

Supporting Information

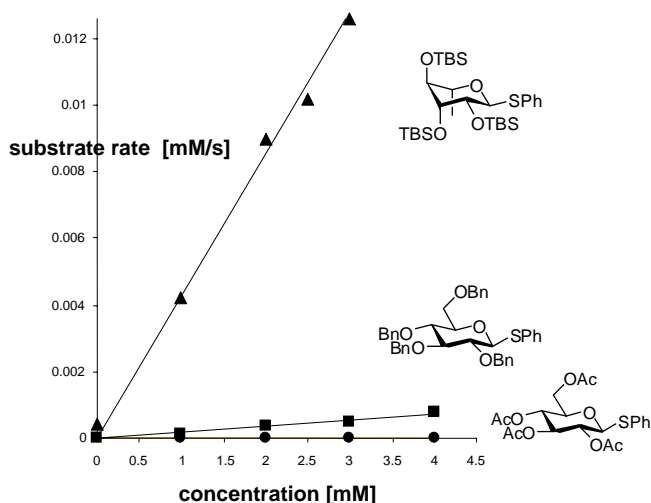
Conformationally armed glycosyl donors: Reactivity quantification, new donors and one pot reactions.

5 Christian Marcus Pedersen, Lavinia G. Marinescu, and Mikael Bols

Department of Chemistry, University of Copenhagen, Universitetsparken 5, 2100 København Ø, Denmark.

General Information: ^{13}C -, ^1H - and H,H-COSY NMR were recorded on a Varian Mercury 400 (400MHz) NMR Instruments. The spectra were referenced to solvent residues. ES-MS was recorded on a Micromass LC-TOF instrument and MALDI-TOF MS was recorded on a Bruker Deltronics mass spectrometer using cinnamic acid (HCCA) based matrix. Optical rotations were measured on a PE-314 polarimeter at 20 ± 1 °C. Chromatography was performed in Merck 60 silica. TLC was performed on Merck silica 60 E₂₅₄ coated glass plates and developed using Ce-mol (10 g Ce(IV)SO₄ and 15 g (NH₄)₂MoO₄ in 1 L 10% H₂SO₄ med) or phosphomolybic acid (MoO₃-H₃PO₄xH₂O 5 % in EtOH) and 15 subsequent heating.

Figure S1. Glycosylation reactivities of different types of donors.



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Determining the relative rate of glycosylation: Each reaction was performed on 6 samples of 2 mL; each sample contained a solution of the appropriate donor in dichloromethane (different

concentrations), TfOH (0.1 eq), MeOH (80 eq.). NIS (10 eq.) was added to these samples and the reaction was followed by UV at 505 nm and typically monitored for 5 to 30 min at room temperature. For the background reaction were prepared 6 samples of dichloromethane containing the same amount of TfOH, MeOH and NIS but no donor. Velocities were determined as the slope of the progress curve of each reaction and subtracting the background velocities from the total velocities of the appropriate donor sample. k_{glyc} was determined as the slope from the plot of v_{glyc} vs. donor concentrations. The extinction coefficient for iodine in dichloromethane at room temperature and 505 [nm] was $\epsilon = 0.8$ [mM⁻¹cm⁻¹].

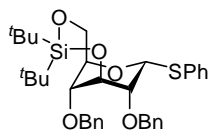
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General procedure for NIS / TfOH activated cross couplings:

When not otherwise noticed equivalent amounts of the glycosyl donor and acceptor were co-evaporated with toluene 3 times followed by drying under vacuum together with powdered 4 Å ms. CH₂Cl₂ was added and the mixture was stirred under argon atm. for 2 h at rt. followed by cooling to -15 85 °C where NIS (1.1 eq.) was added by an in situ addition system followed by a catalytical amount of TfOH (5 µl), which was injected by syringe. The reaction was stirred one hour at -85 °C and allowed to reach -50 to -60 °C, when the donor was “superarmed” and up to rt. with less reactive donors, where it was quenched by addition of Et₃N. The mixture was diluted with EtOAc and filtered through celite. The organic phase was washed with NaHSO₃ (sat.) and brine, dried (MgSO₄) and concentrated *in vacuo* to give a crude product which was purified further by flash chromatography (pentane:EtOAc 25:1 to 10:1).

