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New class of quaternary ammonium salts, derivatives of methyl D-glucopyranosides[☆]

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Abstract—Reactions of two aromatic and two aliphatic amines with methyl 6-*O*-*p*-toluenesulfonyl-α-D-glucopyranoside or methyl 6-*O*-*p*-toluenesulfonyl-β-D-glucopyranoside were performed on a micro-scale. The synthesis and preparative isolation methods have been developed for quaternary *N*-(methyl 2,3,4-tri-*O*-acetyl-6-deoxy-α- and -β-D-glucopyranoside-6-yl)ammonium salts derived from three amines: trimethylamine, 2-methylpyridine, and pyridine. The reaction products were examined with ^{1}H, ^{13}C NMR spectroscopy. *N*-(Methyl 2,3,4-tri-*O*-acetyl-6-deoxy-β-D-glucopyranoside-6-yl)trimethylammonium tosylate was additionally analyzed with X-ray crystallography.
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1. Introduction

Quaternary ammonium salts (quats) constitute a huge group of organic compounds. N-Substituted salts of pyridine and related compounds constitute the most important and versatile investigated products of chemical syntheses.[1,2] Menschutkin[3] in 1890 reported first preparations of quaternary ammonium salts by the reaction of an alkyl halide with a tertiary amine. This reaction, named the Menschutkin reaction, is the most convenient method for synthesis of these compounds (QACs). In contrast to the large body of literature on the N-alkylated (arylated) salts of pyridine and related compounds, two dozen or so papers are found in the literature on the N-glycosylated analogues, only. Per-*O*-acetyl-glycopyranosyl halides (mostly bromides and chlorides), as well as methyl iodide, offer a possibility of

reaction with tertiary amine giving the appropriate quaternary salts with the new N–C$_{an}$ bond. Fischer and Raske[4] in 1910 first reported the synthesis of *N*-(tetra-*O*-acetyl-D-glucopyranosyl)pyridinium bromide, but its structure was elucidated only from the elemental analysis. Their work was continued by Karrer and co-workers,[5,6] and structures of the compounds were also insufficiently documented. Lemieux and Morgan in 1963 identified two anomers of *N*-(tetra-*O*-acetyl-D-glucopyranosyl)pyridinium bromide in the reaction mixture for which the structures were exhaustively documented,[7] and a simplified mechanism of their formation was proposed.[7,8] Every product of the reaction formed a conformational equilibrium mixture.

Lemieux discovered the reverse anomeric effect,[9] which prefers the equatorial orientation of an aglycone in molecules with C-1–N$^+$ bond. He studied an influence of the reactant concentration and the presence of phenol or tetra-*n*-butylammonium bromide or tetra-*n*-butylammonium perchlorate on the mutual concentration of the α and β anomer of *N*-(tetra-*O*-acetyl-D-glucopyranosyl)pyridinium bromide in the post-reaction mixture. The above-mentioned influence of phenol addition was

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reported earlier by Fischer and Raske.[4] Sinnott and co-workers[10–13] studied, inter alia, enzymatic hydrolysis of the O-deacetylated analogous salt. The authors used the Lemieux[14] procedure for O-deacetylation of *N*-(per-*O*-acetyl-glycopyranosyl)pyridinium salts. Paulsen et al.[15] and Finch and Nagpurkar[16] studied conformational equilibria of *N*-(per-*O*-acetyl-aldopyranosyl)pyridinium and -imidazolium salts with ^{1}H NMR spectroscopy, and the reverse anomeric effect was discussed.

However, Abel et al.[17] reported the effectiveness of modified surfaces for antibacterial activity against a series of seven Gram-positive and Gram-negative bacteria. In that paper authors demonstrated that broad antibacterial activity can be imported to carbohydrate surfaces through the covalent attachment of cationic agents with lipophilic adjuncts. First, they functionalized primary hydroxyl group with *p*-toluenesulfonyl chloride.

The purpose of the present contribution is to synthesize and determine the structure of some quaternary ammonium salts. Another purpose is to study their biological activities in order to select antibacterial compounds that are not harmful to humans and the environment.

2. Results and discussion

In recent years our research group has worked on the formation of quaternary *N*-(D-glycopyranosyl)ammonium salts.[18–21] We thought that QACs with a sugar moiety could be very interesting and promising kind of compounds. We determined their chemical and crystal structures. Some of them exhibit biological activity.

The synthesis of *N*-(methyl 2,3,4-tri-*O*-acetyl-6-deoxy-α-D-glucopyranoside-6-yl)ammonium tosylate and *N*-(methyl 2,3,4-tri-*O*-acetyl-6-deoxy-β-D-glucopyranoside-6-yl)-ammonium tosylate started from commercially available methyl α-D-glucopyranoside and methyl β-D-glucopyranoside, respectively. The selective esterification of the primary hydroxyl groups of methyl D-glucopyranoside with *p*-toluenesulfonyl chloride in pyridine has been described.[22] Reaction methyl 6-*O*-tosyl-D-glucopyranosides with trimethylamine, 2-methylpyridine or pyridine gave quaternary salts, demonstrating that the amines were effective nucleophilic reagents. All new synthesized *N*-(methyl 2,3,4-tri-*O*-acetyl-6-deoxy-D-glucopyranoside-6-yl)ammonium-tosylates are water soluble. The structures were determined by 2D ^{1}H NMR (400 MHz). The chemical shifts and coupling constants for *N*-(methyl 2,3,4-tri-*O*-acetyl-6-deoxy-D-glucopyranoside-6-yl)-ammonium tosylate protons are listed in Table 1.

