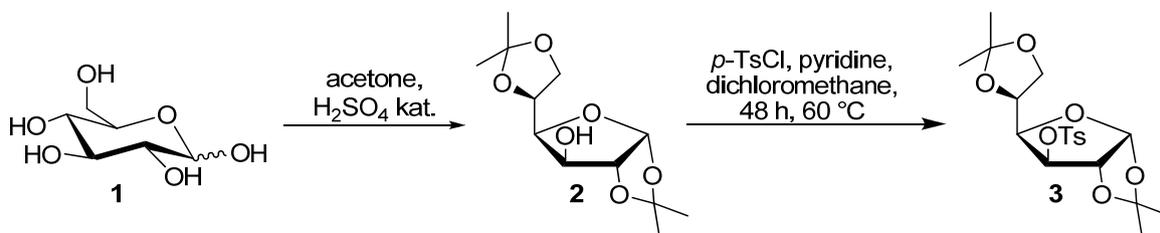
Monosaccharides with good leaving groups like mesylate, tosylate or nosylate play a major role for the introduction of various functional groups, as building blocks for the formation of di- and oligosugars, as chiral pool materials or for the preparation of bioactive glycoconjugates [1]. This offers the possibility for the preparation of rare carbohydrate derivatives. For this purpose, protected carbohydrate building blocks like carbohydrate **2** were prepared from D-glucose (**1**) with the potential for the convenient selective introduction of sulfonate leaving groups in high yields under mild basic

conditions. Thus, D-glucose (**1**) is protected with two isopropylidene moieties in the first step [2]. Next, the introduction of the tosylate leaving group occurs under basic conditions [3]. Interestingly, in subsequent reactions the replacement of the tosyl leaving group against the resulting functional group proceeds under inversion of the configuration of the respective carbon atom C-3 (Walden-inversion) in most of the cases [4]. In addition, side reactions like eliminations were observed as well [5].

2. Results and Discussion

The introduction of isopropylidene protecting groups under acid catalysis occurs chemoselectively and the 1,2:5,6-diisopropylidene- α -D-glucose (**2**) as furanose form was prepared in high yields [2]. Treatment of glucose **2** with *p*-TsCl in the presence of pyridine as base afforded the desired carbohydrate building block **3** in a high yield of 78% (Figure 1). Crystals of **3** were grown during the purification step from a saturated petroleum ether/ethyl acetate solution.

Figure 1. The synthesis of tosylated glucose derivative **3**.



The crystal and instrumental parameters of the structure determination are summarized in Table 1. The drawing of the molecular structure of compound **3** with the used atom-labeling scheme is shown in Figure 2. The displacement thermal ellipsoids are drawn at the 30% probability level. Selected bond lengths and angles comprising the key features of 1,2:5,6-di-*O*-isopropylidene-3-*O*-toluenesulfonyl- α -D-glucopyranose (**3**) are given in Table 2.

Figure 2. A view of molecule **3** showing the atom-labeling scheme. Displacement ellipsoids are drawn at the 30% probability level.

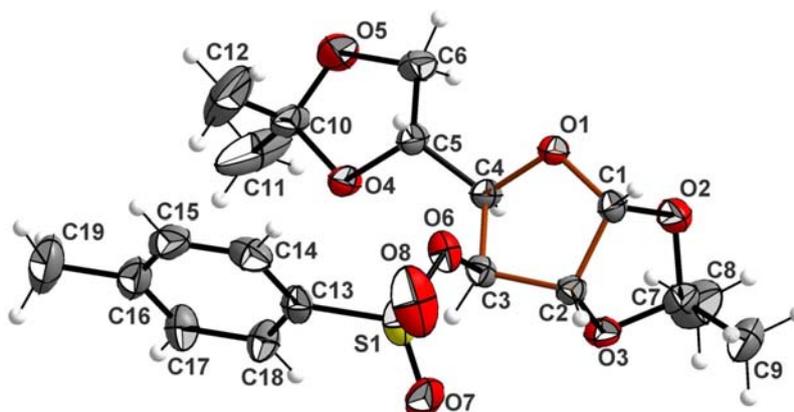
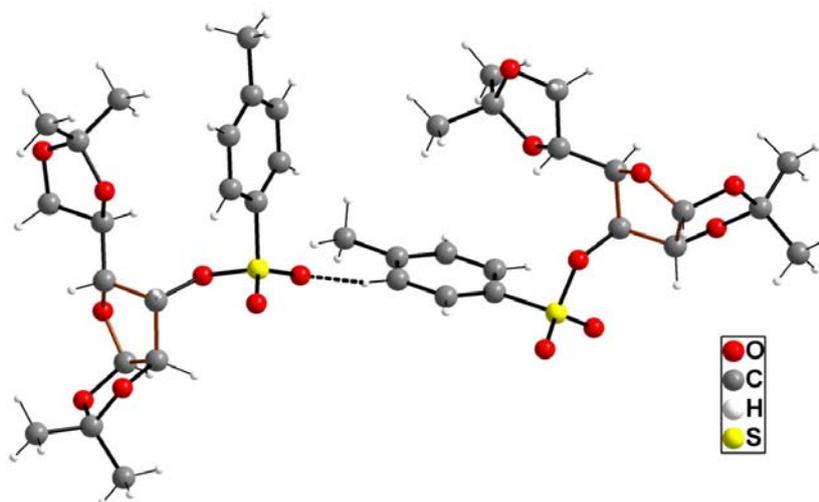


