

Supporting Information

A Novel and Highly Stereoselective Synthesis of 2-Substituted Perhydrofuro[2,3-*b*]pyran Derivatives

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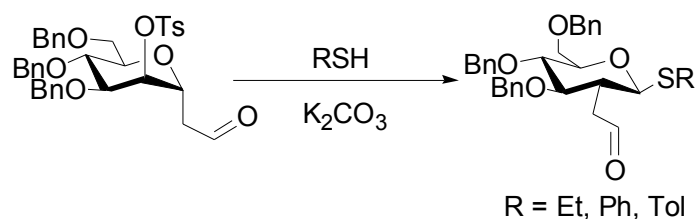
1. General

All reactions sensitive to air or moisture were carried out under nitrogen or argon atmosphere with anhydrous solvents. All reagents were purchased from commercial suppliers and used without further purification unless otherwise noted. Thin-layer chromatography was performed using silica gel GF254 precoated plates (0.20–0.25 mm thickness) with a fluorescent indicator. Visualization on TLC was achieved by UV light (254 nm) and a typical TLC indication solution (10% sulfuric acid / ethanol solution). Column chromatography was performed on silica gel 90, 200–300 mesh. Optical rotations were measured with a Perkin Elmer M341 Digital Polarimeter. ^1H and ^{13}C NMR (600 and 150 MHz, respectively) spectra were recorded on a Bruker Avance 600 spectrometer. ^1H NMR chemical shifts are reported in ppm (δ) relative to tetramethylsilane (TMS) with the solvent resonance employed as the internal standard (CDCl_3 , δ 7.26 ppm; CD_3COCD_3 , δ 2.05 ppm). Data are reported as follows: chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet), coupling constants (Hz) and integration. ^{13}C NMR chemical shifts are reported in ppm from tetramethylsilane (TMS) with the solvent resonance as the internal standard (CDCl_3 , δ 77.0 ppm; CD_3COCD_3 , δ 39.5). ESI-HRMS spectra were recorded on BioTOFQ.

2. Synthetic Procedures and Spectral Data

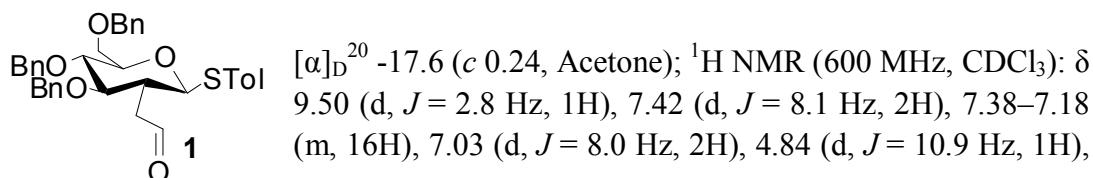
Generally procedures for the synthesis of glycosyl donors

To a solution of aldehyde (2 g, 3.2 mmol) and nucleophile (2–3 equiv) (EtSH, PhSH, 4-MePhSH) in MeOH or DMF (15–20 mL) was added K_2CO_3 (10 equiv). The suspension was stirred at room temperature 2–5 h. The reaction mixture was concentrated. Purification was then performed on a silica gel column.



2.1 *p*-Tolyl 3, 4, 6-tri-*O*-benzyl-2-*C*-formylmethyl-2-deoxy- β -D-thiogluco pyranoside (**1**)

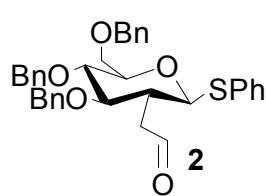
To a solution of aldehyde 2.0 g and 4-MePhSH 0.79 g in DMF 15 mL was added K_2CO_3 (4.37 g). The suspension was stirred at room temperature for 4 h. The reaction mixture was concentrated. Purification was then performed on a silica gel column (petroleum ether/ethyl acetate, 10:1) to afford major product **1** (1.29 g, 70%) as white powder.



