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Note

Synthesis and properties of 1,1,3,3-tetramethyl-2-(2,3,4,6-tetra-*O*-acetyl-α-D-glucopyranosyl)uronium triflate

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An efficient method for the synthesis of 1,2-*trans*-glycosides, introduced by Hanessian and Banoub [1], involves treatment of acetylated glycosyl halides with partially protected sugar derivatives in the presence of silver triflate (promoter) and 1,1,3,3-tetramethylurea (proton acceptor).

However, 1,1,3,3-tetramethylurea in this reaction acts not only as a base but also reacts with the glycosyl halide, particularly at higher temperatures, to form an ionic compound that can be detected by TLC. Thus, 1,1,3,3-tetramethyl-2-(2,3,4,6-tetra-*O*-acetyl-α-D-glucopyranosyl)uronium triflate (**2**) was isolated crystalline (56%) after treatment of 2,3,4,6-tetra-*O*-acetyl-α-D-glucopyranosyl bromide (**1**) in dichloromethane with silver triflate and 1,1,3,3-tetramethylurea at room temperature for 15 min. However, if the reaction mixture was kept for 1 h at −70°, then filtered, and concentrated, ^{1}H-NMR spectroscopy of a solution of the residue in D_2O revealed 1,3,4,6-tetra-*O*-acetyl-α-D-glucopyranose (**5**) together with < 10% of **2**. This finding indicates that, at low temperature, the equilibrium **3a** ⇌ **3b** favours the acetoxonium ion **3b**, which yields **5** on quenching, whereas, at higher temperatures, **2** is formed.

Structure **2** was deduced primarily from the NMR data and its chemical reactivity. Thus, **2** was soluble in water, and the ^{1}H- and ^{13}C-NMR data for solutions in D_2O, $CDCl_3$, and CD_3OD are presented in Tables I and II (the assignments were based on COSY and heteronuclear 2D correlated experiments). The $^3J_{H,H}$ values indicated a $^4C_1$(D) conformation and ruled out the orthoester structure **4**, the NMR data of which would be expected to be similar to those of

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TABLE I

^{1}H-NMR data (δ in ppm, J in Hz in brackets) for **2**, **5**, **6**, **7**, and **9** at 500 MHz

Compound	Solvent	H-1	H-2	H-3	H-4	H-5	H-6a	H-6b	NME/OMe
2	D_2O	6.07 (3.4)	5.38 (10.2)	5.58 (9.6)	5.29 (10.2)	4.49 (3.9) (2.0)	4.39 (12.8)	4.23	3.16
	$CDCl_3$	6.02	5.25	5.50	5.22	4.37	4.25	4.18	3.27
	CD_3OD	6.12 (3.3)	5.35 (10.2)	5.60 (9.5)	5.30 (10.2)	4.45 (5.0) (2.4)	4.34 (12.8)	4.26	3.27
5	D_2O	6.20	4.08	5.36	5.07	4.29	4.38	4.13	
	$CDCl_3$	6.23 (4.0)	3.89 (10.8)	5.23 (10.8)	5.10 (10.8)	4.02 (4.4) (2.0)	4.28 (13.6)	4.05	
6α	D_2O	5.42 (3.5)	5.00 (10.2)	5.44 (9.7)	5.08 (10.1)	4.35 (3.6) (2.2)	4.37 (12.6)	4.13	
	$CDCl_3$	5.38 (3.6)	4.81 (10.2)	5.46 (10.2)	5.01 (10.7)	4.20 (3.9) (1.8)	4.17 (12.0)	4.06	
6β	D_2O	4.97 (8.3)	4.90 (9.7)	5.32 (9.5)	5.08 (10.1)	4.02 (4.1) (2.2)	4.33 (12.6)	4.17	
7	CD_3OD	4.61 (7.9)	4.90 (9.7)	5.28 (9.9)	5.06 (10.0)	3.90 (4.6) (2.4)	4.32 (12.2)	4.18	3.35
9 [a]	$CDCl_3$	4.70 (8.1)	4.95 (9.4)	5.06	5.06	3.34 (4.1) (2.3)	4.16 (12.4)	3.91	
9 [b]	$CDCl_3$	4.31 (7.8)	3.42 (9.1)	3.60 (8.6)	3.98 (9.9)	3.38	3.78	3.78	3.69

[a] Non-reducing unit. [b] Reducing unit.

