Stereoselective Synthesis of 2-*S*-Phenyl-2-deoxy-β-glycosides Using Phenyl 2,3-*O*-Thionocarbonyl-1-thio-glycoside Donors via 1,2-Migration and Concurrent Glycosidation

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Supporting Information

General Remarks. Solvents were distilled from the appropriate drying agents before use. Unless stated otherwise, all reactions were carried out under a positive pressure of argon and were monitored by TLC on silica gel HF_{254} (0.5 mm, Qingdao, China). Spots were detected under UV light or by charging with 10% H_2SO_4 in MeOH. Flash column chromatography was carried out on silica gel H (400 mesh, Qingdao, China). Optical rotations were measured on a Perkin-Elmer 241 MC polarimeter. ^{1}H NMR spectra were recorded on a Bruker AM-300 spectrometer using $CDCl_3$ as solvent and tetramethylsilane as internal reference. Mass spectra were recorded on a HP5989A mass spectrometer.

Phenyl 4-*O*-methyl-2,3-*O*-thionocarbonyl-1-thio-α-L-rhamnopyranoside (2). A solution of **1** (0.85 g, 3.14 mmol) and 1,1'-thiocarbonyldiimidazole (tech. 90%. 0.84 g, 4.72 mmol) in dry tetrahydrofuran (11 mL) under nitrogen was refluxed for 2 h. Tetrahydrofuran was then removed in vacuo. The residue was applied to a silica gel column chromatography (petroleum ether-ethyl acetate 12:1) to give **2** (798 mg, 81%) as a white amorphous solid. $[\alpha]_D^{20}$ = -218.5 ^{o} (*c* 1.0, $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.46-7.32 (m, 5 H), 5.82 (s, 1 H), 4.95 (m, 2 H), 4.14 (m, 1 H), 3.58 (s, 3 H), 3.16 (dd, 1H, *J* = 9.6, 6.1), 1.28 (d, 3 H, *J* = 6.1). ^{13}C NMR (150 MHz, $CDCl_3$): δ 17.45, 59.70, 65.68, 81.45, 81.70, 81.89, 82.83, 128.53, 129.36, 131.50, 132.61, 189.80. EIMS (m/z, %): 312 (M^+, 3.0), 235 (M^+-Ph, 79.8), 203 (M^+-SPh, 58.0). IR (film): 2993, 2979, 2938, 2914, 2828 cm^{-1} . Anal. Calcd for $C_{14}H_{16}O_4S_2$: C, 53.82; H, 5.16. Found: C, 54.22; H, 5.24.

A typical procedure for the reaction of the Phenyl 4-*O*-methyl-2,3-*O*-thionocarbonyl-1-thio-α-L-rhamnopyranoside (2) with alcohol acceptors.

A solution of donor **2** (60 mg ~ 210 mg, 1.0 or 1.2 equiv), an alcohol acceptor (30 mg ~ 150 mg, 1.2 or 1.0 equiv), (with or without) 2,6-di-tert-butyl-4-methylpyridine (1.5 equiv), and 4Å MS (300 mg ~ 1.0 g) in anhydrous CH_2Cl_2 (2 mL ~ 6 mL) was stirred at room temperature under argon for 1 h, followed by the addition of a solution of MeOTf in CH_2Cl_2 (1.0 M, 1.2 equiv). After being stirred for 5 h at rt, the reaction mixture was diluted with dichloromethane, and filtered through a pad of celite. The filtrates were concentrated, and the residue was applied to a silica gel column chromatography with petroleum ether – ethyl acetate as eluent to give the corresponding 2-thioglycosides as a white amorphous solid.

Benzyl 3-*O*-(methylthio)carbonyl-4-*O*-methyl-2-*S*-phenyl-2,6-di-deoxy-β-L-glucopyranoside (6). $[\alpha]_D^{20} = +12.2^{o}$ (*c* 1.0, $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.56-7.20 (m, 10 H), 5.06 (dd, 1H, *J* = 11.4, 8.9), 4.87 (dd, 1 H, *J* = 11.7, 1.3), 4.60 (dd, 1H, *J* = 11.8, 1.4), 4.35 (dd, 1 H, *J* = 8.9, 1.4), 3.46 (s, 3 H), 3.31 (m, 1 H), 3.08 (dd, 1 H, *J* = 11.4, 8.8), 2.94 (t, 1 H, *J* = 9.1), 2.41 (s, 3 H), 1.34 (d, 3 H, *J* = 7.5). EIMS (m/z, %): 434 (M^+, 8.7), 343 (M^+-Bn or-OC(O)SMe, 5.9), 91 (Bn or OC(O)SMe, 100). IR (film): 2932, 2861, 1712, 1498, 1475 cm^{-1}.