Reaction of methyl α-D-glucopyranoside (**1a**) with *p*-toluenesulfonyl chloride in pyridine (Scheme 1) for 24 h at rt afforded, after conventional processing, methyl 6-*O*-*p*-toluenesulfonyl-α-D-glucopyranoside (**2a**) in 45% yield; $[\alpha]_D^{20}$ 73.1 (EtOH). In the same procedure methyl

Table 1. Chemical shifts and coupling constants (Hz) for ammonium salts in D_2O solution

	H-1	H-2	H-3	H-4	H-5	H-6a	H-6b	−OCH₃	PhCH₃	3×OAc	Ph	Amineᵃ	CH₃–Py
3a	δ 5.13 (d) $J_{1,2}$ 3.6	δ 5.25 (t) $J_{2,3}$ 9.6	δ 5.09 (t, br)	δ 5.04 (t) $J_{4,5}$ 9.8	δ 4.62 (t) $J_{5,6a}$ 9.4	δ 3.72 (dd) $J_{6a,6b}$ 8.4	δ 3.48 (dd)	δ 3.57 (s)	δ 2.42 (s)	δ 2.14–2.09 (3×s)	δ 7.73–7.39 (2d)	δ 3.25 (s)	
4a	δ 5.04 (d) $J_{1,2}$ 3.6	δ 5.45 (t) $J_{2,3}$ 9.6	δ 5.11 (m)	δ 5.08 (t, br)	δ 4.43 (ddd) $J_{5,6a}$ 3.0, $J_{5,6b}$ 7.2	δ 4.98 (dd) $J_{6a,6b}$ 11.6	δ 4.81 (dd)	δ 3.03 (s)	δ 2.42 (s)	δ 2.21–2.10 (3×s)	δ 7.73–7.38 (2d)	δ 8.92–8.13 (m)	
5a	δ 5.01 (d) $J_{1,2}$ 3.6	δ 5.44 (t) $J_{2,3}$ 9.8	δ 5.24 (t) $J_{3,4}$ 9.6	δ 5.16 (t) $J_{4,5}$ 10.2	δ 4.36 (ddd) $J_{5,6a}$ 2.4, $J_{5,6b}$ 7.6	δ 4.89 (dd) $J_{6a,6b}$ 11.6	δ 4.78 (dd)	δ 2.92 (s)	δ 2.42 (s)	δ 2.21–2.09 (3×s)	δ 7.72–7.38 (2d)	δ 8.81–7.92 (m)	δ 2.91 (s)
3b	δ 4.77 (d) $J_{1,2}$ 8.0	δ 5.28 (t) $J_{2,3}$ 9.4	δ 4.95 (t) $J_{3,4}$ 9.2	δ 4.93 (t) $J_{4,5}$ 8.0	δ 4.39 (t) $J_{5,6a}$ 9.2	δ 3.62 (dd) $J_{6a,6b}$ 10.0	δ 3.44 (dd)	δ 3.47 (s)	δ 2.33 (s)	δ 2.05–1.99 (3×s)	δ 7.64–7.30 (2d)	δ 3.17 (s)	
4b	δ 4.61 (d) $J_{1,2}$ 8.0	δ 5.02 (m)	δ 5.38 (t) $J_{3,4}$ 9.6	δ 5.11 (t) $J_{4,5}$ 9.6	δ 4.29 (ddd) $J_{5,6a}$ 2.8, $J_{5,6b}$ 6.6	δ 4.98 (dd, br)	δ 4.79 (dd)	δ 3.32 (s)	δ 2.42 (s)	δ 2.21–2.02 (3×s)	δ 7.72–7.38 (2d)	δ 8.89–8.13 (m)	
5b	δ 4.55 (d) $J_{1,2}$ 8.4	δ 5.03 (q) $J_{4,5}$ 8.4	δ 5.37 (t) $J_{3,4}$ 9.6	δ 5.23 (t) $J_{4,5}$ 9.6	δ 4.28 (ddd) $J_{5,6a}$ 2.4, $J_{5,6b}$ 7.6	δ 4.91 (dd) $J_{6a,6b}$ 12.4	δ 4.76 (dd)	δ 3.28 (s)	δ 2.41 (s)	δ 2.21–2.10 (3×s)	δ 7.71–7.37 (2d)	δ 8.76–7.91 (m)	δ 2.90 (s)

ᵃTrimethylamine (**3a** and **3b**), pyridine (**4a** and **4b**), 2-methylpyridine (**5a** and **5b**).
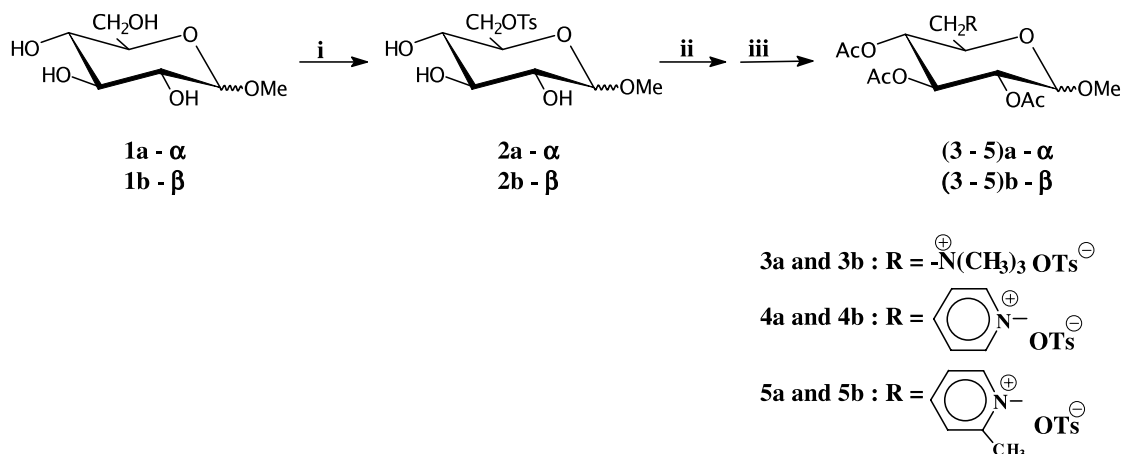
Scheme 1. Reagents and conditions: (i) TsCl, pyridine; (ii) Me₃N in 33% EtOH (compounds **3a** and **3b**), pyridine (compounds **4a** and **4b**), 2-methylpyridine (compounds **5a** and **5b**); (iii) Ac₂O, pyridine. Ts = *p*-toluenesulfonyl.

6-*O*-*p*-toluenesulfonyl-β-D-glucopyranoside (**2b**) was obtained. Both of these esters (**2a** and **2b**) are stable for several months if kept at 0 °C. The next steps were the quaternization reactions of **2a** and **2b**.