TABLE II

^{13}C-NMR data for **2**, **5**, **6**, and **9** at 125.7 MHz

Compound	Solvent	C-1	C-2	C-3	C-4	C-5	C-6	NMe/OMe
2	D_2O	100.6	70.4	70.9	67.8	71.5	62.3	40.8
	$CDCl_3$	100.3	69.1	69.1	66.7	71.0	61.1	40.8
5	$CDCl_3$	91.3	69.8	73.2	67.4	69.7	61.6	
6α	D_2O	90.3	72.0	71.5	69.0	67.5	62.5	
	$CDCl_3$	89.8	71.0	69.7	68.3	66.8	61.8	
6β	D_2O	94.7	73.5	74.0	69.0	72.0	62.5	
9 [a]	$CDCl_3$	99.9	71.9	73.1	68.0	71.5	61.5	
9 [b]	$CDCl_3$	104.6	81.7	82.5	77.1	74.6	67.7	57.0

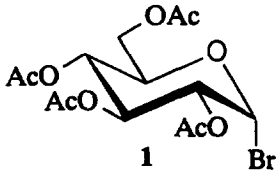
[a] Non-reducing unit. [b] Reducing unit.

3,4,6-tri-*O*-acetyl-α-D-glucopyranose 1,2-(ethyl orthoacetate) [2,3]. The $J_{C\text{-}1,H\text{-}1}$ value (181.5 Hz), which is similar to that (185 Hz) [4] for **1**, indicates a strong anomeric effect by the 1-substituent due to the partial positive charge on the oxygen atom. In agreement with this view, no β anomer of **2** has been detected.

The ^{1}H-NMR spectra of a solution of **2** in D_2O revealed only **2** after 5 min, after 2 h at room temperature, ~ 50% of **2** had been hydrolysed to **6**, and, after 20 h, **6** with only traces of **2** were present. In contrast, the ^{1}H-NMR of a solution of **2** in $CDCl_3$ showed that, after 30 min, ~ 50% of **2** had been hydrolysed to **5**, presumably via **3**, and, after 2 h, a complex mixture of products had been formed. The NMR data for **5** and **6** were comparable to those of authentic samples [5–7]. The NMR spectrum of a solution of **2** in CD_3OD showed that ~ 50% transformation into trideuteriomethyl 2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranoside (**7**) had occurred after 5 min.

Glycosylation of methanol with **2** under homogeneous conditions gave 62% of **7** and of methyl 2,4,6-tri-*O*-benzyl-β-D-glucopyranoside (**8**) in dichloromethane gave 55% of the β-linked disaccharide derivative **9**. The yields were not improved significantly when the original heterogeneous procedure was used but, in other examples (not reported), more complex mixtures of products were obtained, suggesting that the use of **2** as a glycosylating agent is limited.

Attempts to prepare 1,1,3,3-tetramethyl-2-(2,3,4,6-tetra-*O*-benzoyl-α-D-gluco- or -galacto-pyranosyl)uronium triflate from 2,3,4,6-tetra-*O*-benzoyl-α-D-gluco- or -galacto-pyranosyl bromide did not yield any crystalline products.



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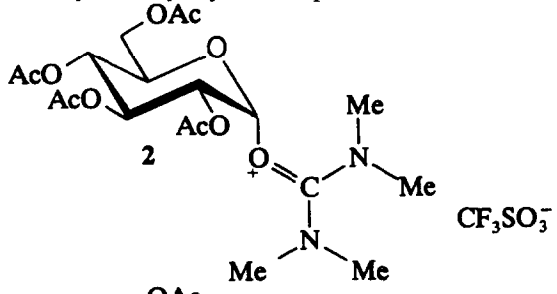

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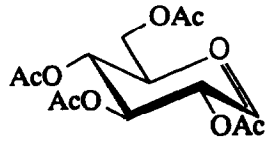

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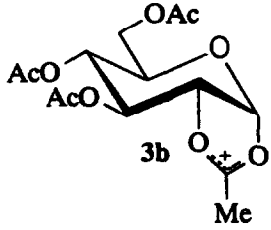

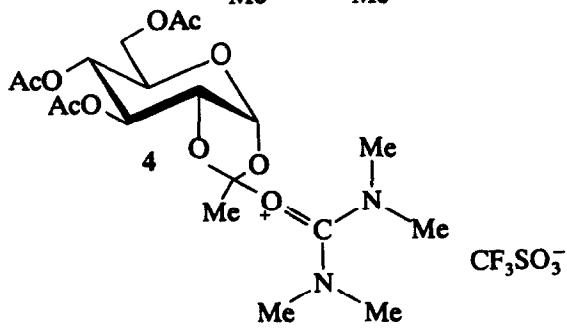

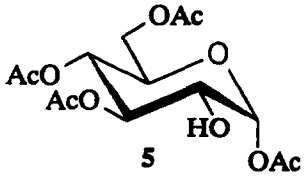

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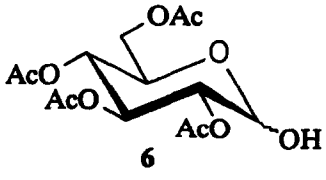