4.77 (d, $J = 11.0$ Hz, 1H), 4.64 (d, $J = 5.5$ Hz, 1H), 4.62 (d, $J = 4.6$ Hz, 1H), 4.58 (d, $J = 10.6$ Hz, 1H), 4.56 (d, $J = 11.9$ Hz, 1H), 4.51 (d, $J = 10.9$ Hz, 1H), 3.81–3.75 (m, 2H), 3.64 (t, $J = 9.3$ Hz, 1H), 3.52–3.45 (m, 2H), 2.84 (dd, $J = 16.9, 3.7$ Hz, 1H), 2.44 (ddd, $J = 17.0, 7.5, 3.2$ Hz, 1H), 2.29–2.23 (m, 1H); ^{13}C NMR(150 MHz, CDCl_3): δ 200.1, 138.4, 138.2, 138.0, 137.7, 133.2, 129.8, 128.5, 128.4, 128.2, 127.9, 127.8, 127.7, 127.7, 127.6, 86.9, 83.8, 79.6, 79.4, 77.3, 77.1, 76.9, 74.8, 73.5, 69.0, 44.1, 42.7, 21.1; ESI-HRMS: m/z calcd for $\text{C}_{36}\text{H}_{38}\text{NaO}_5\text{S}$ $[\text{M}+\text{Na}]^+$: 605.2338; found: 605.2318.

2.2 Phenyl 3, 4, 6-tri-*O*-benzyl-2-*C*-formylmethyl-2-deoxy- β -D-thioglucopyranoside (**2**).

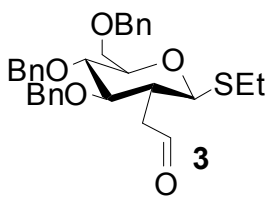
To a solution of aldehyde **2.0** g and PhSH 0.70 g in MeOH 20 mL was added K_2CO_3 (4.37 g). The suspension was stirred at room temperature 5 h. The reaction mixture concentrated. Purification was then performed on a silica gel column (petroleum ether/ethyl acetate, 10:1) to afford the product **2** (1.44 g, 80%) as white powder.



$[\alpha]_{\text{D}}^{20} +22.4$ (c 0.21, CHCl_3); ^1H NMR (600 MHz, CDCl_3): δ 9.50 (d, $J = 2.7$ Hz, 1H), 7.52 (dd, $J = 7.8, 1.1$ Hz, 2H), 7.36–7.31(m, 4H), 7.30–7.20 (m, 14H), 4.85 (d, $J = 10.9$ Hz, 1H), 4.78 (d, $J = 10.9$ Hz, 1H), 4.67–4.62 (m, 3H), 4.56 (d, $J = 11.9$ Hz, 1H), 4.52 (d, $J = 10.9$ Hz, 1H), 3.81–3.76 (m, 2H), 3.66 (t, $J = 9.2$ Hz, 1H), 3.54–3.49 (m, 2H), 2.83 (dd, $J = 16.9, 3.8$ Hz, 1H), 2.44 (ddd, $J = 17.1, 7.4, 3.1$ Hz, 1H), 2.33–2.31 (m, 1H).

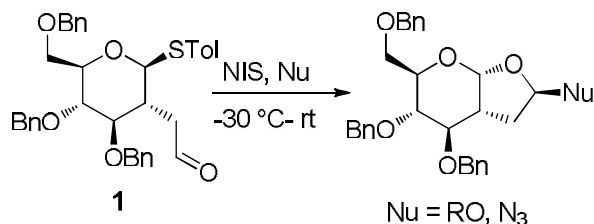
2.3 Ethyl 3, 4, 6-tri-*O*-benzyl-2-*C*-formylmethyl-2-deoxy- β -D-thioglucopyranoside (**3**).

To a solution of aldehyde **2.0** g and EtSH 0.71 mL in DMF 15 mL was added K_2CO_3 (4.37 g). The suspension was stirred at room temperature 3 h. The reaction mixture concentrated. Purification was then performed on a silica gel column (petroleum ether/ethyl acetate, 8:1) to afford major product **3** (1.25 g, 76%) as colorless syrup.