Data for compounds **1 – 8** can be found in reference 5.

Phenyl-2,4-di-O-benzyl-3,6-O-di-^tBusilylene-1-thio- α -D-glucopyranoside (**9**)



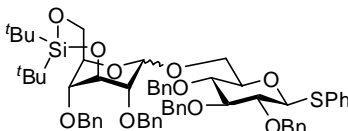
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Phenyl 2,4-di-O-benzyl-3,6-di-O-acetyl-1-thio- α -D-glucopyranoside (190 mg, 0.42 mmol) was dissolved in DMF (5 mL) and 2,6-lutidine (180 mg, 1.68 mmol) was added together with TBDPS triflate (203 mg, 0.46 mmol) and stirred over night. TLC showed full conversion of SM and 2 products. After additional 24 h. the reaction was quenched by MeOH, diluted with EtOAc, washed 30 thoroughly with water, HCl (1 M, 10 mL), NaHCO₃ (sat, 10 mL), brine, dried (MgSO₄) and concentrated *in vacuo* to give a crude product which could be purified by flash chromatography

(pentane : EtOAc 10:1) to give the title product (45 mg, 18 %) and the Si-O-Me derivative (151 mg, 58 %).

$^1\text{H-NMR}$ (400 MHz, CDCl_3): δ 7.44 (m, 2 H), 7.39 (m, 2 H), 7.29-7.10 (m, 11 H), 5.96 (d, $J = 6.1$ Hz, 1 H, H-1), 4.78 (d, $J = 11.5$ Hz, 1 H), 4.62 (d, $J = 11.5$ Hz, 1 H), 4.60 (d, $J = 12.2$ Hz, 1 H), 4.55 (d, $J = 12.2$ Hz, 1 H), 4.43 (bs, 1 H), 4.37 (bs, 1 H), 4.12 (dd, $J = 1.7$ Hz, 12.8 Hz, 1 H), 3.94-3.89 (m, 3 H), 0.84 (s, 9 H), 0.81 (s, 9 H); $^{13}\text{C-NMR}$ (100 MHz, CDCl_3): δ 138.2, 138.0, 137.4, 130.6, 128.8, 128.4, 128.3, 127.9, 127.7, 127.6, 126.5, 84.8, 78.0, 75.4, 73.6, 73.2, 71.2, 70.0, 68.3, 28.4, 28.1, 21.8, 21.2
HRMS(ES) m/z calcd. for $\text{C}_{34}\text{H}_{44}\text{O}_5\text{SSiNa}$: 615.2576, m/z found: 615.2570

10 Phenyl 6-O-(2,4-di-O-benzyl-3,6-di-O-di-^tbutylsilylene-D-glucopyranosyl)-2,3,4-tri-O-benzyl-1-thio- β -D-glucopyranoside (10)



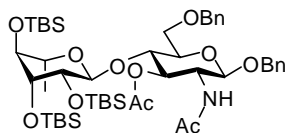
Standard procedure was giving 55% of an inseparable mixture of anomers (α/β 3:1).

α : $^{13}\text{C-NMR}$ (100 MHz, CDCl_3): δ 139.2, 139.0, 138.9, 138.2, 138.1, 134.4, 132.2, 131.9, 129-126 15 (16C), 96.9 (C-1'), 87.8, 86.6, 80.9, 78.6, 77.2, 77.2, 75.5, 75.3, 74.6 (2 C), 74.4, 72.1, 71.5, 70.6, 68.1, 67.6, 28.2, 28.1, 21.9, 21.5

β : $^{13}\text{C-NMR}$ (100 MHz, CDCl_3): δ 138.7, 138.6, 138.3, 138.2, 137.8, 133.8, 132.2, 128.9, 102.2 (C-1'), 87.3, 86.8, 83.5, 80.3, 79.0, 78.1, 77.1, 75.8, 75.5, 75.3, 74.9, 72.8, 72.5, 71.7, 68.5, 67.3, 28.3, 27.9, 21.8, 21.7

