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APPLICATION OF STERICALLY CROWDED ALKYL SULFONATES: S_N2-SUBSTITUTION IN THE DIACETONE GLUCOSE SYSTEM *

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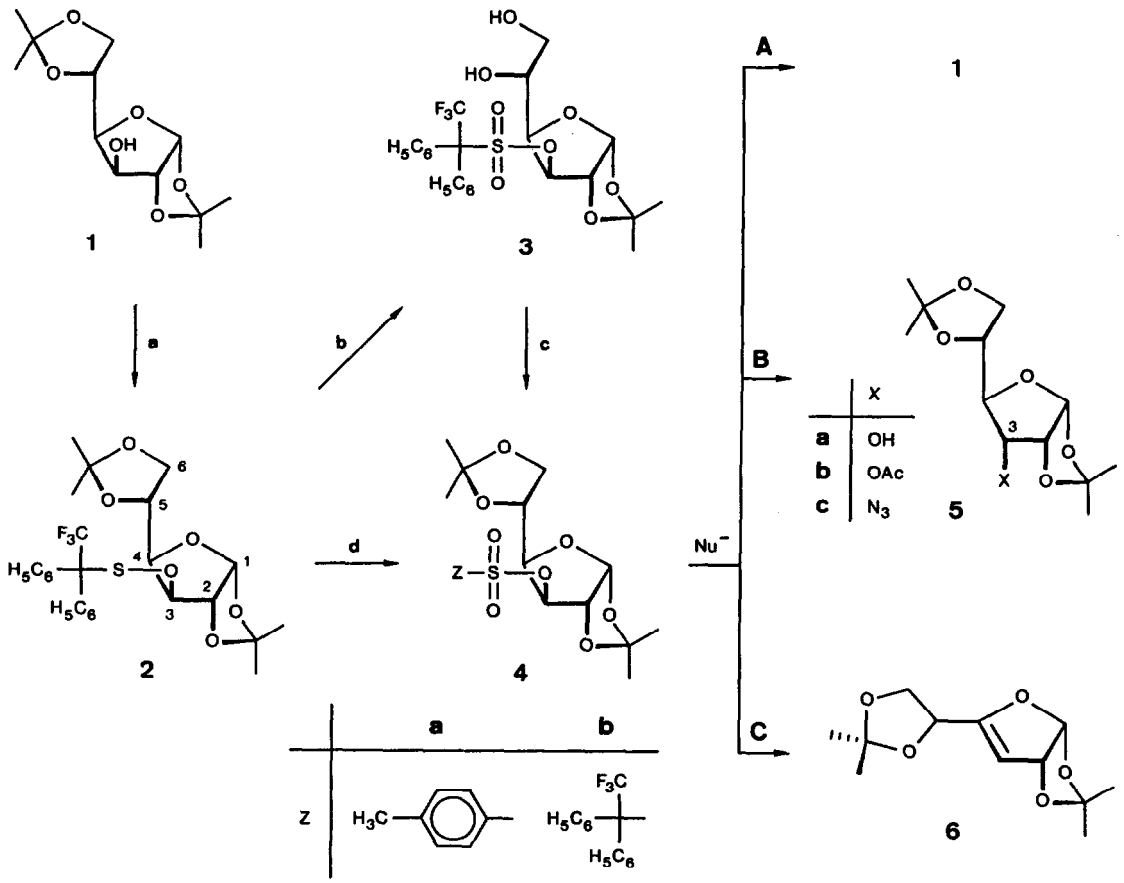
Abstract. The hitherto unaccessible C-substitution by O-nucleophiles in glucose sulfonates **4** was achieved by high nucleofugality of the leaving group and steric hindrance within the ester part of **4b**.

Alkyl sulfonates belong to the most important alkylation reagents in organic chemistry. Nevertheless, their utility in S_N2-substitution reactions at the sp^3-carbon atom of sterically/electronically demanding substrates is limited [2,3)]. In a typical example, it has been long known [4)] that treatment of glucose tosylate **4a** [5)] with O-nucleophiles results in attack on sulfur exclusively (**A**, scheme 1). The "abnormal" displacement under inversion at C-3 (**B**) can now be realized for the first time with the use of the ester **4b** which contains the novel, very nucleofugic 2,2,2-trifluoro-1,1-diphenylethane (TDE-) sulfonate group [6)]. As a consequence of the appreciable steric hindrance about the sulfur atom, competing S-O-scission is retarded efficiently.

