S-BenzoxazolyI (SBox) glycosides as novel, versatile glycosyl donors for stereoselective 1,2-*cis* glycosylation

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Preparation of the glycosyl donors, SBox glycosides

Synthesis of 2a: Solution of **1a** (2.0 mmol) in dry toluene was added dropwise to a stirred mixture of 2-mercaptobenzoxazole (2.4 mmol) and K₂CO₃ (2.4 mmol) in dry acetone at 40°C. The reaction mixture was kept for 2h at 40°C and then for 16 h at rt. Upon completion, mixture was diluted with toluene and washed with 1% aq. NaOH and water, the organic phase was separated, dried and concentrated *in vacuo*. The residue was purified by silica gel column chromatography.

Analytical data for **2a**: ¹H-n.m.r: 7.10-7.65 (m, 9H), 5.54 (d, 1H, J=10.0 Hz), 5.35 (dd, 1H, J=9.2 Hz), 5.08 (dd, 1H, J=9.2 Hz), 4.73 (dd, 2H, J=11.2 Hz), 4.27 (dd, 1H, J=4.8, J=12.4 Hz), 4.12 (dd, 1H, J=2.2, J=12.4 Hz), 3.92 (m, 2H), 2.04, 2.00, 1.96 (3 s, 9H) ppm; ¹³C-n.m.r: 170.79, 170.11, 169.94, 160.90, 152.09, 141.92, 137.21, 128.69, 128.69, 128.33, 128.33, 124.78, 124.71, 119.27, 110.31, 84.79, 78.31, 77.43, 76.41, 75.86, 75.46,

68.51, 62.12, 20.91, 20.84, 20.84 ppm, HR-FAB MS $[M + H]^+$ calcd for $C_{26}H_{28}NO_9S$ 530.1485, found 530.1487.

Synthesis of 2b: SBox galactoside **2b** was obtained from **1b** as described for the synthesis of **2a**. Analytical data for **2b**: 1H -n.m.r: 7.27-7.66 (m, 9H), 5.60 (d, 1H, $J=10.0$ Hz), 5.49 (d, 1H, $J=3.3$ Hz), 5.17 (dd, 1H, $J=9.7$ Hz), 4.78 (dd, 2H, $J=11.0$ Hz), 4.13 (ps, 3H), 3.98 (dd, 1H, $J=10.0$ Hz), 2.17, 1.99, 1.98 (3 s, 9H) ppm; ^{13}C -n.m.r: 170.53, 170.27, 169.96, 161.11, 152.08, 141.93, 137.42, 128.58, 128.21, 128.09, 124.74, 124.66, 119.21, 110.26, 85.21, 75.78, 75.51, 75.05, 74.34, 69.69, 67.78, 61.50, 54.01, 31.92, 29.58, 29.47, 20.84, 20.78 ppm, HR-FAB MS $[M + H]^+$ calcd for $C_{26}H_{28}NO_9S$ 530.1485, found 530.1487.

Preparation of di-and trisaccharides

Typical MeOTf-promoted glycosylation procedure: a mixture the glycosyl donor (0.11 mmol), glycosyl acceptor (0.10 mmol), and freshly activated molecular sieves ($3\text{\AA}$, 200 mg) in CH_2Cl_2 (2 mL) was stirred for 2 h under an atmosphere of argon. MeOTf (0.33 mmol) was added and the reaction mixture was stirred for 2-24 h at room temperature; then Et_3N (0.5 mL) was added, mixture was diluted with CH_2Cl_2 (30 mL), the solid was filtered-off and the residue was washed with CH_2Cl_2 . The combined filtrate was washed with water, the organic phase was separated, dried, filtered and the filtrate was concentrated *in vacuo*. Crude residue was purified by size exclusion column chromatography on Sephadex LH-20.

Typical AgOTf-promoted glycosylation procedure: a mixture the glycosyl donor (0.11 mmol), glycosyl acceptor (0.10 mmol), and freshly activated molecular sieves ($3\text{\AA}$, 200

mg) in CH₂Cl₂ (2 mL) was stirred for 1.5 h under an atmosphere of argon. Freshly conditioned AgOTf (0.22 mmol) was added and the reaction mixture was stirred for 1 - 2 h at rt, then diluted with CH₂Cl₂, the solid was filtered-off and the residue was washed with CH₂Cl₂. The combined filtrate was washed with 20% aq. NaHCO₃ and water, the organic phase was separated, dried and concentrated *in vacuo*. The residue was purified by size exclusion column chromatography on Sephadex LH-20. All synthesized di- and trisaccharides have adequate ¹H-, ¹³C-n.m.r., and HRMS data.

Analytical data for **11** prepared from **2a** and **10** in the presence of AgOTf: ¹H-n.m.r: 7.20-8.10 (m, 20H), 5.90 (d, 1H, J=3.3 Hz), 5.81 (dd, 1H, J=5.0 Hz), 5.60 (dd, 1H, J=3.3, J=10.0 Hz), 5.44 (dd, 1H, J=9.6 Hz), 4.97 (dd, 1H, J=10.4 Hz), 4.85 (d, 1H, J=10.0 Hz), 4.77 (d, 1H, J=3.5 Hz), 4.62 (dd, 2H, J=12.5 Hz), 4.24-4.30 (m, 2H), 4.17 (m, 1H), 4.04 (dd, 1H, J=2.0, J=12.4 Hz), 3.86 (dd, 1H, J=7.2, 10.4 Hz), 3.74 (ps, 2H), 3.54-3.65 (m, 2H), 2.84 (m, 2H), 2.18, 2.01, 2.01 (3 s, 9H), 1.35 (dd, 3H) ppm; ¹³C-n.m.r: 170.77, 170.24, 169.94, 165.82, 165.61, 165.56, 137.80, 133.89, 133.49, 133.42, 130.11, 129.91, 129.44, 129.01, 128.90, 128.72, 128.57, 128.46, 128.31, 128.21, 96.90, 84.42, 76.73, 76.58, 73.27, 73.00, 71.98, 69.68, 69.29, 68.65, 68.52, 67.60, 67.27, 62.04, 54.01, 32.10, 31.91, 29.87, 29.57, 29.46, 24.88, 21.00, 20.84, 20.82 ppm, HR-FAB MS [M + Na]⁺ calcd for C₄₈H₅₀NaO₁₆S 937.2717, found 937.2717.