20 HRMS(ES) m/z calcd. for $\text{C}_{61}\text{H}_{72}\text{O}_{10}\text{SSiNa}$: 1047.4513, m/z found: 1047.4507

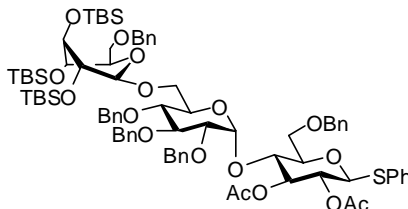
Benzyl 4-O-(2,3,4-tri-O-^tbutyldimethylsilyl-6-deoxy- α -L-mannoside)-2-deoxy-2-N-acetyl-3-O-acetyl-6-O-benzyl- β -D-glucopyranoside (13)



25 1.5 eq donor and 1.0 eq acceptor were cross-coupled under the standard conditions. The crude product was purified by flash chromatography to give 175 mg (quantitative) of the disaccharide as α/β mixture. Due to the multiple conformations in slow equilibrium it was not possible to obtain sharp NMR spectres. In order to analyse the disaccharide it was desilylated and acetylated following the standard procedure.

HRMS(ES) m/z calcd. for $C_{49}H_{81}NO_{11}Si_3Na$: 954.5015, m/z found: 954.4988

Phenyl 4-*O*-(2,3,4-tri-*O*-benzyl-6-*O*-(2,3,4-tri-*O*-*t*-butyldimethylsilyl-6-*O*-benzyl- β -D-glycopyranosyl)- α -D-glucopyranosyl)-2,3-di-*O*-acetyl-6-*O*-benzyl-1-thio- β -D-glucopyranoside (16)



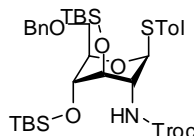
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The "super armed" donor **14** (140 mg, 0.20 mmol), the armed acceptor **4** (98 mg, 0.18 mmol) and the disarmed acceptor **15** (96 mg, 0.22 mmol) were coevaporated with toluene (3 times) and dried under vacuum overnight together with powdered 4 Å ms and NIS (89 mg, 0.40 mmol) in a separate container. The sugar building blocks were dissolved in CH_2Cl_2 (5 mL) and stirred 2 h at rt before it was cooled to $-88\text{ }^\circ\text{C}$, where NIS was added together with TfOH (5 μL). The reaction was slowly warmed to $-50\text{ }^\circ\text{C}$ where it was quenched by addition of Et_3N , filtered and diluted with EtOAc. The organic phase was washed with HCl (1M), $NaHSO_3$ (sat), $NaHCO_3$ (sat.) and brine followed by drying ($MgSO_4$) and concentration *in vacuo* to give the crude product, which was purified by flash chromatography (pentane/EtOAc 50:1 to 15:1) to give the title product together with the trisaccharide **15** missing a TBS group and a small portion lacking two TBS groups (adjusted yield 163 mg, 64 %).

