Dibutyl Tin Oxide Mediated, Regioselective Alkylation and Acylation of Siloxane Protected Glycopyranosides

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Abstract: Treatment of alkyl and aryl 4,6-*O*-(1,1,3,3-tetraisopropyl-1,3-disiloxane-1,3-diyl)-D-glycopyranosides **2** with dibutyltin oxide followed by benzoyl chloride, benzyl bromide and allyl bromide afforded regioselectively the corresponding mono acylated and alkylated glycosides. The regioselective acylation of the stannylene intermediates is inverted as compared to the direct acylation of **2**. Regioselective alkylations of **2** proceeded without affecting the siloxane residue.

Key words: protecting groups, silylation, siloxanes, glycopyranosides, saccharides, alkylation, acylation, benzoylation

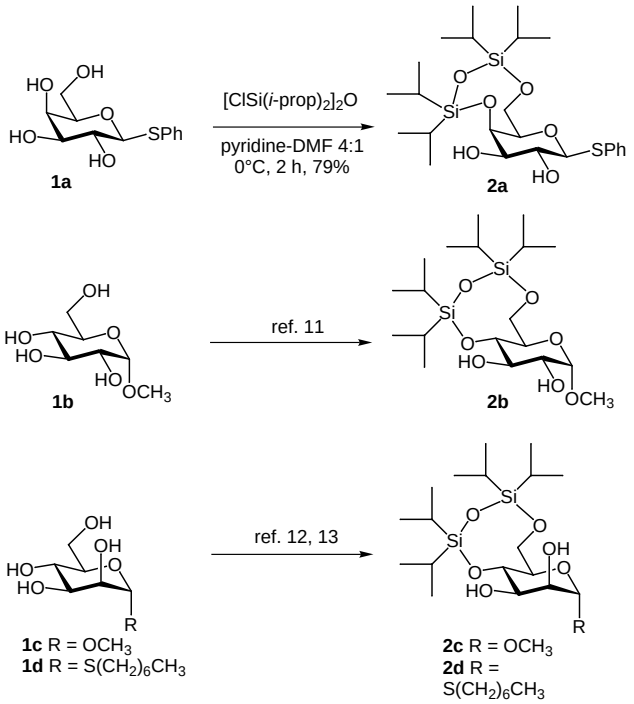
One of the most remarkable developments in protecting group chemistry of carbohydrates in the past decades are without any doubt the silyl ether groups. Due to the viable stability and the ease of cleavage of silyl ether groups virtually under all reaction conditions simply by varying the substitution patterns at the silicon atoms makes silyl ether protecting groups almost ideal for saccharide syntheses. In this respect, the bifunctional 1,1,3,3-tetraisopropyl-1,3-disiloxane-1,3-diyl (TIPS) group which was introduced by Markiewicz in 1979 for the synchronous protection of contiguous hydroxyls in nucleosides[1] appears to be an especially useful protecting group. In general, otherwise unprotected pentofuranosides and hexopyranosides, can be selectively blocked by the TIPS group at hydroxy groups 3 and 5 of furanosides and 4 and 6 of pyranosides.[2] Furthermore, 3,5-TIPS protected furanosides and 4,6-TIPS protected pyranosides are easily rearranged to the corresponding 2,3 protected and 3,4 protected counterparts by simple treatment with acid.[2–6] Thus, the TIPS group may be regarded as a "silyl" equivalent to the classical acetal protecting groups for carbohydrates which, in addition, allows for the protection of trans-diequatorial hydroxyl groups as well. Another useful feature of 4,6-TIPS protected pyranosides is the regioselective acylation of position 2 of the latter and the regioselective ring opening with hydrofluoric acid or glycosyl fluorides that makes protecting group strategies using TIPS groups highly flexible and advantageous for oligosaccharide synthesis.[2,7]

However, a major draw back of TIPS protected pyranosides lies in the incompatibility of TIPS with conditions which are commonly necessary for the introduction of benzyl and allyl protecting groups (i.e. destruction of the siloxane moiety during alkylation of TIPS protected sugars under strongly basic conditions[5]). Solely, allyl groups have been successfully introduced into TIPS-protected glycopyranosides by initial allyloxycarbonylation followed by Pd-catalyzed decarboxylative rearrangement of the acylated intermediates to the corresponding allylated glycosides.[5] Therefore, it would be highly desirable to find reaction conditions which allow for the selective alkylation of 4,6-TIPS protected glycopyranosides without affecting the TIPS group. In this paper, we now present a flexible procedure based on dibutyl stannylene derivatives of TIPS protected D-gluco-, D-manno-, and D-galactopyranosides which allows the regioselective alkylation and acylation of 4,6-TIPS protected sugars.