Cyclohexanyl 3-*O*-(methylthio)carbonyl-4-*O*-methyl-2-*S*-phenyl-2,6-di-deoxy-β-L-glucopyranoside (7). $[\alpha]_D^{20} = +32.3^{o}$ (*c* 1.2, $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.57-7.23 (m, 5 H), 5.08 (dd, 1 H, *J* = 11.5, 8.8), 4.45 (d, 1 H, *J* = 8.8), 3.65 (m, 1 H), 3.48 (s, 3 H), 3.35 (m, 1 H), 3.08 (dd, 1 H, *J* = 11.5, 8.8), 2.94 (t, 1 H, *J* = 9.1), 2.40 (s, 3 H), 1.84 (m, 2 H), 1.68 (m, 2 H), 1.50-1.16 (m, 9 H). EIMS (m/z, %): 426 (M^+, 7.8), 327 (M^+-$OCH(CH_2)_5$, 0.6), 207 (M^+-SPh-OC(O)SMe-H_2O, 100). IR (film): 2935, 2856, 1722, 1584, 1481, 1450 cm^{-1}.

Cholesteryl 3-*O*-(methylthio)carbonyl-4-*O*-methyl-2-*S*-phenyl-2,6-di-deoxy-β-L-glucopyranoside (8). $[\alpha]_D^{20} = -14.5^{o}$ (*c* 1.0, $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.54-7.12 (m, 5 H), 5.34 (m, 1 H), 5.08 (dd, 1 H, *J* = 11.3, 9.1), 4.45 (d, 1 H, *J* = 8.8), 3.54 (m, 1 H), 3.48 (s, 3 H), 3.34 (m, 1 H), 3.08 (dd, 1 H, *J* = 11.5, 8.8), 2.94 (t, 1 H, *J*

= 9.1), 2.40 (s, 3 H), 2.38-2.19 (m, 2 H), 2.08-0.64 (m, 44 H). EIMS (m/z, %): 695 (M^+-H_2O, 9.9), 449 (91.9), 169 (92.6), 69 (100). IR (film): 2935, 2870, 1717, 1440 cm^{-1}. Anal. Calcd for $C_{42}H_{64}O_5S_2$: C, 70.74; H, 9.05. Found: C, 71.05; H, 8.77.

Phenyl 3-*O*-(methylthio)carbonyl-4-*O*-methyl-2-*S*-phenyl-2,6-di-deoxy-β-L-glucopyranosyl-(1→4)-2,3-*O*-isopropylidene-1-thio-α-L-rhamnopyranoside (9). $[\alpha]_D^{20}$ = -107.1 ° (*c* 1.1, $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.48-7.25 (m, 10 H), 5.69 (s, 1 H), 5.10 (dd, 1 H, *J* = 11.5, 8.8), 4.56 (d, 1 H, *J* = 8.8), 4.29 (d, 1 H, *J* = 5.5), 4.15 (dd, 1 H, *J* = 7.1, 5.8), 4.03 (m, 1 H), 3.55 (dd, 1 H, *J* = 9.6, 7.7), 3.48 (s, 3 H), 3.37 (m, 1 H), 3.22 (dd, 1 H, *J* = 11.3, 9.1), 3.02 (t, 1 H, *J* = 9.1), 2.40 (s, 3 H), 1.51, 1.34 (s × 2, 3 H × 2), 1.36-1.26 (m, 6 H). EIMS (m/z, %): 607 (M^+-Me, 0.3), 513 (M^+-SPh, 24.6). IR (film): 2984, 2935, 1721, 1584, 1480, 1440 cm^{-1}. Anal. Calcd for $C_{30}H_{38}O_8S_3 \cdot 0.5H_2O$: C, 57.03; H, 6.22. Found: C, 57.17; H, 6.26.

3-*O*-(Methylthio)carbonyl-4-*O*-methyl-2-*S*-phenyl-2,6-di-deoxy-β-L-glucopyranosyl-(1→6)-1,2;3,4-di-*O*-isopropylidene-α-D-galactopyranoside (10). $[\alpha]_D^{20}$ = -23.9 ° (*c* 1.0, $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.63, 7.28 (m each, 5 H), 5.52 (d, 1 H, *J* = 5.0), 5.05 (dd, 1 H, *J* = 11.3, 8.8), 4.56 (dd, 1 H, *J* = 8.0, 2.5), 4.32-4.24 (m, 3 H), 4.02-3.92 (m, 2 H), 3.73 (m, 1 H), 3.46 (s, 3 H), 3.27 (m, 1 H), 2.98 (dd, 1 H, *J* = 11.3, 8.8), 2.91 (t, 1 H, *J* = 9.1), 2.40 (s, 3 H), 1.48-1.26 (m, 15 H). EIMS (m/z, %): 586 (M^+, 22.3), 571 (M^+-Me, 3.0). IR (film): 2988, 2937, 1722, 1475, 1458, 1440 cm^{-1}. Anal. Calcd for $C_{27}H_{38}O_{10}S_2 \cdot 0.5H_2O$: C, 54.43; H, 6.60. Found: C, 54.08; H, 6.34.