$^1\text{H-NMR}$ (400 MHz, $CDCl_3$): δ 7.50 (m, 2 H), 7.35-7.15 (m, 28 H), 5.28 (t, $J = 9.2$ Hz, 1 H), 4.93 (d, $J = 3.7$ Hz, 1 H), 4.91 (t, $J = 9.2$ Hz, 1 H), 4.84 (d, $J = 11.2$ Hz, 1 H), 4.79 (d, $J = 11.0$ Hz, 1 H), 4.73 (d, $J = 11.2$ Hz, 1 H), 4.61-4.51 (m, 3 H), 4.49 (d, $J = 12.1$ Hz, 1 H), 4.47 (d, $J = 11.9$ Hz, 1 H), 4.45 (d, $J = 12.1$ Hz, 1 H), 4.07 (dd, $J = 3.8$ Hz, 11.3 Hz, 1 H), 3.94 (t, $J = 9.3$ Hz, 1 H), 3.94 (m, 2 H), 3.86 (t, $J = 9.3$ Hz, 1 H), 3.82-3.70 (m, 4 H), 3.59 (m, 2 H), 3.52 (m, 2 H), 3.36 (dd, $J = 4.9$ Hz, 9.9 Hz, 1 H), 3.34 (bd, $J = 9.7$ Hz, 1 H), 2.05 (s, 3 H), 1.83 (s, 3 H), 0.83 (s, 18 H), 0.81 (s, 9 H), 0.04 (s, 3 H), 0.04 (s, 3 H), 0.01 (s, 9 H), 0.00 (s, 3 H); $^{13}\text{C-NMR}$ (100 MHz, $CDCl_3$): δ 170.2, 169.6, 139.1, 138.6, 138.5, 138.4, 138.0, 133.1, 132.2, 128.9, 128.5, 128.5 (2 C), 128.4, 128.4, 128.3, 128.2, 128.1, 127.9 (2 C), 127.9, 127.7, 127.6, 127.6, 127.6, 127.4, 103.5 ($J_{\text{CH}} = 161$ Hz, C-1''), 98.0 ($J_{\text{CH}} = 166$ Hz, C-1'), 85.4 (25 C-1), 81.2, 80.2, 80.1, 79.5, 78.6, 78.2, 77.0, 75.5, 75.4, 75.3, 74.8, 73.2, 73.1, 73.0, 71.8, 71.4, 70.8, 70.7, 69.5, 69.0, 26.0, 25.9, 25.9, 21.0, 20.9, 18.1, 18.0, 18.0, -3.8, -4.1, -4.3, -4.5, -4.5, -4.7

HRMS(ES) m/z calcd. for $C_{81}H_{122}O_{17}SSi_3Na$: 1495.6826, m/z found: 1495.6313

***p*-Methylphenyl 6-*O*-benzyl-3,4-tetra-*O*-^tbutyldimethylsilyl-2-deoxy-2-[[[(2,2,2-trichloroethoxy)carbonyl]amino]-1-thio- β -D-glucopyranoside (17)**

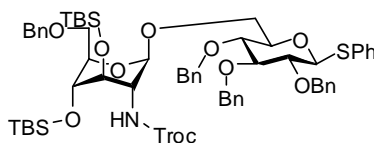


p-Methylphenyl 2-deoxy-2-[[[(2,2,2-trichloroethoxy)carbonyl]amino]-6-*O*-benzyl-1-thio- β -D-glucopyranoside (0.540 mg, 0.98 mmol) was together with DMAP (40 mg) dissolved in pyridine (5 mL) and cooled to 0 °C, where after TBSOTf (1.04 g, 0.40 mmol, 0.9 mL) was added by syringe. The reaction mixture was heated to 60 °C overnight and worked up. A regioisomeric mixture was isolated and the reaction procedure was repeated. After aqueous workup the crude product was purified by flash chromatography to give app. 20 % of the desired product together with a mixture of product and 10 byproducts.

¹H-NMR (400 MHz, CDCl₃): δ 7.43 (d, *J* = 8.0 Hz, 2 H), 7.35-7.25 (m, 5 H), 7.09 (d, *J* = 8.0 Hz, 2 H), 6.36 (d, *J* = 9.7 Hz, 1 H, NH), 5.09 (d, *J* = 4.0 Hz, 1 H, H-1), 4.80 (d, *J* = 11.9 Hz, 1 H), 4.62 (d, *J* = 11.9 Hz, 1 H), 4.57 (d, *J* = 11.8 Hz, 1 H), 5.54 (d, *J* = 11.8 Hz, 1 H), 4.18 (dd, *J* = 8.7 Hz, 8.7 Hz, 1 H), 4.09 (m, 2 H), 3.97 (dd, *J* = 5.4 Hz, 8.8 Hz, 1 H), 3.93 (bd, *J* = 3.3 Hz, 1 H), 3.87 (bs, 1 H), 2.32 (s, 3 15 H), 0.93 (s, 9 H), 0.93 (s, 9 H), 0.14 (s, 3 H), 0.12 (s, 6 H), 0.10 (s, 3 H); ¹³C-NMR (100 MHz, CDCl₃): δ 153.7, 138.4, 137.2, 132.6, 131.8, 129.7, 128.3, 127.6 (2 C), 95.6, 85.0, 79.7, 74.7, 73.3, 71.5, 71.2, 69.5, 54.5, 25.9, 21.2, 18.2, 17.9, -4.7, -4.8, -4.8, -4.9