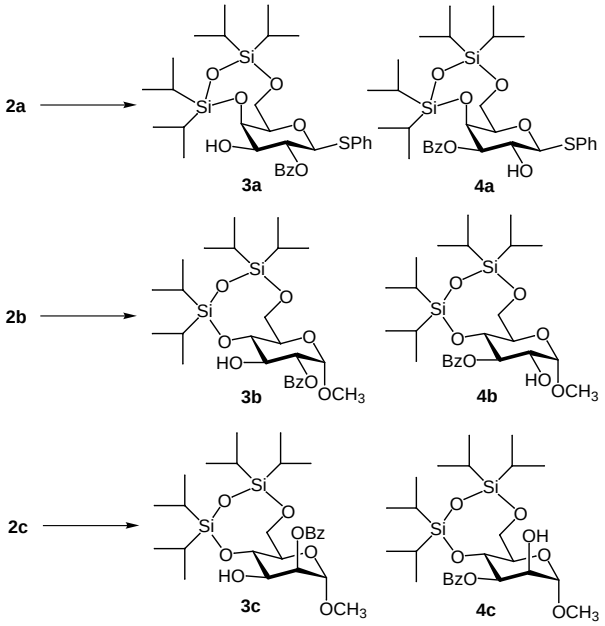
The acylation and alkylation of dibutyl stannylene intermediates of simple glycopyranosides is a well established procedure for the regioselective protection of sugars.[8,9] Although examples for the regioselective manipulation of functional groups of carbohydrates via tin intermediates are abundant, there is only one single example described in the literature where the stannylation procedure was used in combination with the TIPS group. Here, a regioselective stannylene mediated 3-*O* benzylation of the β-(1→4)-linked 4,6-*O*-benzylidene-D-glucopyranosyl side chain of 2,3-TIPS protected levoglucosene was performed thus demonstrating that the TIPS group remains uneffected by intermediate stannylene derivatives.[10]

For stannylations and regioselective acylations and alkylations, we chose 4,6-*O*-(1,1,3,3-tetraisopropyl-1,3-disiloxane-1,3-diyl)-glycopyranosides **2** in the D-galacto, D-gluco and D-manno series (Scheme 1). TIPS protected glycosides **2b**,[11] **2c**,[12] and **2d**[13] were prepared from the corresponding glycosides **1** using 1,3-dichloro-1,1,3,3-tetraisopropyl-1,3-disiloxane and imidazole as previously described. For the preparation of phenyl 1-thiogalactoside **2a** this procedure failed as was previously encountered for other galactosides.[12] Therefore, a modified procedure[14] using pyridine/DMF mixtures as the solvent was applied here. Thus, phenyl 1-thio-β-D-galactopyranoside **1a** was converted into the corresponding TIPS protected galactoside **2a** in 79% yield.

Next, benzoylation of TIPS-protected glycosides **2** was performed either by treatment of **2** directly with benzoyl chloride in pyridine (Table, Procedure A) or by first stannylation followed by benzoylation with benzoyl chloride (Table, Procedure B). As was expected from previous acylations of 4,6-TIPS protected glycosides[2–7] direct benzoylations afforded solely the corresponding 2-*O*-benzoylated glycosides **3**. In contrast, when the intermediate stannylene derivative of galactoside **2a** was benzoylated an almost complete inversion of the regioselectivity was



Scheme 1



For reaction conditions and yield of product(s), see Table

Scheme 2

observed. Thus, the corresponding 3-*O*-benzoylgalactoside **4a** (77%) was formed as the main product (Scheme 2). Benzoylation of the stannylene derivatives of glucoside **2b** and mannoside **2c** gave mixtures of the 2-*O*- and 3-*O*-benzoylated products which, however, were easily separated by chromatography. The respective position of benzoylation was unambigously assigned for all benzoylation products **3** and **4** by simple inspection of the ^{1}H NMR spectra of compounds **3** and **4** which showed a significant downfield shift for H-2 and H-3, respectively when a benzoyl group was present at this position.