Reaction of **2a** with 33% ethanolic solution of tri-methylamine at 70 °C for 96 h produced, after O-acetylation (O-Ac), *N*-(methyl 2,3,4-tri-*O*-acetyl-6-deoxy-α-D-glucopyranoside-6-yl)trimethylammonium tosylate (**3a**) in 19% yield. The same reaction in ultrasonic conditions at rt for 20 h gave **3a** in 42% yield; $[\alpha]_D^{20}$ 92.46 (*c* 0.3, H₂O). Under similar conditions (ultrasonic conditions, rt, 20 h) *N*-(methyl 2,3,4-tri-*O*-acetyl-6-deoxy-β-D-glucopyrano-side-6-yl)trimethylammonium tosylate (**3b**) in 33% yield; mp 210–220 °C; $[\alpha]_D^{20}$ −2.28 (*c* 0.175, H₂O) was obtained. Their identities were confirmed by the ¹H NMR and ¹³C NMR spectra evidence and X-ray diffraction for compound **3b** (Tables 2–5; Figs. 1 and 2).

In the ¹H NMR spectrum for compound **3a**, the signal for the anomeric proton is a doublet at $\delta = 5.13$ ppm with coupling constant of $J_{1,2} = 3.6$ Hz, which is characteristic for H_e–H_a. The chemical shift for H-2 is a triplet at $\delta = 5.25$ ppm with a coupling constant of $J_{2,3} = 9.6$ Hz. Signals of protons for H-3 and H-4 are at $\delta = 5.09$ ppm and $\delta = 5.04$ ppm, respectively. Coupling constants of $J_{2,3}$, $J_{3,4}$ and $J_{4,5}$ at about 9.5 Hz are characteristic for H_a–H_a system. The structure of the sugar protons and values of coupling constants for H-1, H-2, H-4 allows one to assert that the pyranose ring for compound **3a** is in the $^4C_1$ conformation.

In the spectrum of **3b** compound, H-1 appears as a doublet with a $J_{1,2} = 8.0$ Hz (H_a–H_a). We found coupling constants $J_{2,3}$, $J_{3,4}$ and $J_{4,5}$ to be 9.4, 9.2, 8.0 Hz, respectively. The pyranose ring for compound **3b** is thus in the $^4C_1$ conformation. The chemical shifts are given in Table 1, the sequence of protons of compound **3a** (H-2, H-1, H-3, H-4, H-5, H-6a, H-6b) are different from compound **3b** (H-2, H-3, H-4, H-1, H-5, H-6a, H-6b).

Table 2. Crystal data and structure refinement for *N*-(methyl 2,3,4-tri-*O*-acetyl-6-deoxy-β-D-glucopyranoside-6-yl)trimethylammonium tosylate (**3b**)

Empirical formula	C₂₃H₃₅NO₁₁S
Formula weight	533.58
Temperature (K)	200(2)
Wavelength (Å)	0.71073
Crystal system, space group	Orthorhombic, $P2_12_12_1$
Unit cell dimensions	
a (Å)	8.859(2)
b (Å)	9.120(2)
c (Å)	34.465(7)
Volume (Å³)	2784.6(10)
Z	4
Calculated density (Mg m⁻³)	1.273
Absorption coefficient (mm⁻¹)	0.172
F(000)	1136
Crystal size (mm)	0.40×0.30×0.30
Theta range for data collection (°)	$1.18 < \theta < 26.00$
Index ranges, h, k, l	$-6 \to 10$, $-11 \to 6$, $-28 \to 42$
Reflections collected/unique	3205/3177
Reflections [$I > 2\sigma(I)$]	1655
Completeness to $\theta = 27.55$	0.993
Refinement method	Full-matrix least-squares refinement based on F^2
Data/restraints/parameters	3177/0/334
Goodness-of-fit on F^2	0.977
Final *R* indices [$I > 2\sigma(I)$]	R1 = 0.066, wR2 = 0.1905
R indices (all data)	R1 = 0.1874, wR2 = 0.2751
Absolute structure parameter	0.0(4)
Largest difference peak and hole (e Å⁻³)	0.407/−0.438

In the crystal asymmetric unit of *N*-(methyl 2,3,4-tri-*O*-acetyl-6-deoxy-β-D-glucopyranoside-6-yl)trimethyl-ammonium tosylate (**3b**) contains one ammonium cation and one tosylate anion (see Fig. 1). The intermolecular interactions between these ion pairs are shown in the drawing of the elemental cell (Fig. 2). Several C–H···O short contacts are formed. Most of them can be regarded as charge-assisted hydrogen bonds between C–H donors from positively charged trimethylammonium groups and

Table 3. Atomic coordinates and equivalent isotropic displacement parameters (Å^2) for *N*-(methyl 2,3,4-tri-*O*-acetyl-6-deoxy-β-D-glucopyranoside-6-yl)trimethylammonium tosylate[a]

	x	y	z	U_{eq}
S-1	0.7876(3)	0.5690(3)	0.06579(7)	0.0483(6)
O-20	0.6666(7)	0.5766(8)	0.03830(19)	0.0560(18)
O-21	0.9270(7)	0.5220(9)	0.0482(2)	0.062(2)
O-22	0.8017(12)	0.7004(9)	0.0875(3)	0.095(3)
C-50	0.6023(16)	0.0886(18)	0.1772(4)	0.096(5)
C-51	0.6496(11)	0.2140(16)	0.1498(3)	0.065(3)
C-52	0.652(2)	0.181(2)	0.1099(5)	0.133(8)
C-53	0.692(2)	0.2919(18)	0.0856(4)	0.125(7)
C-54	0.7348(10)	0.4264(13)	0.0986(3)	0.055(3)
C-55	0.7364(13)	0.4537(13)	0.1370(3)	0.065(3)
C-56	0.6985(17)	0.3428(16)	0.1619(4)	0.090(4)
O-1	0.2700(7)	0.4236(6)	0.08232(16)	0.0422(14)
C-1	0.1672(11)	0.3058(9)	0.0903(3)	0.045(2)
C-2	0.1954(10)	0.2547(9)	0.1312(2)	0.0391(19)
C-3	0.1856(10)	0.3760(9)	0.1596(2)	0.0384(19)
C-4	0.2822(10)	0.5047(9)	0.1476(2)	0.0351(18)
C-6	0.3473(9)	0.6684(9)	0.0924(2)	0.0340(18)
C-7	0.153(2)	0.2227(14)	0.0270(3)	0.098(5)
O-7	0.1980(9)	0.1937(6)	0.06480(19)	0.0590(18)
C-8	0.1217(13)	0.0085(10)	0.1469(3)	0.052(3)
O-8	0.0791(7)	0.1481(6)	0.14085(19)	0.0450(16)
C-81	−0.0125(14)	−0.0849(12)	0.1567(3)	0.069(3)
O-81	0.2493(9)	−0.0332(7)	0.1432(2)	0.065(2)
C-9	0.1472(12)	0.3197(11)	0.2273(3)	0.055(3)
O-9	0.2375(6)	0.3145(7)	0.19625(16)	0.0440(15)
C-91	0.2090(14)	0.2268(13)	0.2592(3)	0.065(3)
O-91	0.0347(10)	0.3905(12)	0.2286(2)	0.098(3)
C-10	0.3534(13)	0.6720(16)	0.1978(3)	0.077(4)
O-10	0.2507(6)	0.6246(6)	0.17413(17)	0.0430(15)
O-11	0.4617(18)	0.582(2)	0.2076(5)	0.086(7)
O-11	0.495(2)	0.671(2)	0.1856(6)	0.070(8)
C-12	0.3078(15)	0.7876(12)	0.2237(3)	0.071(3)
N-1	0.3078(8)	0.7431(8)	0.0551(2)	0.0385(16)
C-21	0.3098(11)	0.6358(10)	0.0215(2)	0.045(2)
C-22	0.1565(9)	0.8162(11)	0.0562(3)	0.048(2)
C-23	0.4252(11)	0.8601(10)	0.0478(3)	0.051(3)

