Glycoside-Syntheses; III[1]. Stereoselective Synthesis of Protected 1-*O*-Trimethylsilyl-α-D-glucopyranosides

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1-*O*-Trimethylsilyl-glucopyranosides such as **1** or **2** are valuable educts in the synthesis of disaccharides[2,3] and of glucosides with the 1,1′-diacetal-structure[1,4]. However, the synthe-

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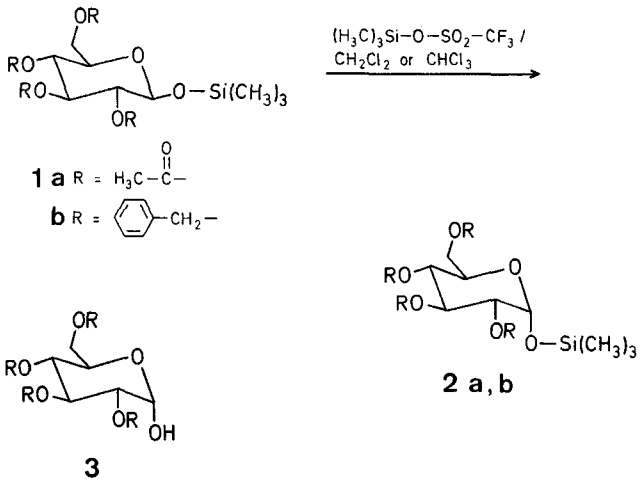
sis of protected trimethylsilyl-α-D-glucopyranosides has been difficult so far, because protected α-glucopyranose **3**, the required precursor, is either not available in the desired anomeric purity[5,6] or can only be synthesized in low yields[7].

We now report on a convenient method to convert the easily available mixture of acetyl-protected α- and β-trimethylsilylglucosides **1a** and **2a** or of the pure β-glucoside **1a**[8] selectively and in very good yields into the α-anomer **2a**. For the transformation, a solution of the mixture **1a** and **2a** or of pure **1a** in dichloromethane or chloroform is treated with catalytic amounts of trimethylsilyl trifluoromethanesulfonate at temperatures of 0 to 40 °C for 5 to 1 h, depending on the reaction temperature. The α-anomer **2a** can be isolated after workup in 90% yield, containing less than 4% of the β-anomer. Purification can easily be performed by crystallisation. The described procedure is simple to carry out and superior to all known methods.

The selectivity of the transformation of **1b** into **2b** is less pronounced. Thus, the reaction of **1b** at temperatures from −20 to 40 °C gives only a 4 : 1 mixture of **2b** and **1b** in 95% yield. A separation of the two anomers could not be achieved by crystallisation. A separation by chromatography on silica gel is possible but difficult.



Both acetyl- and benzyl-protected silylglucosides form disaccharides at prolonged reaction times. The anomerisation and the following disaccharide formation could be monitored by ^{1}H- and ^{13}C-N.M.R. spectroscopy. Hereby, a distinct influence of reaction temperature, solvent, and amount of catalyst could be observed. For instance, **1b** can be converted completely into disaccharides of the trehalose-type within 4 h at ~40 °C using 3 mol-% of trimethylsilyl trifluoromethanesulfonate. One gets a mixture of octa-*O*-benzyl-α,β-D-trehalose, -α,α-D-trehalose and -β,β-D-trehalose in a proportion of 6 : 3 : 1 in 96% yield. As an additional product, hexamethyldisiloxane is formed in this reaction.

The mixture of **1a** and **2a** was easy available by reaction of 2,3,4,6-tetra-*O*-acetyl-D-glucose with hexamethyldisilazane and chlorotrimethylsilane in pyridine[2]. The synthesis of **1b** was performed analogous to the known procedure for the formation of methyl-protected trimethylsilyl-β-D-glucopyranosides[2].

1-*O*-Trimethylsilyl-2,3,4,6-tetra-*O*-benzyl-β-D-glucopyranoside (1b)[9]:
To a solution of 2,3,4,6-tetra-*O*-benzyl-α-D-glucose (**3b**; 1.00 g, 1.85 mmol) in benzene (20 ml), triethylamine (1.50 ml) is added. The mixture is stirred and gently boiled under reflux while chlorotrimethylsilane (0.20 g, 1.90 mmol) is added dropwise. Boiling under reflux and stirring are continued for 2 h, then the mixture is filtered and evaporated in vacuo. Filtration on silica gel (hexane/ethyl acetate 3 : 1) affords the β-glucopyranoside **1b** with 97% anomeric purity; yield: 0.79 g (70%); m.p. 55 °C; R_F: 0.43 (hexane/ethyl acetate 3 : 1); $[\alpha]_D^{20}$: 14.6° (*c* 1.1, chloroform).

$C_{37}H_{44}O_6Si$	calc.	C 72.52	H 7.24
(612.8)	found	72.67	7.11

M.S. (70 eV): *m/e* (relative intensity) = 521 (M^+ − benzyl, 0.5); 431 [521 − $(H_3C)_3SiOH$, 1]; 254 (10); 253 (55); 240 (10); 235 (12); 210 (12); 209 (73); 181 (31); 92 (68); 91 (benzyl, 100); 73 [$(H_3C)_3$—Si, 20]; 65 (28).

I.R. (KBr): ν = 3090, 3070, 3040 (CH_{arom}); 1260, 850 cm^{-1} (Si—CH_3).