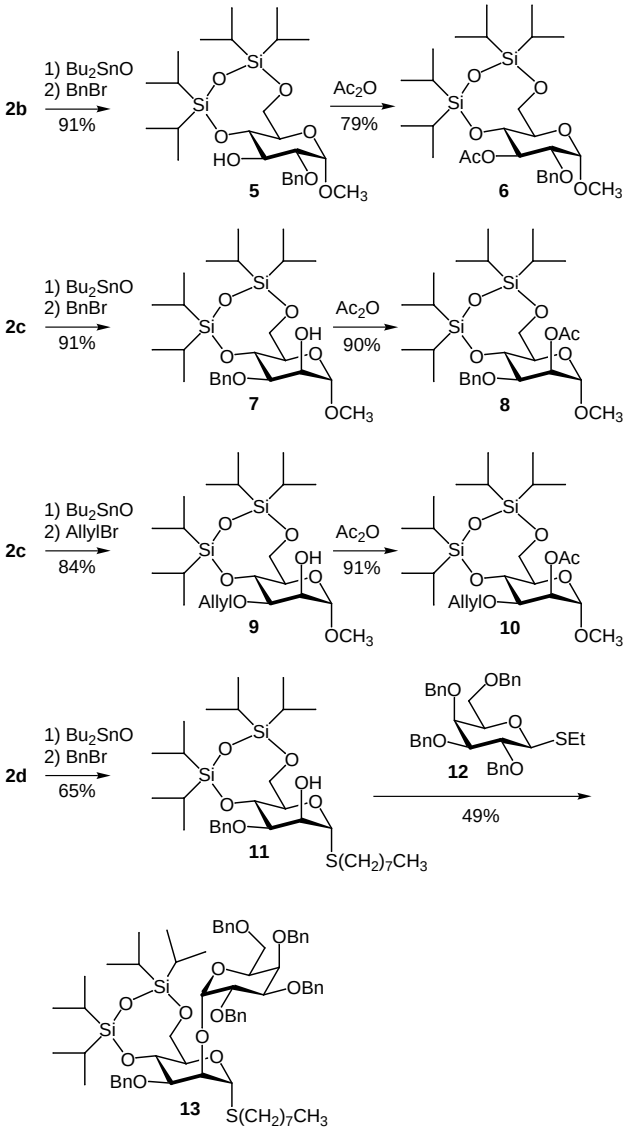
In contrast to the benzoylations of stannylene intermediates of TIPS protected glycosides **2**, alkylations (i.e. benzylation and allylation) proceeded with high selectivity in all cases (Scheme 3). All reactions proceeded smoothly and no decomposition of the TIPS group was observed. Treatment of glucoside **2b** with dibutyl tin oxide followed by benzyl bromide afforded the 2-*O*-benzyl-glucoside **5** in 91% yield. Therefore, a significantly higher regioselectivity compared to the respective benzoylation of **2b** was found in this case since the latter gave a 2:1 mixture of the corresponding 2-*O*-benzoyl- **3b** and 3-*O*-benzoylglucoside **4b** (cf. Table). In contrast, both mannosides **2c** and **2d** afforded the corresponding 3-*O*-alkylated products **7**, **9** and **11** exclusively upon benzylation or allylation. This regioselectivity is surprising since the sterically more demanding position reacted here (i.e. position 3). It should be also noted that all attempts to benzylate compound **2c** with benzyl bromide and silver oxide[10,15] resulted in a 1:1 mixture of **7** and the corresponding 2-*O*-benzylated counterpart (experimental data are not given). A similar case has been previously found as well.[10] All alkylation positions were unambigously assigned as outlined above by acetylation of compounds **5**, **7**, and **9** followed by inspection of the NMR spectra of the thus obtained products **6**, **8**, and **10**, respectively. Furthermore, octyl 1-thio-mannoside **11** was used as glycosyl acceptor for coupling with ethyl 2,3,4,6-tetra-*O*-benzyl-1-thio-α-D-galactopyranoside[16] **12** under promotion by methyl trifluoromethanesulfonate to give the corresponding α-(1→2)-linked disaccharide **13**, related to the GPI-anchor of *Trypanosoma brucei*.[13]

Obviously, the regioselectivity of alkylations of stannylene intermediates of TIPS-protected glycosides is strongly governed by the relative configuration of hydroxy groups at position 2 and 3 whereas benzoylations depend more on steric factors due to the sterically de-

Table Benzoylation of Glycopyranosides **2a–c**

Substrate	Benzoylation Procedure[a]	Product(s)			
		3	Yield (%)	**4**	Yield (%)
2a	A	**3a**	77	**4a**	0
2a	B	**3a**	8	**4a**	77
2b	A	**3b**	89	**4b**	0
2b	B	**3b**	62	**4b**	31
2c	A	**3c**	67	**4c**	0
2c	B	**3c**	69	**4c**	31

[a] A: BzCl in pyridine. Procedure A corresponds to the General Procedure I described in the experimental part. B: 1. Bu_2SnO; 2. BzCl. Procedure B corresponds to the General Procedure II described in the experimental part.



Scheme 3

manding TIPS group. Thus, regioselective alkylations of TIPS protected glycosides via stannylene intermediates may be regarded as a useful extension for TIPS-protected glycosides in oligosaccharide synthesis.

Mps were determined with a Büchi apparatus and are uncorrected. Optical rotations were measured with a Perkin-Elmer 241 polarimeter. ^{1}H and ^{13}C NMR spectra were recorded with a Bruker AC 300F spectrometer at 300 MHz and 75.46 MHz, respectively. TLC was performed on precoated silica gel plates (Merck, $60F_{254}$) using appropriately adjusted mixtures of toluene/ethyl acetate. Detection of the products was achieved by charring with 5% H_2SO_4 in MeOH. Column chromatography was carried out on silica gel using columns of different length (10-20 cm). Solvents were destilled prior to use. Compounds **2b**, **2c** and **2d** were prepared as previously described.[11–13]

Phenyl 4,6-*O*-(1,1,3,3-Tetraisopropyl-1,3-disiloxane-1,3-diyl)-1-thio-β-D-galactopyranoside (2a)

A solution of 1,3-dichloro-1,1,3,3-tetraisopropyl-1,3-disiloxane (4.04 g, 12.8 mmol) and phenyl 1-thio-β-D-galactopyranoside[17] (**1a**; 2.9 g, 10.65 mmol) in a mixture of DMF (23 mL) and pyridine (85 mL) was stirred at 0°C for 2 h, poured into H_2O and extracted with CH_2Cl_2. The combined extracts were washed with aq HCl and aq $NaHCO_3$ solution, dried and concentrated. Chromatography (eluent: CCl_4/acetone 10:1) of the residue afforded **2a** (4.36 g, 79%); $[\alpha]_D^{20}$ –30 (*c* = 1.0, MeOH).