[a] U_{eq} is defined as one-third of the trace of the orthogonalized U_{ij} tensor.

Table 4. Selected bond lengths (Å) for *N*-(methyl 2,3,4-tri-*O*-acetyl-6-deoxy-β-D-glucopyranoside-6-yl)trimethylammonium tosylate

	Bond length
O-1–C-5	1.412(9)
O-1–C-1	1.435(10)
C-1–O-7	1.375(11)
C-1–C-2	1.504(12)
C-2–O-8	1.455(10)
C-2–C-3	1.479(12)
C-3–O-9	1.458(9)
C-3–C-4	1.509(12)
C-4–O-10	1.452(10)
C-4–C-5	1.521(11)
C-5–C-6	1.507(11)
C-6–N-1	1.496(10)
C-7–O-7	1.390(13)
C-8–O-81	1.200(12)
C-8–O-8	1.344(11)
C-8–C-81	1.502(15)
C-9–O-91	1.188(12)
C-9–O-9	1.337(11)
C-9–C-91	1.492(14)
C-10–O-11	1.320(2)
C-10–O-11	1.307(17)
C-10–O-10	1.297(12)
C-10–C-12	1.439(15)
N-1–C-22	1.498(11)
N-1–C-21	1.515(11)
N-1–C-23	1.511(11)
S-1–O-22	1.417(8)
S-1–O-20	1.433(7)
S-1–O-21	1.442(7)

negatively charged O-atoms from the tosylate anion. These interactions are relatively strong with donor–acceptor distances of about 3.3 Å. Other interactions are weaker and probably play a less important role.

The reaction of compound **2** with triethylamine did not give the expected quaternary ammonium salt. Evidently, the tertiary aliphatic amine with ethyl substituents enlarges the steric hindrance so much that the expected salts cannot be formed even in trace amounts.

Secondly, we tried to synthesize quaternary ammonium salts with aromatic amines. The reactions of the α and β anomer of methyl 6-*O*-tosyl-D-glucopyranoside with pyridine and 2-methylpyridine gave four new quaternary ammonium salts (**4a** and **4b**, **5a** and **5b**, Scheme 1). Reaction of **2a** with pyridine at rt (6 days) and after that at 70 °C for next 6 days gave *N*-(methyl 2,3,4-tri-*O*-acetyl-6-deoxy-α-D-glucopyranoside-6-yl)pyridinium tosylate (**4a**) in 35% yield; $[\alpha]_D^{20}$ 11.74 (*c* 0.23, H$_2$O). Methyl 6-*O*-tosyl-β-D-glucopyranoside (**2b**) in reaction

with pyridine at 70 °C for 3 days, after O-Ac produced *N*-(methyl 2,3,4-tri-*O*-acetyl-6-deoxy-β-D-glucopyranoside-6-yl)pyridinium tosylate (**4b**) in 62.5% yield; mp 163 °C; $[\alpha]_D^{20}$ −15.13 (*c* 0.37, H$_2$O). The reaction of **2b** with pyridine first at rt for 6 weeks, then 3 days at 70 °C and after O-Ac, gave the same product in 73.5% yield.

Converting of **2a** to the appropriate *N*-(methyl 2,3,4-tri-*O*-acetyl-6-deoxy-α-D-glucopyranoside-6-yl)-2-methylpyridinium tosylate (**5a**) was successful in 48% yield; $[\alpha]_D^{20}$ 52.38 (*c* 0.21, H$_2$O) after 11 days at 70 °C and after O-Ac. *N*-(Methyl 2,3,4-tri-*O*-acetyl-6-deoxy-β-D-glucopyranoside-6-yl)-2-methylpyridinium tosylate (**5b**) was produced in reaction of **2b** with the 2-methylpyridine at rt for 6 weeks, first, and next at 70 °C for 16 days and after O-Ac; $[\alpha]_D^{20}$ −22.55 (*c* 0.51, H$_2$O). The yields of these syntheses were higher for the β anomer than for methyl α-D-glucopyranoside. In that case we also tested a number of reaction conditions, but the best results we obtained were at higher temperature (70 °C) and when the reaction mixture was kept in a screw-capped ampoule.