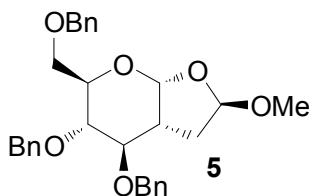
$[\alpha]_{\text{D}}^{20} +12.0$ (c 0.24, CHCl_3); ^1H NMR (600 MHz, CDCl_3): δ 9.56 (d, $J = 1.7$ Hz, 1H), 7.348–7.18 (m, 15H), 4.86 (d, $J = 11.0$ Hz, 1H), 4.77 (d, $J = 11.0$ Hz, 1H), 4.61(dd, $J = 12.5, 3.8$ Hz, 2H), 4.53 (dd, $J = 11.0, 3.0$ Hz, 2H), 4.43 (d, $J = 10.7$ Hz, 1H), 3.74 (d, $J = 3.9$ Hz, 2H), 3.65 (t, $J = 9.2$ Hz, 1H), 3.49–3.45 (m, 2H), 2.74–2.61 (m, 3H), 2.44–2.40 (m, 1H), 2.36–2.30 (m, 1H), 1.26 (t, $J = 7.6$ Hz, 3H); ^{13}C NMR (150 MHz, CDCl_3): δ 200.0, 138.2, 138.0, 137.8, 128.0, 127.8, 127.8, 127.8, 127.6, 84.5, 83.8, 79.8, 79.4, 74.7, 74.7, 73.5, 69.1, 43.7, 43.3, 24.5, 15.0; ESI-HRMS: m/z calcd for $\text{C}_{31}\text{H}_{36}\text{NaO}_5\text{S}$ $[\text{M}+\text{Na}]^+$: 543.2181; found: 543.2178.

2.4 Experimental Procedures and Spectral Data



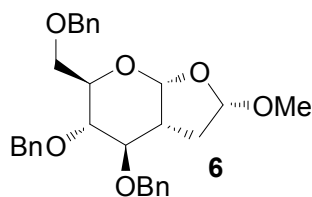
(2*R*, 3*aR*, 4*R*, 5*S*, 6*R*, 7*aR*)-4, 5-bis(benzyloxy)-6-[(benzyloxy)methyl]-2-methoxyhexahydro-furo[2,3-*b*]pyran (**5**)

A suspension of glycosyl donor **1** (58.2 mg), and MeOH **4** (8.1 μ L), containing activated 4 Å molecular sieves (50 mg) in dry CH₂Cl₂ (2.0 mL) was stirred under argon at room temperature for 30 minutes. After cooling to –30 °C, NIS (33 mg) was added. The reaction mixture was then warmed slowly to room temperature, stirred for 2 h, and then quenched by the addition of NaS₂O₃. The suspension was diluted with CH₂Cl₂ (5.0 mL), and filtered through Celite. The filtrate was washed successively with H₂O, saturated NaCl solution and dried with Na₂SO₄. The crude product was purified by flash column chromatography (petroleum ether/ethyl acetate, 5:1→4:1) to afford major product **5** (37.7 mg, 77%) and **6** (7.3 mg, 15%).



$[\alpha]_D^{20} + 11.4$ (*c* 0.39, Acetone); ¹H NMR (600 MHz, Acetone-*d*₆): δ 7.42–7.25 (15H, m), 5.46 (1H, d, *J* = 5.5 Hz), 5.08 (1H, dd, *J* = 5.5 Hz, 2.9 Hz), 4.79 (1H, d, *J* = 11.2 Hz), 4.73 (1H, d, *J* = 11.3 Hz), 4.69 (1H, d, *J* = 11.8 Hz), 4.60–4.52 (3H, m), 3.79–3.76 (1H, m), 3.73 (1H, dd, *J* = 10.98 Hz, 4.7 Hz), 3.68–3.62 (3H, m), 3.29 (3H, m), 2.53–2.51 (1H, m), 2.23–2.19 (1H, m), 1.88–1.84 (1H, m); ¹³C NMR (150 MHz, *d*₆-Acetone): δ 139.0, 138.8, 138.6, 128.2(2), 127.8(2), 127.6, 127.5(2), 127.4, 127.3, 103.1, 100.3, 79.2, 77.3, 72.9(2), 72.7, 71.5, 69.8, 54.3, 41.0, 34.4; ESI-HRMS: *m/z* calcd for C₃₀H₃₄NaO₆ [M+Na]⁺: 513.2253; found: 513.2252.