HRMS(ES) *m/z* calcd. for C₃₅H₅₄Cl₃NO₆SSi₂Na: 800.2174, *m/z* found: 800.2202

20 Phenyl 6-*O*-(2-deoxy-2-[[[(2,2,2-trichloroethoxy)carbonyl]amino]-6-*O*-benzyl-3,4-di-*O*-^tbutyldimethylsilyl- β -D-glucopyranosyl)-2,3,4-tri-*O*-benzyl-1-thio- β -D-glucopyranoside (18)



Following the standard procedure **18** was obtained (85%, only β).

¹H-NMR (400 MHz, CDCl₃): δ 7.39 (m, 4 H), 7.32-7.19 (m, 18 H), 7.04 (d, *J* = 8.0 Hz, 2 H), 6.33 (d, *J* = 9.7 Hz, 1 H), 4.92 (d, *J* = 11.2 Hz, 1 H), 4.92 (d, *J* = 12.0 Hz, 1 H), 4.88 (d, *J* = 11.2 Hz), 4.87 (d, *J* = 10.8 Hz, 1 H), 4.76 (bs, 1 H), 4.75 (d, *J* = 10.8 Hz, 1 H), 4.68 (d, *J* = 11.9 Hz, 1 H), 4.63 (d, *J* = 11.9 Hz, 1 H), 4.62 (d, *J* = 12.0 Hz, 1 H), 4.61 (d, *J* = 9.7 Hz, 1 H), 4.43 (s, 2 H), 4.18 (d, *J* = 10.3 Hz, 1 H), 4.09 (t, *J* = 8.7 Hz, 1 H), 3.99 (dbb, *J* = 6.4 Hz, 8.1 Hz, 1 H), 3.87 (m, 2 H), 3.83 (dd, *J* = 5.9 Hz, 9.0

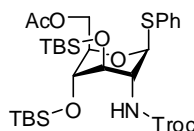
Hz, 1 H), 3.80 (bs, 1 H), 3.68 (m, 2 H), 3.58 (dd, $J = 4.4$ Hz, 10.9 Hz, 1 H), 3.42 (m, 2 H), 2.27 (s, 3 H), 0.92 (s, 9H), 0.91 (s, 9 H), 0.14 (s, 3 H), 0.10 (s, 6 H), 0.09 (s, 3 H)

^{13}C -NMR (100 MHz, CDCl_3): δ 153.8, 138.8, 138.8, 138.2, 138.2, 137.4, 131.9, 131.0, 129.8, 128.6, 128.5, 128.5, 128.4, 128.3, 128.2, 128.1, 128.1, 128.0, 127.9, 127.8, 127.6, 127.4, 127.3, 100.4, 95.6, 5 88.8, 86.9, 81.4, 78.5, 77.6, 77.0, 75.6, 75.6, 75.2, 74.7, 72.9, 71.3, 70.3, 69.3, 68.0, 52.7, 26.0, 25.9, 21.2, 18.1, 18.0, -4.6, -4.7, -4.8, -4.8,

HRMS(ES) m/z calcd. for $\text{C}_{61}\text{H}_{80}\text{Cl}_3\text{NO}_{11}\text{SSi}_2\text{Na}$: 1218.3954, m/z found: 1218.4012

$^3J_{\text{CH}} = 154$ Hz of the desilylated disaccharide.