^{1}H-N.M.R. ($CDCl_3$): δ = 7.5–7.1 (m, 20 H, phenyl); 5.1–4.45 (m, 9 H, 1-H, CH_2); 3.9–3.3 (m, 6 H, 2-H, 3-H, 4-H, 5-H, 6-H); 0.24 ppm [s, 9 H, $Si(CH_3)_3$].

^{13}C-N.M.R. ($CDCl_3$): δ = 138.56–138.10, 128.21–127.38 (phenyl); 97.94 (C-1); 84.51, 83.80, 77.81, 74.82 (C-2 to C-5); 75.52, 74.65, 73.27 (CH_2); 68.97 (C-6); 0.17 ppm (CH_3).

General Procedure for the Transformation into Protected 1-*O*-Trimethylsilyl-α-D-glucopyranosides (2):
A 0.10 molar solution of trimethylsilyl trifluoromethanesulfonate (0.60 ml) in dichloromethane is added to a solution containing **1** (2 mmol) in anhydrous dichloromethane (5 ml) under an inert gas at 20 °C and the mixture is stirred at this temperature for ~4 h. After addition of triethylamine (0.20 ml) the reaction mixture is filtered on silica gel (hexane/ethyl acetate) and evaporated.

1-*O*-Trimethylsilyl-2,3,4,6-tetra-*O*-acetyl-α-D-glucopyranoside (2a):
Yield after recrystallisation: 0.64 g (76%); m.p. 41.8 °C (ether/petroleum ether) (Lit.[3], m.p. 87–88 °C); R_F: 0.47 (silica gel, hexane/ethyl acetate 1 : 1); $[\alpha]_D^{20}$: 128.9° (*c* 1, chloroform) {Lit.[3], $[\alpha]_D^{20}$: 100.4° (*c* 1, chloroform)}.

$C_{17}H_{28}O_{10}Si$	calc.	C 48.56	H 6.71
(420.5)	found	48.52	6.66

M.S. (70 eV): *m/e* (relative intensity) = 405 ($M^+ - CH_3$, 4); 331 (1); 303 (2); 302 (2); 300 (10); 243 (40); 242 (13); 227 (20); 200 (17); 183 (20); 169 (11); 158 (12); 141 (63); 140 (26); 109 (26); 103 (46); 98 (43); 81 (100); 73 (62); 44 (100).

I.R. (KBr): ν = 1750 (C=O); 1255 (Si—CH_3); 1230 (C—O); 850 cm^{-1} (Si—CH_3).

^{1}H-N.M.R. ($CDCl_3$): δ = 5.5–5.4 (m, 1 H, 3-H); 5.38 (d, 1 H, *J* = 3.5 Hz, 1-H); 5.04 (dd, 1 H, J_1 = 10.0 Hz, J_2 = 9.5 Hz, 4-H); 4.82 (dd, 1 H, J_1 = 10.0 Hz, J_2 = 3.5 Hz, 2-H); 4.3–4.0 (m, 3 H, 5-H, 6-H); 2.09, 2.05, 2.03, 2.01 (4s, 12 H, 4 CO—CH_3); 0.16 ppm [s, 9 H, $Si(CH_3)_3$].

^{13}C-N.M.R. ($CDCl_3$): δ = 169.94, 169.58, 169.44, 169.03 (CO—CH_3); 89.96 (C-1); 71.48, 69.82, 68.42, 66.81 (C-2 to C-5); 61.80 (C-6); 20.37 (CO—CH_3); −0.52 ppm [$Si(CH_3)_3$].

1-*O*-Trimethylsilyl-2,3,4,6-tetra-*O*-benzyl-α-D-glucopyranoside (2b):
Yield: 1.16 g (95%) (contains ~20% β-anomer); R_F (α-anomer): 0.42; R_F (β-anomer): 0.43 (silica gel, hexane/ethyl acetate 3 : 1); separation was performed by column chromatography on silica gel (hexane/ethyl acetate 3 : 1); oil; $[\alpha]_D^{20}$: 41.2° (*c* 0.9, chloroform).

M.S. (70 eV): *m/e* (relative intensity) = 521 (M^+ − benzyl, 1.4); 431 [521 − $(H_3C)_3SiOH$, 3.7]; 253 (33); 209 (37); 193 (11); 181 (25); 92 (50); 91 (benzyl, 100); 73 [$(H_3C)_3$—Si, 18]; 65 (17).

I.R. (film): ν = 3090, 3070, 3040 (CH_{arom}); 1260, 850 cm^{-1} (Si—CH_3).

^{1}H-N.M.R. ($CDCl_3$): δ = 7.5–7.1 (m, 20 H, phenyl); 5.25 (d, 1 H, *J* = 3.75 Hz, 1-H); 5.15–4.35 (m, 8 H, CH_2); 4.2–3.5 (m, 6 H, 2-H, 3-H, 4-H, 5-H, 6-H); 0.20 ppm (s, 9 H, CH_3).

^{13}C-N.M.R. ($CDCl_3$): δ = 138.62–137.60, 128.02–127.15 (phenyl); 91.38 (C-1); 81.43, 80.51, 77.44, 69.72 (C-2 to C-5); 75.19, 74.74, 73.06, 72.61 (CH_2); 68.15 (C-6); −0.24 ppm (CH_3).

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[9] For the synthesis of benzyl-protected trimethylsilyl-β-D-glucopyranoside according to Lit.[2], we obtained only a 5:4 mixture of **1b** and **2b**; $[\alpha]_D^{20}$: 24.2° (*c* 1, chloroform) instead of pure **1b** as described {Lit.[2], $[\alpha]_D^{21}$: 24.4° (*c* 1.3, chloroform)}.

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