^{1}H NMR ($CDCl_3$): δ = 3.66–3.56 (m, 3 H, H-2,3,5), 3.92–3.80 (m, 2 H, H-6a,6b), 4.25 (d, 1 H, $J_{3,4}$ = 1.3 Hz, H-4), 4.46 (d, 1 H, $J_{1,2}$ = 9.2 Hz, H-1).

^{13}C NMR ($CDCl_3$): δ = 59.3 (C-6), 68.2 (C-2), 69.2 (C-4), 74.9 (C-3), 77.9 (C-5), 87.6 (C-1).

Anal. Calcd for $C_{24}H_{42}O_6SSi_2$: C, 55.99; H, 8.22. Found C, 55.72; H, 8.16.

Benzoylation of Glycosides; General Procedure I

Benzoyl chloride (1.1 mmol) was added at 0°C to a solution of **2** (1.0 mmol) in pyridine (5 mL) and the mixture was stirred at r.t. until all starting material was consumed. The mixture was poured into H_2O and extracted with CH_2Cl_2. The combined extracts were washed with aq HCl and aq $NaHCO_3$ solution, dried and concentrated. Chromatography (eluent: toluene/ethyl acetate 15:1) of the residue afforded **3**.

Benzoylation of Stannylene Intermediates; General Procedure II

A solution of **2** (1.0 mmol) and Bu_2SnO (1.1 mmol) in benzene (80 mL) was refluxed in a Dean–Stark apparatus for 16 h and concentrated to 40 ml. Benzoyl chloride (1.1 mmol) was added at 0°C and strirring was continued at r.t. for 16 h. Workup as described in the General Procedure I afforded **3** and **4**, respectively.

Alkylation of Stannylene Intermediates; General Procedure III

A solution of **2** (1.0 mmol) and Bu_2SnO (1.1 mmol) in benzene (80 mL) were treated as described in the General Procedure II. Benzyl bromide (2.0 mmol) or allyl bromide (2.0 mmol), Bu_4NI (1.0 mmol) and 4 Å molecular sieves (1 g) were added and the mixture was refluxed for 24 h. After cooling to r.t., the mixture was filtered through a layer of Celite and concentrated. Chromatography (eluent: toluene/ethyl acetate 10:1) of the residue afforded **5**, **7**, **9**, and **11**.

Acetylation of Glycosides; General Procedure IV

Ac_2O (2 mL) was added at r.t. to a solution of **5**, **7**, and **9** (0.2 mmol) in pyridine (5 mL) and the mixture was stirred for 6 d at r.t. Workup as described for the General Procedure I afforded **6**, **8**, and **10**, respectively.

Phenyl 2-*O*-Benzoyl-4,6-*O*-(1,1,3,3-tetraisopropyl-1,3-disiloxane-1,3-diyl)-1-thio-β-D-galactopyranoside (3a)

Treatment of **2a** (445 mg, 0.86 mmol) according to the General Procedure I afforded **3a** (408 mg, 77%); $[\alpha]_D^{20}$ –22.8 (*c* = 0.85, $CHCl_3$).

^{1}H NMR ($CDCl_3$): δ = 3.73–3.67 (m, 1 H, H-5), 3.79 (dd, 1 H, H-3), 3.98–3.88 (m, 2 H, H-6a,6b), 4.32 (d, 1 H, $J_{3,4}$ = 2.6 Hz, H-4), 4.78 (d, 1 H, $J_{1,2}$ = 9.8 Hz, H-1), 5.14 (t, 1 H, $J_{2,3}$ = 9.7 Hz, H-2).

^{13}C NMR ($CDCl_3$): δ = 59.2 (C-6), 68.9 (C-4), 71.2 (C-2), 74.3 (C-3), 77.8 (C-5), 85.3 (C-1).

Anal. Calcd for $C_{31}H_{46}O_7SSi_2$: C, 60.16; H, 7.49. Found C, 60.03; H, 7.57.

Phenyl 3-*O*-Benzoyl-4,6-*O*-(1,1,3,3-tetraisopropyl-1,3-disiloxane-1,3-diyl)-1-thio-β-D-galactopyranoside (4a)
Treatment of **2a** (266 mg, 0.52 mmol) according to the General Procedure II afforded **3a** (24 mg, 8%) and **4a** (250 mg, 77%); $[\alpha]_D^{20}$ –12.9 (*c* = 1.1, $CHCl_3$).

^{1}H NMR ($CDCl_3$): δ = 3.95–3.77 (m, 3 H, H-5,6a,6b), 4.06 (t, 1 H, $J_{2,3}$ = 9.8 Hz, H-2), 4.55 (d, 1 H, H-4), 4.60 (d, 1 H, $J_{1,2}$ = 9.5 Hz, H-1),5.14 (t, 1 H, $J_{3,4}$ = 2.8 Hz, H-3).

^{13}C NMR ($CDCl_3$): δ = 59.1 (C-6), 66.4 (C-2), 66.7 (C-4), 77.1 (C-3), 77.9 (C-5), 88.3 (C-1).

Anal. Calcd for $C_{31}H_{46}O_7SSi_2$: C, 60.16; H, 7.49. Found C, 60.08; H, 7.51.