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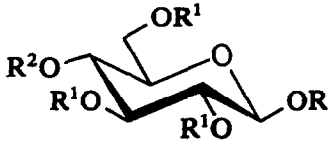
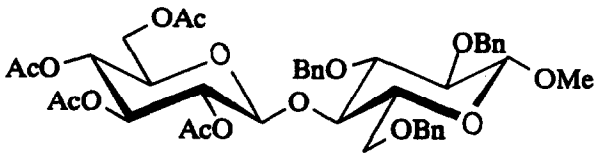


7 R = CD_3, $R^1 = R^2 = Ac$

8 R = CH_3, R^1 = Bn, R^2 = H



9

EXPERIMENTAL

General methods.—Melting points are uncorrected. NMR spectra were recorded with a Bruker AM-500 spectrometer at 27° on solutions in $CDCl_3$, CD_3OD, and D_2O (^1H, internal DOH, δ 4.75; ^{13}C, internal dioxane, 67.4 ppm). TLC was performed on Silica Gel HF_{254} (Merck) with detection by charring with H_2SO_4.

*1,1,3,3-Tetramethyl-2-(2,3,4,6-tetra-*O*-acetyl-α-*D*-glucopyranosyl)uronium triflate* (**2**).—To a stirred mixture of silver triflate (5.10 g, 19.8 mmol), 1,1,3,3-tetramethylurea (2.75 mL, 22.9 mmol), and 3A molecular sieves (5 g) in CH_2Cl_2 (25 mL) was added, at room temperature under N_2, 2,3,4,6-tetra-*O*-acetyl-α-D-glucopyranosyl bromide (**1**; 8.17 g, 19.8 mmol). The mixture was stirred for 15 min at room temperature under N_2, then filtered through a mixture of Celite and $MgSO_4$, and the insoluble material was washed with dry CH_2Cl_2 (50 mL). The combined filtrate and washings were concentrated at 30°, and the residue was treated with cold EtOH to give immediately a mass of crystals which was filtered quickly and dried over P_2O_5. Compound **2** (6.61 g, 11.08 mmol, 56%) had mp 86–89° (dec), R_F 0.34 (9:1 CH_2Cl_2–MeOH). See Tables I and II for the NMR data. The $[\alpha]_D$ value could not be obtained due to the instability of **2** in most solvents.

Anal. Calcd. for $C_{20}H_{31}F_3N_2O_{13}S$: C, 40.27; H, 5.23; N, 4.70. Found: C, 39.71; H, 5.38; N, 4.55.

Glycosylations with **2**.—*(a) Methanol.* A solution of **2** (100 mg, 0.17 mmol) in dry MeOH (2 mL) was kept over 3A molecular sieves (300 mg) for 3 h at room temperature, then filtered, and concentrated to dryness, and the residue was crystallised from EtOH to yield methyl 2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranoside (**7**; 38 mg, 62%), mp 104–105°; lit. [8] 104–105°.

*(b) Methyl 2,3,6-tri-*O*-benzyl-β-*D*-glucopyranoside* (**8**).—A solution of **2** (300 mg, 0.5 mmol) in CH_2Cl_2 (3 mL) was stirred with 3A molecular sieves under N_2, a solution of **8** (264 mg, 0.57 mmol) in CH_2Cl_2 (1.5 mL) was added, and the mixture was stirred overnight. The mixture was diluted with CH_2Cl_2 (25 mL), filtered, and

washed with water (20 mL), satd aq $NaHCO_3$ (5 mL), and water (10 mL), dried ($MgSO_4$), and concentrated. Preparative TLC 1:2 EtOAc–hexane) of the residue gave **8** (70 mg, 0.15 mmol, 25%) and methyl 2,3,6-tri-*O*-benzyl-4-*O*-(2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosyl)-β-D-glucopyranoside (9; 223 mg, 0.28 mmol, 55%), mp 86–90°; $[\alpha]_D^{25}$ −4.4° (*c* 1.39, $CHCl_3$) {lit. [9] $[\alpha]_D^{25}$ −5° ($CHCl_3$)}, which was identified by the ^1H- and ^{13}C-NMR data in Tables I and II.

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