Apart for the sugar-proton signals in the ^{1}H NMR spectra (compounds **4a**, **4b**, **5a** and **5b**, Table 1) proton signals also exist that correspond to the pyridinium (Py) ring (**4a** and **4b**) or the 2-methylpyridinium ring (**5a** and **5b**). The coupling constants $J_{3,4} =\sim 9.0$ Hz and $J_{4,5} =\sim 9.0$ Hz taken from their ^{1}H NMR spectra verify the $^4C_1$ conformation of compounds **4a**, **4b**, **5a** and **5b**. The

Table 5. Selected torsion angles (°) for *N*-(methyl 2,3,4-tri-*O*-acetyl-6-deoxy-β-D-glucopyranoside-6-yl)trimethylammonium tosylate
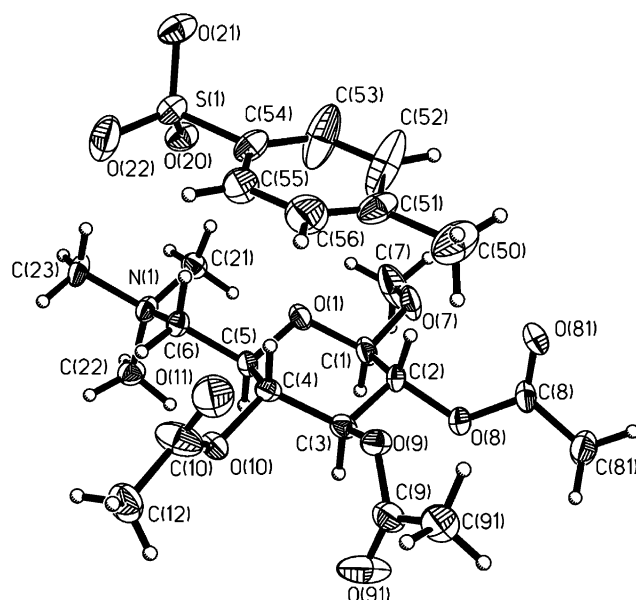
	Torsion angles
C-5–O-1–C-1–O-7	177.9(7)
C-5–O-1–C-1–C-2	−63.8(9)
O-7–C-1–C-2–O-8	−69.7(9)
O-1–C-1–C-2–O-8	173.0(6)
O-7–C-1–C-2–C-3	171.8(7)
O-1–C-1–C-2–C-3	54.5(9)
O-8–C-2–C-3–O-9	70.0(8)
C-1–C-2–C-3–O-9	−171.6(7)
O-8–C-2–C-3–C-4	−169.5(6)
C-1–C-2–C-3–C-4	−51.1(10)
O-9–C-3–C-4–O-10	−70.0(8)
C-2–C-3–C-4–O-10	172.7(6)
O-9–C-3–C-4–C-5	169.3(6)
C-2–C-3–C-4–C-5	51.9(9)
C-1–O-1–C-5–C-6	−174.2(6)
C-1–O-1–C-5–C-4	66.4(9)
O-10–C-4–C-5–O-1	−176.9(6)
C-3–C-4–C-5–O-1	−58.1(8)
O-10–C-4–C-5–C-6	65.3(9)
C-3–C-4–C-5–C-6	−175.9(7)
O-1–C-5–C-6–N-1	73.5(9)
C-4–C-5–C-6–N-1	−168.7(7)
O-1–C-1–O-7–C-7	−72.5(12)
C-2–C-1–O-7–C-7	170.3(11)
O-81–C-8–O-8–C-2	−3.0(15)
C-81–C-8–O-8–C-2	179.6(7)
C-3–C-2–O-8–C-8	−124.7(9)
C-1–C-2–O-8–C-8	114.0(9)
O-91–C-9–O-9–C-3	−11.4(15)
C-91–C-9–O-9–C-3	169.3(8)
C-2–C-3–O-9–C-9	−123.2(8)
C-4–C-3–O-9–C-9	115.8(8)
O-11–C-10–O-10–C-4	−24.4(17)
O-11–C-10–O-10–C-4	34.8(19)
C-12–C-10–O-10–C-4	−177.8(9)
C-3–C-4–O-10–C-10	113.7(10)
C-5–C-4–O-10–C-10	−126.6(10)
C-5–C-6–N-1–C-22	60.5(9)
C-5–C-6–N-1–C-23	179.5(7)
C-5–C-6–N-1–C-21	−61.6(9)
O-22–S-1–C-54–C-55	−8.8(11)
O-20–S-1–C-54–C-55	−128.3(9)
O-21–S-1–C-54–C-55	112.9(9)
O-22–S-1–C-54–C-53	170.7(13)
O-20–S-1–C-54–C-53	51.2(13)
O-21–S-1–C-54–C-53	−67.6(13)

Figure 1. The X-ray structure of *N*-(methyl 2,3,4-tri-*O*-acetyl-6-deoxy-β-D-glucopyranoside-6-yl)trimethylammonium tosylate.

on Kieselgel 60 F_{254} Silica Gel plates (E. Merck, 0.20 mm thickness). The spots were detected by spraying with 5% ethanolic H_2SO_4 and charring. A Mercury-400BB (400 MHz) spectrometer with D_2O as a solvent and acetone as an external standard, and 2D COSY, HSQC technique at temperature of 25 °C was used.

3.2. X-Ray crystallography

X-Ray measurements were carried out on a KUMA KM-4 four circle diffractometer. The structures were solved by direct methods with the SHELXS program[23] and refined employing full-matrix least-squares method implemented in the SHELXL program.[24] Anisotropic displacement coefficients were applied to all non-hydrogen atoms. The atomic scattering factors were taken from the International Tables for X-ray Crystallography (1993). Molecular illustrations were drawn using the ORTEP program.[25] Optical rotations were measured with a JASCO J-20 polarimeter. Elemental analyses were made with a Carlo Erba apparatus. Positive-ion mode MALDITOF mass spectra were obtained using a Bruker Biflex III spectrometer with α-cyano-4-hydroxycinnamic matrix.

3.3. *N*-(Methyl 2,3,4-tri-*O*-acetyl-6-deoxy-α-D-glucopyranoside-6-yl)trimethylammonium tosylate (3a)