Analytical data for **13** prepared from **2a** and **12** in the presence of AgOTf (obtained as an anomeric mixture, α/β 8/1): ¹H-n.m.r: 7.20-7.40 (m, 20H), 5.83 (m, 1H), 5.46 (dd, 1H, J=9.6 Hz), 4.58-5.09 (m, 13H), 4.38 (d, 1H, 7.8 Hz), 4.24 (dd, 1H, J=3.4 Hz), 3.90-4.04

(m, 3H), 3.78 (pd, 2H), 3.38-3.68 (m, 7H), 3.27 (dd, 1H, J=7.8 Hz), 2.18 (m, 2H), 2.07, 2.02, 2.01 (3 s, 9H), 1.76 (m, 2H) ppm; selected ^{13}C -n.m.r. data: 109.92, 97.23 ppm, HR-FAB MS $[\text{M} + \text{Na}]^+$ calcd for $\text{C}_{51}\text{H}_{60}\text{NaO}_{14}$ 919.3881, found 919.3893.

Analytical data for **14** prepared from **11** and **12** in the presence of MeOTf: ^1H -n.m.r.: 7.10-8.15 (m, 35H), 5.87 (dd, 1H, J=3.2 Hz), 5.76-5.84 (m, 2H), 5.53 (dd, 1H, J=3.5, J=10.4 Hz), 5.42 (dd, 1H, J=9.6 Hz), 4.78-5.03 (m, 7H), 4.44-4.67 (m, 6H), 4.22-4.29 (m, 3H), 3.97-4.12 (m, 3H), 3.80-3.86 (m, 3H), 3.63 (dd, 1H, J=6.0, J=10.5 Hz), 3.51-3.56 (m, 2H), 3.31-3.46 (m, 4H), 2.05-2.18 (m, 2H), 1.98, 1.97, 1.94 (3 s, 9H), 1.61-1.74 (m, 2H) ppm; ^{13}C -n.m.r.: 170.72, 170.16, 169.93, 165.87, 165.57, 165.40, 138.76, 138.61, 138.24, 137.85, 133.84, 133.39, 130.25, 129.94, 129.86, 129.22, 128.88, 128.67, 128.56, 128.48, 128.27, 127.96, 127.86, 127.72, 115.17, 103.71, 101.81, 97.23, 84.73, 82.28, 77.82, 76.60, 75.65, 75.06, 74.92, 73.10, 72.58, 71.96, 70.15, 69.44, 68.84, 68.71, 68.36, 67.75, 66.60, 61.97, 32.12, 30.43, 29.90, 29.09, 21.00, 20.83 ppm, HR-FAB MS $[\text{M} + \text{Na}]^+$ calcd for $\text{C}_{78}\text{H}_{82}\text{NaO}_{22}$ 1393.5196, found 1393.5216.

Protecting group compatibility studies

In order to further evaluate the versatility of the SBox glycosides for block oligosaccharide synthesis and their ability to withstand rather harsh reaction conditions associated with major protecting group manipulations, we performed a number of pilot experiments. Thus, SBox derivatives were found to be compatible with typical acetylation (Ac_2O /Pyridine), deacetylation (MeONa/MeOH), benzylation (BnBr/NaH , DMF), triphenylmethylation ($\text{TrCl}/\text{Pyridine}$), as well benzylidene acetal formation $\{\text{PhCH}(\text{OMe})_2, \text{CSA}\}$ and cleavage ($20\% \text{ TFA}/\text{CH}_2\text{Cl}_2$) conditions (see Scheme below).

Current Data Parameters
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 PROCNO 1

F2 - Acquisition Parameters
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 SOLVENT CDCl3
 NS 32
 DS 2
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 FIDRES 0.158946 Hz
 AQ 3.145779 sec
 RG 715
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 NUCLEUS 1H

F2 - Processing Parameters
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1D NMR plot parameters
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 F2P 1.800 ppm
 F2 900.23 Hz
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 HZCM 163.78697 Hz/cm

Current Data Parameters

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PROCNO	1

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 SOLVENT CDCl3
 NS 32

DS 2
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 NUCLEUS 1H

F2 - Processing parameters

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PC	1.00

1D NMR plot parameters

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 PROCNO 1

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 DS 2
 SMH 6578.947 Hz
 FIDRES 0.100387 Hz
 AQ 4.9807858 sec
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 NUCLEUS ¹H

F2 - Processing parameters
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1D NMR plot parameters
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 F2P -0.025 ppm
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 HZCM 206.22749 Hz/cm

14

Current Data Parameters
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EXPNO 2
PROCNO 1

F2 - Acquisition Parameters
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TD 65536
SOLVENT CDCl3
NS 2048
DS 4
SWH 25000.000 Hz
FIDRES 0.381470 Hz
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DE 25.00 usec
TE 300.0 K
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DL6 50.00 dB
D1 2.00000000 sec
CPDPRG waitz16
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D11 0.0300000 sec
DL5 18.00 dB
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SF01 125.7684284 MHz
NUCLEUS 13C

F2 - Processing parameters
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SSB 0
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GB 0
PC 1.40

1D NMR plot parameters
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