Methyl 2-*O*-Benzoyl-4,6-*O*-(1,1,3,3-tetraisopropyl-1,3-disiloxane-1,3-diyl)-α-D-glucopyranoside (3b)
Treatment of **2b** (437 mg, 1.0 mmol) according to the General Procedure I afforded **3b** (481mg, 89%); $[\alpha]_D^{20}$ +72.5 (*c* = 1.7, $CHCl_3$).

^{1}H NMR ($CDCl_3$): δ = 3.95–3.77 (m, 3 H, H-5,6a,6b), 4.06 (t, 1 H, $J_{2,3}$ = 9.8 Hz, H-2), 4.55 (d, 1 H, H-4), 4.60 (d, 1 H, $J_{1,2}$ = 9.5 Hz, H-1), 5.14 (t, 1 H, $J_{3,4}$ = 2.8 Hz, H-3).

^{13}C NMR ($CDCl_3$): δ = 59.1 (C-6), 66.4 (C-2), 66.7 (C-4), 77.1 (C-3), 77.9 (C-5), 88.3 (C-1).

Anal. Calcd for $C_{26}H_{43}O_8Si_2$: C, 57.75; H, 8.20. Found C, 57.60; H, 8.20.

Methyl 3-*O*-Benzoyl-4,6-*O*-(1,1,3,3-tetraisopropyl-1,3-disiloxane-1,3-diyl)-α-D-glucopyranoside (4b)
Treatment of **2b** (437 mg, 1 mmol) according to the General Procedure II afforded first **3b** (336 mg, 62%). Compound **4b** was eluted next (119 mg, 22%); $[\alpha]_D^{20}$ +51.5 (*c* = 1.0, $CHCl_3$).

^{1}H NMR ($CDCl_3$): δ = 1.15-0.56 (m, 28 H, TIPS), 2.14 (s, 1 H, OH), 3.44 (s, 3 H, CH_3), 3.66 (d, 1 H, $J_{5,4}$ = 9.5 Hz, H-5), 3.69 (dd, 1 H, $J_{2,1}$ = 4.0 Hz, $J_{2,3}$ = 9.7 Hz, H-2), 3.95 (dd, 1 H, $J_{5,6b}$ = 1.3 Hz, H-6b), 4.09 (t, 1 H, $J_{3,4}$ = 9.4 Hz, H-4), 4.18 (dd, 1 H, $J_{5,6a}$ = 1.9 Hz, $J_{6a,6b}$ = 12.6, H-6a), 4.85 (d, 1 H, $J_{1,2}$ = 3.9 Hz, H-1), 5.50 (t, 1 H, $J_{3,4}$ = 9.6 Hz, H-3).

^{13}C NMR ($CDCl_3$): δ = 99.6 (C-1), 76.0 (C-2), 72.2 (C-4), 71.9 (C-5), 67.1 (C-3), 60.7(C-6).

Anal. Calcd for $C_{26}H_{43}O_8Si_2$: C, 57.75; H, 8.20. Found C, 57.70; H, 8.20.

Methyl 2-*O*-Benzoyl-4,6-*O*-(1,1,3,3-tetraisopropyl-1,3-disiloxane-1,3-diyl)-α-D-mannopyranoside (3c)
Treatment of **2c** (1.60 g, 3.7 mmol) according to the General Procedure I afforded **3c** (1.32 g, 67%); $[\alpha]_D^{20}$ –19.5 (*c* = 1.2, $CHCl_3$).

^{1}H NMR ($CDCl_3$): δ = 3.58 (d, 1 H, *J* = 9.4, H-5), 3.94 (dd, 1 H, $J_{6b,5}$ = 1.1 Hz, H-6b), 4.14 (dd, 1 H, $J_{2,3}$ = 3.8 Hz, $J_{3,4}$ = 9.5 Hz,H-3), 4.20 (dd, 1 H, $J_{6a,5}$ = 2.0 Hz, $J_{6a,6b}$ = 12.7 Hz, H-6a), 4.29 (t, 1 H, $J_{3,4}$ = $J_{4,5}$ = 9.4 Hz, H-4), 4.85 (d, 1 H, $J_{1,2}$ = 1.2 Hz, H-1), 5.42 (dd, 1 H, $J_{1,2}$ = 1.5 Hz, $J_{2,3}$ = 3.5 Hz, H-2).

^{13}C NMR ($CDCl_3$): δ = 99.3 (C-1), 72.8 (C-2), 72.7 (C-3), 70.6 (C-4), 67.6 (C-5), 60.9 (C-6).

Anal. Calcd for $C_{26}H_{44}O_8Si_2$: C, 57.75; H, 8.20. Found C, 57.67; H, 8.18.

Methyl 3-*O*-Benzoyl-4,6-*O*-(1,1,3,3-tetraisopropyl-1,3-disiloxane-1,3-diyl)-α-D-mannopyranoside (4c)
Treatment of **2c** (437 mg, 1.0 mmol) according to the General Procedure II afforded first **3c** (370 mg, 69%). Compound **4c** was eluted next (170 mg, 31%); $[\alpha]_D^{20}$ –9.9 (*c* = 1.2, $CHCl_3$).