Sugar sulfonate **4b** [7)] was prepared from 1,2:5,6-di-O-isopropylidene-α-D-glucofuranose (**1**) via the sulfenate **2** [8)] (quant. from **1** and the readily available TDE-sulfenyl chloride [9)]). When **2** was oxidized by trifluoroperacetic acid (standard procedure [9)]), the diol **3** [10)] arising from 5,6-deprotection under the weakly acidic conditions [11)] was isolated from the reaction mixture as the main product (57% after chromatography), in spite of buffering by disodiumhydrogene phosphate. Rather than resorting to the ketalization of **3** (85% crystalline **4b**), this complication could be avoided by oxidizing **2** with alkaline permanganate solution in a two-phase system (70% **4b** from **1**).

In reactions with O-nucleophiles (table 1), the TDE-sulfonate **4b** manifests a completely different behaviour from conventional alkyl / aryl sulfonate esters [12)], represented by tosylate **4a** in comparative experiments. In the case of **4b**, S-O-scission by ethanolic hydroxide solution was not detected (≈100%

6 [13]) whereas tosylate **4a** was transformed into alcohol **1** quantitatively [4,14]. The remarkable C-substitution in the diacetone glucose system yielding allofuranose derivative **5a** [15] (no **1** detectable) was accomplished by the highly nucleophilic reagent potassium superoxide / crown ether in dimethyl sulfoxide [16]. Under the same conditions, the corresponding tosylate underwent only S-O-cleavage (**A**, **1**) in addition to the generally observed elimination reaction (**C**, **6**). According to preliminary experiments, the TDE-sulfonate group in **4b** can be substituted even by acetate at increased temperature (110°C, dimethyl formamide), although in low yield (up to 7% **5b**).



Scheme 1. a) NaH, THF, TDE-sulfenyl chloride [9], 20°C; b) CF_3CO_3H, Na_2HPO_4, CH_2Cl_2, 0→20°C; c) acetone, $CuSO_4$ [11], 20°C, 24 h; d) $KMnO_4$, NaOH, TEBA-Br, THF / water, 20°C, 2 h.

In view of further preparative applications, it is noteworthy that the high nucleofugality of the leaving group [17], compared to tosylate, is documented by the synthesis of azide **5c** from **4a/4b**. Less aggressive conditions are

Table 1. Treatment of Glucose Sulfonates **4a/4b** with O-Nucleophiles

Educt Sulfonate **4**	Z	Reagents	Products, Yield [%] **1**	**5**	**6**
a	Tol	KOH, ethanol [4]	≈100	- [a]	-
b	TDE	KOH, ethanol	-	- [a]	≈100
a	Tol	KO_2, 18C6, DMSO	15	- [a]	81
b	TDE	KO_2, 18C6, DMSO	-	37 [a]	55
b	TDE	NMe_4OAc, DMF	-	7 [b]	63

[a] alcohol **5a** [15]. [b] acetate **5b** (reference probe from **5a**/ acetic acid anhydride / pyridine). Tol = 4-methylphenyl-, TDE = 2,2,2-trifluoro-1,1-diphenylethyl-, 18C6 = [18]crown-6.

required for comparable yields on going from **4b** [30 h, 90°C, 43% **5c** / 40% **6**] than from **4a** [15 d, 115°C, 53% **5c** / 10% **6** / 10% educt [20] or 40% **5c** / 31% **6** using the carcinogenic hexamethylphosphoric triamide, HMPA [21]].

From the results described herein, an impressive and clear demonstration of the unique potential and advantage of sterically hindered sulfonate leaving groups [22,23] over conventional sulfonates has been shown, particularly in the field of polyfunctionalized systems.

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REFERENCES AND NOTES

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7) **4b**: m.p. = 131°C; correct microanalysis (C,H,S); ^{1}H NMR (250 MHz, $CDCl_3$): δ = 5.56 (d, 1-H), 4.96 (d, 3-H), 4.06 (dd, 4-H), 3.81 (d, 2-H), $J_{1,2}$ = 3.5, $J_{3,4}$ = 3.0, $J_{4,5}$ = 10.0 Hz; IR (KBr): ν = 2980, 1380, 1180 cm^{-1}.

8) **2**: ^{1}H NMR (250 MHz, $CDCl_3$): δ = 5.67 (d, 1-H), 4.22 (d, 2-H), 4.13 (d, 3-H), 4.07 (dd, 4-H), $J_{1,2}$ = 3.5, $J_{3,4}$ = 3.0, $J_{4,5}$ = 6.0 Hz.

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10) **3**: m.p. = 62-65°C; correct microanalysis (C,H,S); ^{1}H NMR (250 MHz, $CDCl_3$): δ = 5.53 (d, 1-H), 5.05 (d, 3-H), 4.10 (dd, 4-H), 3.67 (d, 2-H), $J_{1,2}$ = 3.5, $J_{3,4}$ = 3.0, $J_{4,5}$ = 9.0 Hz; IR (KBr): ν = 3440, 1370, 1175 cm^{-1}.

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