Table 1. Crystal data and structure refinement parameters for compound 3.

Crystal data		Refinement	
Formula	C ₁₉ H ₂₆ O ₈ S	Refinement method	Full-matrix least-squares on F^2
Formula weight	414.48 g·mol ⁻¹	Data/restraints/parameters	6469/0/254
Temperature	173(2) K	Measured reflections	18550
Wavelength	0.71073 Å	Goodness-of-fit on F^2	1.032
Crystal system	orthorhombic	Final R indices	$R_1 = 0.0509$
Space group	P2 ₁ 2 ₁ 2 ₁	$[I > 2\sigma(I)]$	$wR_2 = 0.1238$
Unit cell dimensions	$a = 9.7945(7)$ Å $b = 10.1945(7)$ Å $c = 21.306(1)$ Å	R indices (all data)	$R_1 = 0.0660$ $wR_2 = 0.1357$
Volume	2127.4(2) Å ³	Largest diff. peak/hole	0.417/−0.375 eÅ ⁻³
Z	4		
Density (calcd.)	1.294 g·cm ⁻³		
Absorption coefficient	0.193 mm ⁻¹		
F(000)	880		
Crystal size	0.70 × 0.22 × 0.11 mm ³		

Figure 3. View of two neighboring molecules in 3 with the shortest intermolecular contact drawn as a dashed line.

In the title compound, the conformation of the furanose ring is fixed by the two isopropylidene protecting groups. Each of the protecting groups form a five membered ring with the furanose skeleton. The first group is attached to O2 (C1) and O3 (C2), both carbon atoms have the R configuration. The second isopropylidene protecting group is attached to O4 (C5) and O5 (C6). The atom C3 has S configuration, whereas C4 is R-configured. The furanose ring has a distorted envelope conformation, in which C1, C2, C3 and O1 are located almost in a plane, and atom C4 is the one out of this plane. The (C1, C2, C3, O1) plane has a dihedral angle of 35.5° relative to the mean plane through O1, C4 and C3. Figure 2 shows, that atom C11, which is part of the isopropylidene group attached to O4 and O5, has an unusual ratio of the anisotropic displacement parameters. Attempts to use split positions did not improve the model. Therefore, it is concluded that the various energetically very close positions of

this methyl group, as averaged over all the unit cells of the used crystal, are best described by a cigar-type ellipsoid.

Between the molecules there are no classical hydrogen bonds, because all the O-bonded H atoms are substituted by protecting and leaving groups, respectively. The shortest intermolecular contact is between O8 and H14A (C14) of the neighboring molecule at an O–C distance of 2.941(4) Å. Figure 3 shows the two adjacent molecules with this short intermolecular contact.