^{1}H NMR ($CDCl_3$): δ = 3.67 (d, 1 H, *J* = 9.4 Hz, H-5), 3.95 (dd, 1 H, $J_{5,6b}$ = 1.4 Hz, H-6b), 4.09 (dd, 1 H, H-2), 4.20 (dd, 1 H, $J_{5,6a}$ = 2.1 Hz, $J_{6a,6b}$ = 12.5 Hz, H-6a), 4.50 (t, 1 H, $J_{3,4}$ = $J_{4,5}$ = 9.7 Hz, H-4), 4.78 (d, 1 H, $J_{1,2}$ = 1.7 Hz, H-1), 5.48 (dd, 1 H, $J_{3,2}$ = 3.2 Hz, $J_{3,4}$ = 9.9 Hz, H-3).

^{13}C NMR ($CDCl_3$) δ = 61.4 (C-6), 64.7 (C-3), 70.3 (C-4), 73.4 (C-5), 74.8 (C-2), 101.6 (C-1).

Anal. Calcd for $C_{26}H_{44}O_8Si_2$: C, 57.75; H, 8.20. Found C, 57.67; H, 8.18.

Methyl 2-*O*-Benzyl-4,6-*O*-(1,1,3,3-tetraisopropyl-1,3-disiloxane-1,3-diyl)-α-D-glucopyranoside (5)
Treatment of **2b** (437 mg, 1.0 mmol) according to the General Procedure III afforded **5** (480 mg, 91%); $[\alpha]_D^{20}$ +47.8 (*c* = 1.1, $CHCl_3$).

^{1}H NMR ($CDCl_3$) δ = 3.51–3.47 (m, 1 H, H-5), 3.36 (dd, 1 H, H-2), 3.77 (t, 1 H, $J_{3,4}$ = $J_{4,5}$ = 9.2 Hz, H-4), 3.85 (dd, 1 H, $J_{5,6b}$ = 1.3 Hz, H-6b), 3.94 (t, 1 H, $J_{2,3}$ = $J_{3,4}$ = 9.2 Hz, H-3), 4.11 (dd, 1 H, $J_{5,6a}$ = 1.9 Hz, H-6a), 4.63 (d, 1 H, $J_{1,2}$ = 4.0 Hz, H-1).

^{13}C NMR ($CDCl_3$): δ = 60.7 (C-6), 69.3 (C-4), 71.4 (C-5), 73.1 (C-3), 79.9 (C-2), 98.0 (C-1).

Anal. Calcd for $C_{26}H_{46}O_7Si_2$: C, 59.28; H, 8.80. Found C, 59.05; H, 8.72.

Methyl 3-*O*-Acetyl-2-*O*-benzyl-4,6-*O*-(1,1,3,3-tetraisopropyl-1,3-disiloxane-1,3-diyl)-α-D-glucopyranoside (6)
Treatment of **5** (110 mg, 210 μmol) according to the General Procedure IV afforded **6** (93 mg, 73%); $[\alpha]_D^{20}$+67.0 (*c* = 0.7, $CHCl_3$).

^{1}H NMR ($CDCl_3$) δ = 3.41 (dd, 1 H, H-2), 3.58 (d, 1 H, *J* = 9.6 Hz, H-5), 3.87 (dd, 1 H, $J_{5,6b}$ = 1.3 Hz, H-6b), 3.90 (t, 1 H, $J_{3,4}$ = $J_{4,5}$ = 9.4 Hz, H-4), 4.13 (dd, 1 H, $J_{5,6a}$ = 2.0 Hz, $J_{6a,6b}$ = 12.7 Hz, H-6a), 4.68 (d, 1 H, $J_{1,2}$ = 3.6 Hz, H-1), 5.43 (t, 1 H, $J_{2,3}$ = $J_{3,4}$ = 9.6 Hz, H-3).

^{13}C NMR ($CDCl_3$): δ = 60.7 (C-6), 67.7 (C-3), 71.7 (C-5), 73.5 (C-4), 78.2 (C-2), 97.9 (C-1).

Anal. Calcd for $C_{28}H_{48}O_8Si_2$: C, 59.12; H, 8.50. Found C, 58.77; H, 8.50.

Methyl 3-*O*-Benzyl-4,6-*O*-(1,1,3,3-tetraisopropyl-1,3-disiloxane-1,3-diyl)-α-D-mannopyranoside (7)
Treatment of **2c** (437 mg, 1.0 mmol) according to the General Procedure III afforded **7** (481 mg, 91%); $[\alpha]_D^{20}$+44.4 (*c* = 1.0, $CHCl_3$).

^{1}H NMR ($CDCl_3$) δ = 3.47 (d, 1 H, *J* = 9.5 Hz, H-5), 3.71 (dd, 1 H, H-3), 3.89 (dd, 1 H, $J_{5,6b}$ = 1.5 Hz, H-6b), 3.93 (dd, 1 H, $J_{2,3}$ = 3.2 Hz, H-2), 4.15 (dd, 1 H, $J_{5,6a}$ = 2.0 Hz, $J_{6a,6b}$ = 12.6 Hz, H-6a), 4.21 (t, 1 H, $J_{3,4}$ = $J_{4,5}$ = 9.4 Hz, H-4), 4.78 (d, 1 H, $J_{1,2}$ = 1.2 Hz, H-1).