Methyl 6-*O*-*p*-toluenesulfonyl-α-D-glucopyranoside (2a) (40.4 mg, 0.117 mmol) was dissolved in 33% ethanolic solution of Me_3N (0.2 mL). The reaction mixture was kept under ultrasonic conditions at rt. After 20 h under
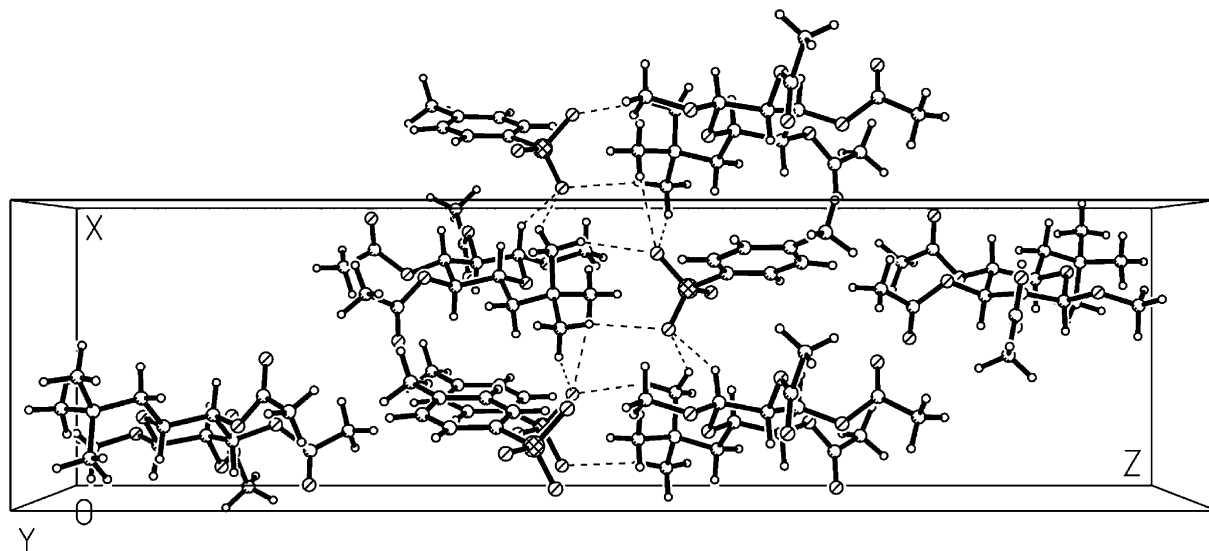
sequence of the proton positions for compounds **4a** and **5a** are the same (H-2, H-3, H-4, H-1, H-6a, H-6b, H-5), and the sequence of proton positions for compounds **4b** and **5b** are similar (H-3, H-4, H-2, H-6a, H-6b, H-1, H-5).

3. Experimental

3.1. General methods

Commercial methyl α-D-glucopyranoside and methyl β-D-glucopyranoside (Fluka) were used. All reactions were monitored by thin-layer chromatography (TLC)

Figure 2. Packing of *N*-(methyl 2,3,4-tri-*O*-acetyl-6-deoxy-β-D-glucopyranoside-6-yl)trimethylammonium tosylate with C–H···O hydrogen bonds.

these conditions and 8 days at rt, the solvent was evaporated to dryness under reduced pressure, and the crude product was dissolved in pyridine (2.5 mL) and Ac$_2$O (2.5 mL) was added. Next, the solution was evaporated to dryness. The residue was dissolved in H$_2$O (10 mL), washed three times with CHCl$_3$. The aqueous layer was evaporated and dried over P$_2$O$_5$ to give an oil of *N*-(methyl 2,3,4-tri-*O*-acetyl-6-deoxy-α-D-glucopyranoside-6-yl)trimethylammonium tosylate (20.1 mg, 42%); $[\alpha]_D^{20}$ 92.46 (*c* 0.3, H$_2$O); ^{1}H NMR (D$_2$O): δ 7.73–7.39 (2d, each 2H, Ph), 5.45 (t, 1H, H-2, $J_{2,3}$ 9.6 Hz), 5.13 (d, 1H, H-1, $J_{1,2}$ 3.6 Hz), 5.09 (t, br, 1H, H-3), 5.04 (t, 1H, H-4, $J_{4,5}$ 9.8 Hz), 4.62 (t, 1H, H-5, $J_{5,6a}$ 9.4 Hz), 3.73 (dd, 1H, H-6a, $J_{6a,6b}$ 8.4 Hz), 3.57 (s, 3H, –OCH$_3$), 3.48 (dd, 1H, H-6b), 3.25 (s, 9H, 3×CH$_3$ of N(CH$_3$)$_3$), 2.42 (s, 3H, PhCH$_3$), 2.14–2.09 (9H, 3×OAc); ^{13}C NMR (H$_2$O): δ 173.34–172.69 (3C, 3×OOCCH$_3$), 142.67–139.82 (2C, Ph), 129.67–125.63 (2C, Ph), 97.32 (C-1), 70.4 (C-2), 69.91 (C-3), 69.88 (C-4), 66.35 (C-6), 64.70 (C-5), 57.82 (–OCH$_3$), 54.51 (9C, N(CH$_3$)$_3$), 20.71 (PhCH$_3$), 20.34–20.20 (3C, COOCH$_3$); R_f = 0 (3:1 CHCl$_3$–MeOH). Anal. Calcd for C$_{23}$H$_{35}$NO$_{11}$S (533.595): C, 51.77; H, 6.61; N, 2.63; S, 6.01; O, 32.98. Found: C, 51.82; H, 6.65; N, 2.70; S, 6.05. MALDITOF-MS (CCA): *m/z* 362.2 ([M−OTs]$^+$).

3.4. *N*-(Methyl 2,3,4-tri-*O*-acetyl-6-deoxy-α-D-glucopyranoside-6-yl)pyridinium tosylate (4a)

Methyl 6-*O*-*p*-toluenesulfonyl-α-D-glucopyranoside (95.7 mg, 0.275 mmol) was dissolved in dry pyridine (2.2 mL), and phenol (catalytic amount) was added to the reaction mixture. That solution was kept in a screw-capped ampoule at rt for 6 days and at 70 °C for the next 6 days. After 12 days the solvent was evaporated, and the residue was dissolved in pyridine (5 mL) and Ac$_2$O (5 mL) was added. Next, the solution was evaporated,