Benzyl 3-*O*-(methylthio)carbonyl-4-*O*-methyl-2-*S*-phenyl-2,6-di-deoxy-β-L-glucopyranosyl-(1→3)-2,4-di-*O*-benzoyl-α-D-xylopyranoside (11). $[\alpha]_D^{20}$ = +62.7 ° (*c* 1.1, $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.15-7.14 (m, 20 H), 5.22-5.13 (m, 2 H), 5.04 (dd, 1 H, *J* = 9.1, 3.7), 4.89 (dd, 1 H, *J* = 11.4, 8.9), 4.76 (d, 1 H, *J* = 12.3), 4.67 (d, 1 H, *J* = 8.9), 4.62 (t, 1 H, *J* = 9.1), 4.52 (d, 1 H, *J* = 12.3), 3.98 (t, 1 H, *J* = 11.0), 3.75 (t, 1 H, *J* = 10.4), 3.39 (s, 3 H), 3.26 (m, 1 H), 2.95 (dd, 1 H, *J* = 11.4, 8.9), 2.78 (t, 1 H, *J* = 9.2), 2.30 (s, 3 H), 1.19 (d, 3 H, *J* = 6.1). EIMS (m/z, %): 774 (M^+, 8.0), 226 (57.6), 207 (50.6), 105 (Bz,100). IR (film): 1725, 1602, 1585, 1453 cm^{-1}.

Phenyl 3-*O*-(methylthio)carbonyl-4-*O*-methyl-2-*S*-phenyl-2,6-di-deoxy-β-L-

glucopyranosyl-(1→4)-2,3-*O*-thionocarbonyl-1-thio-α-L-rhamnopyranoside (12). Compound **9** (112 mg, 0.18 mmol) was dissolved in 80% HOAc (20 mL). After being stirred at 50 ^{o}C for 8 h, the solution was concentrated in vacuo. The residue was purified by flash column chromatography (petroleum ether – ethyl acetate 2:1) to give a white amorphous solid (104 mg, 99%). A solution of the solid (56 mg, 0.096 mmol), 1,1'- thiocarbonyldiimidazole (21 mg, 0.115 mmol) and DMAP (26 mg, 0.211 mmol) was dissolved in dry DMF (1.5 mL). After being stirred at 55 ^{o}C for 2 h, the mixture was diluted with ethyl acetate. The organic layer, washed with water and brine, respectively, was dried over anhydrous Na_2SO_4, and then filtered and concentrated in vacuo. The residue was purified by flash column chromatography (petroleum ether–ethyl acetate 7:1) to give **12** (41 mg, 69%) as a white amorphous solid. $[\alpha]_D^{20} = -66.0^{o}$ (*c* 1.1, $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.48-7.27 (m, 10 H), 5.78 (s, 1 H), 5.14-5.06 (m, 2 H), 4.95 (d, 1 H, *J* = 7.1), 4.50 (d, 1 H, *J* = 9.1), 4.13 (m, 1 H), 3.58 (dd, 1 H, *J* = 9.6, 6.6), 3.52-3.41 (m, 4 H), 3.17 (dd, 1 H, *J* = 11.5, 9.1), 2.99 (t, 1 H, *J* = 9.1), 2.38 (s, 3 H), 1.41, 1.32 (d each, 3 H each, *J* = 6.1). EIMS (m/z, %): 624 (M^+, 12.0), 235 (90.0), 220 (97.0). IR (film): 2978, 2934, 1718, 1584, 1479, 1440 cm^{-1}. Anal. Calcd for $C_{28}H_{32}O_8S_4$: C, 53.82; H, 5.16. Found: C, 54.14; H, 5.40.

Phenyl 4-*O*-methyl-2-*S*-phenyl-2,6-di-deoxy-β-L-glucopyranosyl-(1→4)-2,3-*O*-isopropylidene-1-thio-α-L-rhamnopyranoside (13).