^{13}C NMR ($CDCl_3$): δ = 61.4 (C-6), 66.1 (C-4), 68.9 (C-2), 73.2 (C-5), 80.0 (C-3), 101.2 (C-1).

Anal. Calcd for $C_{26}H_{45}O_7Si_2$: C,59.28; H, 8.80. Found C, 59.00; H,8.80.

Methyl 2-*O*-Acetyl-3-*O*-benzyl-4,6-*O*-(1,1,3,3-tetraisopropyl-1,3-disiloxane-1,3-diyl)-α-D-mannopyranoside (8)
Treatment of **7** (150 mg, 285 μmol) according to the General Procedure IV afforded **8** (147 mg, 90%); $[\alpha]_D^{20}$+17.9 (*c* = 1.5, $CHCl_3$).

^{1}H NMR ($CDCl_3$) δ = 3.50 (d, 1 H, *J* = 9.2 Hz, H-5), 3.81 (dd, 1 H, H-3), 3.88 (dd, 1 H, $J_{5,6b}$ = 1.2 Hz, H-6b), 4.18 (dd, 1 H, $J_{5,6a}$ = 1.7 Hz, $J_{6a,6b}$ = 12.5 Hz, H-6a), 4.29 (t, 1 H, $J_{3,4}$ = $J_{4,5}$ = 9.6 Hz, H-4), 4.71 (d, 1 H, H-1), 5.28 (dd, 1 H, $J_{1,2}$ = 1.8 Hz, $J_{2,3}$ = 3.1 Hz, H-2).

^{13}C NMR ($CDCl_3$): δ = 60.9 (C-6), 65.7 (C-4), 68.9 (C-2), 73.3 (C-5), 76.7 (C-3), 99.1 (C-1).

Anal. Calcd for $C_{28}H_{47}O_8Si_2$: C, 59.12; H, 8.50. Found C, 59.24; H, 8.38.

Methyl 3-*O*-Allyl-4,6-*O*-(1,1,3,3-tetraisopropyl-1,3-disiloxane-1,3-diyl)-α-D-mannopyranoside (9)
Treatment of **2c** (437 mg, 1.0 mmol) according to the General Procedure III afforded **9** (399 mg, 84%); mp 113°C; $[\alpha]_D^{20}$+34.5 (*c* = 1.1, $CHCl_3$).

^{1}H NMR ($CDCl_3$): δ = 3.42–3.37 (m, 1 H, H-5), 3.53 (dd, 1 H, $J_{3,4}$ = 9.3, H-3), 3.82 (dd, 1 H, $J_{5,6b}$ = 1.5, $J_{6a,6b}$ = 12.5 Hz, H-6b),

3.92 (dd, 1 H, $J_{2,3}$ = 3.4, H-2), 4.11–4.04 (m, 4 H, H-4, H6a, Allyl-CH_2), 4.73 (d, 1 H, $J_{1,2}$ = 1.2 Hz, H-1), 5.11 (ddd, 1 H, H3´b), 5.21 (ddd, 1 H, $J_{3'a,3'b}$ = 3.0, $J_{3'a,1'a,b}$ = 1.4, H-3´a), 5.94 (ddt, 1 H, $J_{2',3'a}$ = 17.2 Hz, $J_{2',3'b}$ = 10.3 Hz, $J_{2',1'a,b}$ = 5.7 Hz, H-2´).

^{13}C NMR ($CDCl_3$): δ = 60.96 (C-6), 65.5 (C-4), 68.5 (C-2), 72.7 (C-5), 78.9 (C-3), 100.8 (C-1).

Anal. Calcd for $C_{22}H_{44}O_7Si_2$: C, 55.43; H, 9.30. Found C, 55.28, H, 9.23.

Methyl 2-*O*-Acetyl-3-*O*-allyl-4,6-*O*-(1,1,3,3-tetraisopropyl-1,3-disiloxane-1,3-diyl)-α-D-mannopyranoside (10)

Treatment of **9** (150 mg, 315 μmol) according to the General Procedure IV afforded **10** (149 mg, 91%); $[\alpha]_D^{20}$+17.0 (*c* = 1.2, $CHCl_3$).

^{1}H NMR ($CDCl_3$) δ = 3.50 (d, 1 H, *J* = 9.6 Hz, H-5), 3.88 (dd, 1 H, $J_{5,6b}$ = 1.3 Hz, H-6b), 3.71 (dd, 1 H, H-3), 4.17 (dd, 1 H, $J_{5,6a}$ = 1.9 Hz, $J_{6a,6b}$ = 12.5 Hz, H-6a), 4.07–4.02 (m, 2H Allyl-CH_2), 4.21 (t, 1 H, $J_{3,4}$ = $J_{4,5}$ = 9.6 Hz, H-4), 4.70 (d, 1 H, H-1), 5.13 (ddd, 1 H, H3´b), 5.24 (ddd, 1 H, $J_{3'a,3'b}$ = 3.5, $J_{3'a,1'a,b}$ = 1.4, H-3´a), 5.25 (dd, 1 H, $J_{1,2}$ = 1.8 Hz, $J_{2,3}$ = 3.3 Hz, H-2), 5.86 (ddt, 1 H, $J_{2',3'a}$ = 17.2 Hz, $J_{2',3'b}$ = 10.4 Hz, $J_{2',1'a,b}$ = 5.6 Hz, H-2´).