dissolved in H$_2$O extracted with CHCl$_3$. The aqueous layer was evaporated and the residue was dried over P$_2$O$_5$ to give the title compound as an oil (16.7 mg, 35%); $[\alpha]_D^{20}$ 11.74 (*c* 0.23, H$_2$O); ^{1}H NMR (D$_2$O): δ 8.92–8.13 (m, 5H, Py), δ 7.72–7.38 (2d, each 2H, Ph), 5.45 (t, 1H, H-2, $J_{2,3}$ 9.6 Hz), 5.11 (m, 1H, H-3), 5.08 (t, br, 1H, H-4), 5.04 (d, 1H, H-1, $J_{1,2}$ 3.6 Hz), 4.98 (dd, 1H, H-6a, $J_{6a,6b}$ 11.6 Hz), 4.81 (dd, 1H, H-6b), 4.43 (ddd, 1H, H-5, $J_{5,6a}$ 3.0 Hz, $J_{5,6b}$ 7.2 Hz), 3.03 (s, 3H, –OCH$_3$), 2.42 (s, 3H, PhCH$_3$), 2.21–2.10 (9H, 3×OAc); ^{13}C NMR (H$_2$O): δ 173.39–172.98 (2C, 2×OOCCH$_3$), 147.04–125.60 (6C, Ph), 96.49 (C-1), 70.68 (C-2), 70.24 (C-3), 69.80 (C-4), 67.67 (C-5), 61.08 (C-6), 55.08 (OCH$_3$), 20.69 (PhCH$_3$), 20.39–20.18 (3C, COOCH$_3$); R_f = 0 (3:1 CHCl$_3$–MeOH). Anal. Calcd for C$_{25}$H$_{31}$NO$_{11}$S (553.585): C, 54.24; H, 5.65; N, 2.53; S, 5.79; O, 31.78. Found: C, 54.05; H, 5.80; N, 2.75; S, 5.85. MALDITOF-MS (CCA): *m/z* 382.1 ([M−OTs]$^+$).

3.5. *N*-(Methyl 2,3,4-tri-*O*-acetyl-6-deoxy-α-D-glucopyranoside-6-yl)-2-methylpyridinium tosylate (5a)

Methyl 6-*O*-*p*-toluenesulfonyl-α-D-glucopyranoside (115.6 mg, 0.330 mmol) was dissolved in dry 2-methylpyridine (1.08 mL). That solution was kept in a screw-capped ampoule at 70 °C. After 11 days the solvent was evaporated. That oil was dissolved in the mixture of pyridine (6 mL) and Ac$_2$O (6 mL). After 24 h, at rt the solvent were evaporated. The residue was dissolved in H$_2$O and extracted with CHCl$_3$. The aqueous layer was evaporated, and the residue was dried over P$_2$O$_5$ to give the title compound as an oil (90.8 mg, 48%); $[\alpha]_D^{20}$ 52.38 (*c* 0.21, H$_2$O); ^{1}H NMR (D$_2$O): δ 8.81–7.92 (m, 4H, Py), δ 7.72–7.38 (2d, each 2H, Ph), 5.44 (t, 1H, H-2, $J_{2,3}$ 9.8 Hz), 5.24 (t, 1H, H-3, $J_{3,4}$ 9.6 Hz), 5.16 (t, 1H, H-4, $J_{4,5}$ 10.2 Hz), 5.01 (d, 1H, H-1, $J_{1,2}$ 3.6 Hz), 4.89 (dd, 1H,

H-6a, $J_{6a,6b}$ 11.6 Hz), 4.78 (dd, 1H, H-6b), 4.36 (ddd, 1H, H-5, $J_{5,6a}$ 2.4 Hz, $J_{5,6b}$ 7.6 Hz), 2.92 (s, 3H, –OCH$_3$), 2.91 (s, 3H, PhCH$_3$-picoline), 2.42 (s, 3H, PhCH$_3$), 2.21–2.09 (9H, 3×OAc); ^{13}C NMR (H$_2$O): δ 173.40–172.72 (3C, 3×OOCCH$_3$), 146.48–125.60 (9C, Ph), 96.37 (C-1), 70.74 (C-2), 70.31 (C-3), 70.22 (C-4), 68.06 (C-5), 57.15 (C-6), 54.91 (–OCH$_3$), 20.69 (PhCH$_3$), 20.34–20.19 (3C, COOCH$_3$), 17.03 (PhCH$_3$); R_f = 0 (3:1 CHCl$_3$–MeOH). Anal. Calcd for C$_{26}$H$_{33}$NO$_{11}$S (567.612): C, 55.02; H, 5.86; N, 2.47; S, 5.65; O, 31.00. Found: C, 55.54; H, 5.82; N, 2.72; S, 5.71. MALDITOF-MS (CCA): *m/z* 396.1 ([M−OTs]$^+$).

3.6. *N*-(Methyl 2,3,4-tri-*O*-acetyl-6-deoxy-β-D-glucopyranoside-6-yl)trimethylammonium tosylate (3b)

Solution of trimethylamine (33%) in EtOH (2.3 mL) was added to methyl 6-*O*-*p*-toluenesulfonyl-β-D-glucopyranoside (104.2 mg, 0.300 mmol). The reaction mixture was kept in a screw-capped ampoule under ultrasonic conditions at rt for 20 h and then for 8 days at rt. The reaction mixture was evaporated to the dryness. The oily residue was dissolved in a mixture of pyridine (6.5 mL) and Ac$_2$O (6.5 mL). *N*-(Methyl 2,3,4-tri-*O*-acetyl-6-deoxy-β-D-glucopyranoside-6-yl)trimethylammonium tosylate crystallized from the solution of pyridine and Ac$_2$O (52.6 mg, 33%); mp 210–220 °C; $[\alpha]_D^{20}$ −2.28 (*c* 0.175, H$_2$O); ^{1}H NMR (D$_2$O): δ 7.64–7.30 (2d, each 2H, Ph), 5.28 (t, 1H, H-2, $J_{2,3}$ 9.4 Hz), 4.95 (t, 1H, H-3, $J_{3,4}$ 9.2 Hz), 4.93 (t, 1H, H-4, $J_{4,5}$ 8 Hz), 4.77 (d, 1H, H-1, $J_{1,2}$ 8 Hz), 4.39 (t, 1H, H-5, $J_{5,6a}$ 9.2 Hz;), 3.62 (dd, 1H, H-6a, $J_{6a,6b}$ 10 Hz), 3.47 (s, 3H, –OCH$_3$), 3.44 (dd, 1H, H-6b), 3.17 (s, 9H, N(CH$_3$)$_3$), 2.33 (s, 3H, PhCH$_3$), 2.05–1.99 (9H, 3×OAc); ^{13}C NMR (H$_2$O): δ 173.24–172.66 (3C, 3×OOCCH$_3$), 142.68–139.77 (2C, Ph), 129.68–125.62 (2C, Ph), 100.69 (C-1), 73.08 (C-2), 71.06 (C-4), 69.66 (C-3), 68.20 (C-5), 66.12 (C-6), 57.68 (OCH$_3$), 54.46 (9C, N(CH$_3$)$_3$), 20.70 (PhCH$_3$), 20.32–20.23 (3C, COOCH$_3$); R_f = 0 (3:1 CHCl$_3$–MeOH). Anal. Calcd for C$_{23}$H$_{35}$NO$_{11}$S (533.595): C, 51.77; H, 6.61; N, 2.63; S, 6.01; O, 32.98. Found: C, 51.65; H, 6.64; N, 2.69; S, 6.11. MALDITOF-MS (CCA): *m/z* 362.2 ([M−OTs]$^+$).