10 Phenyl 6-*O*-acetyl-3,4-di-*O*-di-^tButyldimethylsilyl-2-deoxy-2-[(2,2,2-trichloroethoxy)carbonyl]amino]-1-thio-D-glucopyranoside (19)

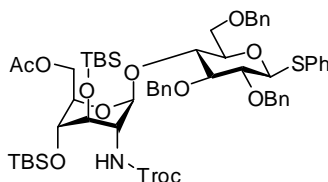


^1H -NMR (400 MHz, CDCl_3): δ 7.53 (d, $J = 7.4$ Hz, 2 H), 7.30-7.20 (m, 3 H), 6.44 (d, $J = 9.7$ Hz, 1 H, NH), 5.22 (d, $J = 3.2$ Hz, 1 H, H-1), 4.76 (d, $J = 11.9$ Hz, 1 H), 4.75-4.65 (m, 2 H), 4.63 (d, $J = 11.9$ Hz, 1 H), 4.11 (m, 1 H), 4.09 (t, $J = 7.3$ Hz, 1 H), 3.88 (dd, $J = 2.6$ Hz, 2.7 Hz, 1 H), 3.81 (d, $J = 3.3$ Hz, 1 H), 2.02 (s, 3 H), 0.94 (2 s, 18 H), 0.17 (s, 3 H), 0.14 (s, 3 H), 0.13 (s, 6 H); ^{13}C -NMR (100 MHz, CDCl_3): δ 170.3, 153.6, 136.4, 131.0, 128.9, 127.1, 95.5, 84.4, 78.0, 74.7, 70.6, 69.2, 64.7, 54.3, 25.8, 25.8, 20.8, 18.1, 17.9, -4.8 (2 C), -4.9, -5.0

HRMS(ES) m/z calcd. for $\text{C}_{29}\text{H}_{48}\text{Cl}_3\text{NO}_7\text{SSi}_2\text{Na}$: 738.1653, m/z found: 738.1635

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Phenyl 4-*O*-(6-*O*-acetyl-2-deoxy-2-[(2,2,2-trichloroethoxy)carbonyl]amino)-3,4-di-*O*-^tButyldimethylsilyl- β -D-glucopyranosyl)-2,3,6-tri-*O*-benzyl-1-thio- β -D-glucopyranoside (20)



Standard procedure was giving 67% of the β -disaccharide.

25 ^1H -NMR (400 MHz, CDCl_3): δ 7.55 (m, 2 H), 7.38-7.19 (m, 18 H), 5.59 (d, $J = 10.2$ Hz, 1 H), 5.10 (d, $J = 10.6$ Hz, 1 H), 4.93 (d, $J = 5.6$ Hz, 1 H), 4.83 (d, $J = 11.9$ Hz, 1 H), 4.81 (d, $J = 10.2$ Hz, 1 H), 4.76 (d, $J = 11.3$ Hz, 1 H), 4.74 (d, $J = 10.6$ Hz, 1 H), 4.59 (d, $J = 11.9$ Hz, 1 H), 4.63 (m, 2 H), 4.27 (dd, $J = 8.4$ Hz, 8.9 Hz, 1 H), 4.19 (dd, $J = 6.0$ Hz, 10.6 Hz, 1 H), 3.94 (t, $J = 9.4$ Hz, 1 H), 3.86 (m, 2 H),

3.78 (m, 3 H), 3.71 (t, $J = 8.9$ Hz, 1 H), 3.49 (dd, $J = 9.1$ Hz, 9.3 Hz, 1 H), 3.45 (bd, $J = 9.9$ Hz, 1 H), 1.99 (s, 3 H), 0.89 (s, 9 H), 0.86 (s, 9 H), 0.12 (s, 3 H), 0.08 (s, 6 H), 0.03 (s, 3 H); ^{13}C -NMR (100 MHz, CDCl_3): δ 170.3, 153.7, 138.9, 138.4, 138.3, 133.6, 132.3, 128.9, 128.4, 128.4, 128.3, 128.2, 128.0, 127.8, 127.6, 127.5, 127.5, 109.9, 102.0, 95.7, 87.4, 85.0, 80.6, 79.2, 78.6, 77.7, 75.4, 74.9, 5 74.6, 73.3, 70.1, 68.3, 65.2, 57.1, 25.9, 25.8, 20.9, 18.1, 17.9, -4.6, -4.7, -4.8, -5.0
MS(ES) m/z calcd. for $\text{C}_{56}\text{H}_{76}\text{Cl}_3\text{NO}_{12}\text{SSi}_2\text{Na}$: 1170.3590, m/z found: 1170.3611

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