To a stirred solution of **9** (27 mg, 0.043 mmol) in MeOH (4 mL) was added sodium methoxide 50wt% solution in methanol (9 mg, 0.083 mmol). After being stirred at 60 ^{o}C for 3 days, the reaction mixture was diluted with ethyl acetate. The organic layer, washed with water and brine, respectively, was dried over anhydrous Na_2SO_4, and then filtered and concentrated in vacuo. The residue was purified by flash column chromatography (petroleum ether–ethyl acetate 4:1) to give **13** (22 mg, 93%) as a colorless syrup. $[\alpha]_D^{20} = -151.7^{o}$ (*c* 0.7, $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.53-7.26 (m, 10 H), 5.70 (s, 1 H), 4.51 (d, 1 H, *J* = 9.1), 4.31 (d, 1 H, *J* = 5.5), 4.20 (dd, 1 H, *J* = 7.1, 5.5), 4.04 (m, 1 H), 3.61 (s, 3 H), 3.57 (dd, 1 H, *J* = 9.9, 7.4), 3.46 (dd, 1 H, *J* = 9.6, 9.3), 3.30 (m, 1 H), 3.11 (dd, 1 H, *J* = 11.0, 8.8), 2.97 (t, 1 H, *J* = 8.8), 1.52, 1.34 (s each, 3 H each), 1.35, 1.29 (d each, 3 H each, *J* = 6.3). EIMS (m/z, %): 530 (M^+-H_2O, 0.4), 439 (M^+-SPh, 42.3), 191 (100). IR (film): 2984, 2935, 2899, 1584,

1481, 1440 cm^{-1}.

*Procedures similar to that for the glycosidation of 2,3-thionocarbonate **2** were employed for the preparation of **14** and **15**.*

Phenyl 3-*O*-(methylthio)carbonyl-4-*O*-methyl-2-*S*-phenyl-2,6-di-deoxy-β-L-glucopyranosyl-(1→4)-3-*O*-(methylthio)carbonyl-2-*S*-phenyl-2,6-di-deoxy-β-L-glucopyranosyl-(1→4)-2,3-*O*-isopropylidene-1-thio-α-L-rhamnopyranoside (14). $[\alpha]_D^{20} = -3.5^{o}$ (*c* 0.7, $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.30-7.24 (m, 15 H), 5.69 (s, 1 H), 5.06 (dd, 1 H, *J* = 11.5, 9.1), 4.99 (dd, 1 H, *J* = 11.3, 8.8), 4.50 (d, 1 H, *J* = 9.3), 4.46 (d, 1 H, *J* = 9.3), 4.28 (d, 1 H, *J* = 5.5), 4.14 (m, 1 H), 4.02 (m, 1 H), 3.58-3.48 (m, 2 H), 3.47 (s, 3 H), 3.35 (m, 1 H), 3.16-3.18 (m, 2 H), 3.12 (dd, 1 H, *J* = 11.3, 8.8), 2.91 (t, 1 H, *J* = 9.1), 2.36, 2.33 (s each, 3 H each), 1.49, 1.34 (s each, 3 H each), 1.44, 1.36, 1.28 (d each, 3 H each, *J* = 6.0). EIMS (m/z, %): 825 (M^+-SPh, 33.6). IR (film): 2934, 1720, 1481, 1440 cm^{-1}. Anal. Calcd for $C_{44}H_{54}O_{12}S_5$: C, 56.51; H, 5.82. Found: C, 56.38; H, 5.88.

Phenyl 3-*O*-(methylthio)carbonyl-4-*O*-methyl-2-*S*-phenyl-2,6-di-deoxy-β-L-glucopyranosyl-(1→3)-4-*O*-methyl-2-*S*-phenyl-2,6-di-deoxy-β-L-glucopyranosyl-(1→4)-2,3-*O*-isopropylidene-1-thio-α-L-rhamnopyranoside (15). $[\alpha]_D^{20} = -97.9^{o}$ (*c* 0.4, $CHCl_3$). ^{1}H NMR (300 MHz, $DCCl_3$): δ 7.52-7.17 (m, 15 H), 5.67 (s, 1 H), 5.23 (d, 1 H, *J* = 8.8), 5.06 (dd, 1 H, *J* = 11.5, 8.8), 4.51 (d, 1 H, *J* = 8.8), 4.26 (d, 1 H, *J* = 5.2), 4.06 (dd, 1 H, *J* = 7.1, 5.5), 3.95-3.84 (m, 2 H), 3.52-3.45 (m, 4 H), 3.41 (s, 3 H), 3.37-3.25 (m, 3 H), 3.01 (dd, 1 H, *J* = 11.8, 8.5), 2.94 (t, 1 H, *J* = 9.1), 2.83 (dd, 1 H, *J* = 9.6, 8.0), 2.38 (s, 3 H), 1.50, 1.34 (s each, 3 H each), 1.35-1.22 (m, 6 H). EIMS (m/z, %): 765 (M^+-SPh, 4.1). IR (film): 2935, 1724, 1481, 1440 cm^{-1}. Anal. Calcd for $C_{43}H_{54}O_{11}S_4$: C, 59.01; H, 6.22. Found: C, 59.39; H, 5.90.