3.7. *N*-(Methyl 2,3,4-tri-*O*-acetyl-6-deoxy-β-D-glucopyranoside-6-yl)pyridinium tosylate (4b)

Methyl 6-*O*-*p*-toluenesulfonyl-β-D-glucopyranoside (72.8 mg, 0.210 mmol) and a catalytic amount of phenol were placed in a screw-capped ampoule. The reactant and catalyst were dissolved in dry pyridine (0.55 mL). The solution was kept in a screw-capped ampoule and heated at 70 °C for 3 days. After that time the solution was evaporated to dryness, and the residue was dissolved in a mixture of pyridine (3 mL) and Ac$_2$O (3 mL). After 24 h the solution was evaporated to dryness. The residue was dissolved in H$_2$O, extracted with CHCl$_3$ and

concentrated to an oil. The oil crystallized from AcOEt to give the title compound; (72.4 mg, 62.5%); mp 163 °C, $[\alpha]_D^{20}$ −15.13 (*c* 0.37, H$_2$O); ^{1}H NMR (D$_2$O): δ 8.89–8.13 (m, 5H, Py), 7.72–7.38 (2d, each 2H, Ph), 5.38 (t, 1H, H-3, $J_{3,4}$ 9.6 Hz), 5.11 (t, 1H, H-4, $J_{4,5}$ 9.6 Hz), 5.02 (m, 1H, H-2), 4.98 (dd, br, 1H, H-6a), 4.79 (dd, 1H, H-6b), 4.61 (d, 1H, H-1, $J_{1,2}$ 8.0 Hz), 4.29 (ddd, 1H, H-5, $J_{5,6a}$ 2.8 Hz, $J_{5,6b}$ 6.6 Hz), 3.32 (s, 3H, –OCH$_3$), 2.42 (s, 3H, PhCH$_3$), 2.21–2.02 (9H, 3×OAc); ^{13}C NMR (H$_2$O): δ 173.27–172.89 (3C, 3×OOCCH$_3$), 147.06–125.61 (6C, Ph), 100.86 (C-1), 73.05 (C-3), 71.38 (C-5), 71.36 (C-2), 69.97 (C-4), 61.17 (C-6), 57.20 (OCH$_3$), 20.70 (PhCH$_3$), 20.38–20.24 (3C, COOCH$_3$); R_f = 0 (3:1 CHCl$_3$–MeOH). Anal. Calcd for C$_{25}$H$_{31}$NO$_{11}$S (553.585): C, 54.24; H, 5.65; N, 2.53; S, 5.79; O, 31.78. Found: C, 54.03; H, 5.84; N, 2.95; S, 5.90. MALDITOF-MS (CCA): *m/z* 382.1 ([M−OTs]$^+$).

3.8. *N*-(Methyl 2,3,4-tri-*O*-acetyl-6-deoxy-β-D-glucopyranoside-6-yl)-2-methylpyridinium tosylate (5b)

Methyl 6-*O*-*p*-toluenesulfonyl β-D-glucopyranoside (68.6 mg, 0.200 mmol) was dissolved in dry 2-methylpyridine (0.64 mL). The solution was kept in a screw-capped ampoule: first at rt for 6 weeks, next at 70 °C for 16 days. After that time the solvent was evaporated. The oil was dissolved in pyridine (3 mL) and Ac$_2$O (3 mL) was added. After 24 h the solution was evaporated. The residue was dissolved in H$_2$O and extracted with CHCl$_3$. The aqueous layer was evaporated and dried over P$_2$O$_5$ to give title compound (64.6 mg, 58%); $[\alpha]_D^{20}$ −22.55 (*c* 0.51, H$_2$O); ^{1}H NMR (D$_2$O): δ 8.76–7.91 (m, 4H, Py), 7.71–7.37 (2d, each 2H, Ph), 5.37 (t, 1H, H-3, $J_{3,4}$ 9.6 Hz), 5.23 (t, 1H, H-4, $J_{4,5}$ 9.6 Hz), 5.03 (q, 1H, H-2, $J_{2,3}$ 8.4 Hz), 4.91 (dd, 1H, H-6a, $J_{6a,6b}$ 12.4 Hz), 4.76 (dd, 1H, H-6b), 4.55 (d, 1H, H-1, $J_{1,2}$ 8.4 Hz), 4.28 (ddd, 1H, H-5, $J_{5,6a}$ 2.4 Hz, $J_{5,6b}$ 7.6. Hz), 3.28 (s, 3H, –OCH$_3$), 2.90 (s, 3H, CH$_3$-picoline), 2.41 (s, 3H, PhCH$_3$), 2.21–2.10 (9H, 3×OAc); ^{13}C NMR (H$_2$O): δ 173.29–172.84 (3C, 3×OOCCH$_3$), 156.36–125.60 (9C, Ph), 100.73 (C-1), 73.13 (C-3), 71.38 (C-5), 71.32 (C-2), 70.39 (C-4), 57.47 (C-6), 57.10 (OCH$_3$), 20.66 (PhCH$_3$), 20.33–20.27 (3C, COOCH$_3$), 20.06 (1C, CH$_3$-picoline); R_f = 0 (3:1 CHCl$_3$–MeOH). Anal. Calcd for C$_{25}$H$_{31}$NO$_{11}$S (553.585): C, 54.24; H, 5.65; N, 2.53; S, 5.79; O, 31.78. Found: C, 54.34; H, 5.57; N, 2.49; S, 5.83. MALDITOF-MS (CCA): *m/z* 396.1 ([M−OTs]$^+$).

4. Supplementary material

Full crystallographic details, excluding structure factors, have been deposited (deposition no. CCDC 222217) with the Cambridge Crystallographic Data Centre. These data may be obtained, on request, from the

CCDC, 12 Union Road, Cambridge, CB2 1EZ, UK. Tel.: +44 1223 336408, fax: +44 1223 336033, e-mail: deposit@ccdc.cam.ac.uk.

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