^{13}C NMR ($CDCl_3$): δ = 60.9 (C-6), 65.5 (C-4), 69.0 (C-2), 73.2 (C-5), 76.3 (C-3), 99.1 (C-1).

Anal. Calcd for $C_{24}H_{46}O_8Si_2$: C, 55.56; H, 8.94. Found C, 55.39; H, 8.92.

Octyl 3-*O*-Benzyl-4,6-*O*-(1,1,3,3-tetraisopropyl-1,3-disiloxane-1,3-diyl)-1-thio-α-D-mannopyranoside (11)

Reaction of a solution of **2d** (2.46 g, 4.5 mmol) in benzene (280 mL) with Bu_2SnO (1.22g, 4.9 mmol), benzyl bromide (2.14 mL, 9 mmol), Bu_4NI (3.33 g, 9 mmol) and 4 Å molecular sieves (5 g) according to the General Procedure III afforded **11** (1.86 g, 65%); $[\alpha]_D^{20}$ +79.5 (*c* = 1.0, $CHCl_3$).

^{1}H NMR ($CDCl_3$): δ = 3.69 (dd, 1 H, $J_{2,3}$ = 3.2 Hz, H-3), 3.89–3.81 (m, 2 H, H-5,6b), 3.98 (d, 1 H, *J* = 2.4 Hz, H-2), 4.16 (dd, 1 H, $J_{5,6a}$ = 1.9 Hz, $J_{6a,6b}$ = 12.4 Hz, H-6a), 4.25 (t, 1 H, $J_{3,4}$ = $J_{4,5}$ = 9.3 Hz, H-4), 5.36 (s, 1 H, H-1).

^{13}C NMR ($CDCl_3$): δ = 61.1 (C-6), 65.9 (C-4), 70.1 (C-2), 73.5 (C-5), 79.9 (C-3), 84.2 (C-1).

Anal. Calcd for $C_{33}H_{60}O_6SSi_2$: C, 61.81; H, 9.43; S, 5.00. Found C, 61.86; H, 9.41; S, 5.05.

Octyl 3-*O*-Benzyl-2-*O*-(2,3,4,6-tetra-*O*-benzyl-α-D-galactopyranosyl)-4,6-*O*-(1,1,3,3-tetraisopropyl-1,3-disiloxane-1,3-diyl)-1-thio-α-D-mannopyranoside (13)

A solution of **11** (254 mg, 0.4 mmol) and **12**[15] (245 mg, 0.4 mmol) in anhyd Et_2O (10 mL) was stirred for 1 h with 4 Å molecular sieves at r.t. under argon. After 0.5 h, 2,4-di-*tert*-butyl pyridine (220 μL, 1.0 mmol) was added and the solution was stirred for 1 h. Then, methyl triflate (110 μL, 1.0 mmol) was added and the mixture was allowed to react for 1.5 h. An additional amount of **12** (122 mg, 0.2 mmol) was then added and stirring was continued for 1.5 h. The mixture was quenched with Et_3N (1 mL) and diluted with CH_2Cl_2. After filtration through a layer of Celite the solution was washed with 1 M aq HCl, neutralized with aq satd $NaHCO_3$ solution, dried (Na_2SO_4), filtered and concentrated. Chromatography of the residue (hexane/EtOAc, 20:1 to 10:1) afforded **13** (228 mg, 49%) as a colorless oil; $[\alpha]_D^{20}$ +48 (*c* = 1.3, $CHCl_3$).

^{1}H NMR ($CDCl_3$): δ = 3.44 (dd, 1 H, $J_{5',6'b}$ = 5.6 Hz, H-6´b), 3.51 (dd, 1 H, $J_{5',6'a}$ = 6.7 Hz, $J_{6'a,6'b}$ = 10.0 Hz, H-6´a), 3.70 (dd, 1 H, $J_{2,3}$ = 2.2 Hz, $J_{3,4}$ = 9.6 Hz, H-3), 3.87–3.81 (m, 2 H, H-5, H-6b), 3.99 (s, 2 H, H-2´, H-4´), 3.91 (s, 1 H, H-3´),4.04 (d, 1 H, *J* = 1.3 Hz, H-2), 4.21–4.17 (m, 2 H, H-6a, H-5´),4.46 (t, 1 H, $J_{3,4}$ = $J_{4,5}$ = 9.7 Hz, H-4), 5.16 (s, 1 H, H-1´), 5.45 (s, 1 H, H-1).

^{13}C NMR ($CDCl_3$): δ = 61.1 (C-6), 66.6 (C-4), 69.6 (C-6´), 70.0 (C-5´), 74,4 (C-5), 75.6 (C-2´), 75.9 (C-4´), 77.4 (C-2), 79.1 (C-2´),79.7 (C-3), 85.3 (C-1, $J_{C1,H1}$ = 166.41 Hz), 99.6 (C-1´, $J_{C1',H1'}$ = 169.45 Hz).

Anal. Calcd for $C_{67}H_{94}O_{11}SSi_2$: C, 69.15; H, 8.14. Found C, 69.01, H, 8.19.

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