Table 2. Selected interatomic distances [Å] in **3**.

atoms	distance	atoms	Distance
O1–C1	1.439(2)	S1–O7	1.431(2)
O1–C4	1.407(2)	S1–O8	1.418(2)
C1–C2	1.518(2)	S1–C1	1.748(2)
C2–C3	1.526(2)	C5–C6	1.508(3)
C3–C4	1.538(2)	C5–O2	1.420(2)
C1–C5	1.506(3)	C6–O3	1.394(3)
C2–O4	1.451(2)	C7–O2	1.437(2)
C3–O5	1.415(2)	C7–O3	1.406(3)
C4–O6	1.406(2)	C17–O5	1.427(3)
S1–O4	1.588(2)	C17–O6	1.431(3)

3. Experimental Section

3.1. General

NMR spectra were recorded on a Varian Inova-400 spectrometer and chemical shifts of the ^1H and ^{13}C spectra were reported in parts per million (ppm) using the solvent shifts. The melting point was determined on a Galen III (Cambridge Instruments) melting point apparatus (Leica, Vienna, Austria) and is uncorrected.

3.2. Synthesis of Compound **3**

1,2:5,6-Di-*O*-isopropylidene- α -D-glucufuranose (2.16 g, 8.3 mmol) was dissolved in pyridine (20 mL) and *p*-toluenesulfonyl chloride (2.6 g, 13.6 mmol) dissolved in anhydrous dichloromethane (20 mL) was added at ambient temperature. The resulting mixture was stirred 48 h at 60 °C. Afterwards, the organic solvents were removed, the residue was dissolved in dichloromethane (20 mL) and washed with saturated hydrogen carbonate solution (20 mL). The organic layer was separated and dried over Na_2SO_4 . Purification was done via column chromatography (petroleum ether/ethyl acetate = 15:1→10:1) to yield **3** as colourless solid (2.68 g, 78%). m.p. 121 °C. ^1H NMR (400 MHz, C_6D_6): δ 0.96 (s, 6H, $^i\text{Pr-CH}_3$), 1.10 (s, 3H, $^i\text{Pr-CH}_3$), 1.28 (s, 3H, $^i\text{Pr-CH}_3$), 1.82 (s, 3H, Tos- CH_3), 3.84 (dd, $^2J = 8.6$ Hz, $^3J = 6.3$ Hz, 1H, H-6b), 3.96 (dd, $^2J = 8.6$ Hz, $^3J = 4.7$ Hz, 1H, H-6a), 4.07–4.12 (m, 1H, H-5), 4.25 (dd, $^3J = 8.0$ Hz, $^3J = 2.8$ Hz, 1H, H-4), 4.90 (d, $^3J = 3.6$ Hz, 1H, H-2), 5.02 (d, $^3J = 2.8$ Hz, 1H, H-3), 5.66 (d, $^3J = 3.6$ Hz, 1H, H-1), 6.67 (d, $^3J = 8.2$ Hz, 2H, H-o), 7.76 (d, $^3J = 8.2$ Hz, 2H, H-m). ^{13}C NMR (101 MHz, C_6D_6): δ 21.1 (Tos- CH_3), 24.7, 25.0, 26.7 ($3 \times ^i\text{Pr-CH}_3$), 26.8 ($^i\text{Pr-CH}_3$), 67.4 (C-6), 72.3 (C-5), 80.4 (C-4), 82.7 (C-3), 84.1 (C-2), 105.6 (C-1), 109.1, 112.3 ($2 \times ^i\text{Pr-C}_{\text{quart}}$), 128.8 (C-m), 129.7 (C-o), 133.8 (C-i), 144.5 (C-p).

3.3. Data Collection and Refinement

Crystallographic data were collected with a Bruker-Nonius Apex-X8 CCD-diffractometer with monochromatic Mo- $K\alpha$ radiation ($\lambda = 0.71073 \text{ \AA}$) and a CCD detector. Preliminary data of the unit cell dimensions were obtained from the reflex positions of 36 frames, measured in three different directions of the reciprocal space. After completion of the data measurements the reflex intensities were corrected for Lorentz, polarization and absorption effects. The structure was solved by direct methods using SHELXS-97 and refined against F^2 on all data by full-matrix least-squares methods using SHELXL-97(2) [6,7]. All non-hydrogen atoms were refined anisotropically; all hydrogen atoms bonded to carbon atoms were placed on geometrically calculated positions and refined using riding models. Crystallographic data has been deposited with the Cambridge Crystallographic Data Centre, CCDC-855989. It can be retrieved free of charge through deposit@ccdc.cam.ac.uk or <http://www.ccdc.cam.ac.uk>.

4. Conclusions

The crystal and molecular structure of the title compound is reported. These data represent a crystallographically characterized example of tosylated carbohydrate building blocks.

References and Notes

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