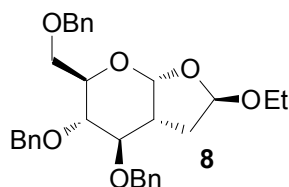
(2*S*, 3*aR*, 4*R*, 5*S*, 6*R*, 7*aR*)-4,5-bis(benzyloxy)-6-[(benzyloxy)methyl]-2-methoxyhexahydro-furo[2,3-*b*]pyran (**6**)



Colorless syrup; $[\alpha]_D^{20} + 32.1$ (c 0.08, Acetone); ^1H NMR (600 MHz, Acetone- d_6): δ 7.40–7.24 (m, 15H), 5.49 (d, J = 5.4 Hz, 1H), 4.92 (dd, J = 5.0 Hz, 0.7 Hz 1H), 4.82 (d, J = 11.6 Hz, 1H), 4.78 (d, J = 11.1 Hz, 1H), 4.70 (d, J = 11.6 Hz, 1H), 4.68 (d, J = 11.1 Hz, 1H), 4.61 (d, J = 12.0 Hz, 1H), 4.57 (d, J = 12.0 Hz, 1H), 4.05 (t, J = 7.9 Hz, 1H), 3.87–3.80 (m, 2H), 3.73 (d, J = 9.0 Hz, 1H), 3.61–3.56 (m, 1H), 3.31 (s, 3H), 2.29 (ddd, J = 7.7, 5.8, 1.9 Hz, 1H), 2.28–2.25 (m, 1H), 2.24–2.17 (m, 1H); ^{13}C NMR (150 MHz, d_6 -Acetone): δ 139.3, 138.9, 138.8, 128.2, 128.1, 127.8, 127.6 (2), 127.4, 127.3 (2), 103.6, 102.9, 82.0, 78.1, 73.8, 73.5, 72.9, 71.6, 69.3, 54.4, 41.7, 35.5; ESI-HRMS: m/z calcd for $\text{C}_{30}\text{H}_{34}\text{NaO}_6$ $[\text{M}+\text{Na}]^+$: 513.2253; found: 513.2250.

(2*R*, 3*aR*, 4*R*, 5*S*, 6*R*, 7*aR*)-4,5-bis(benzyloxy)-6-((benzyloxy)methyl)-2-ethoxyhexahydro-furo[2,3-*b*]pyran (8)

A suspension of glycosyl donor **1** (58.2 mg), and EtOH **7** (17.5 μL), containing activated 4 Å molecular sieves (50 mg) in dry CH_2Cl_2 (2.0 mL) was stirred under argon at room temperature for 30 minutes. After cooling to -30°C , NIS (33 mg) was added. The reaction mixture was then warmed slowly to room temperature, stirred for 2 h, and then quenched by the addition of NaS_2O_3 . The suspension was diluted with CH_2Cl_2 (5.0 mL), and filtered through Celite. The filtrate was washed successively with H_2O , saturated NaCl solution and dried with Na_2SO_4 . The crude product was purified by flash column chromatography (petroleum ether/ethyl acetate, 5:1→4:1) to afford major product **8** (41.9 mg, 83%).

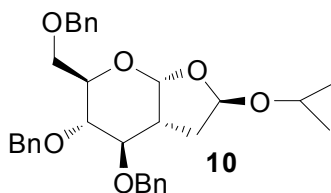


Colorless syrup; $[\alpha]_D^{20} + 16.1$ (c 0.32, Acetone); ^1H NMR (600MHz, Acetone- d_6): δ 7.40–7.25 (15H, m), 5.46 (1H, d, J = 5.5 Hz), 5.04 (1H, d, J = 4.7 Hz), 4.83–4.78 (2H, m), 4.72–4.67 (2H, m), 4.62–4.55 (2H, m), 4.11 (1H, t, J = 7.7 Hz), 3.90–3.87 (1H, m), 3.83–3.79 (1H, m), 3.74–3.71 (2H, m), 3.60 (1H, dd, J = 9.54 Hz, 8.0 Hz), 3.41–3.39 (1H, m), 2.29–2.27 (1H, m), 2.25–2.20 (1H, m), 2.02–1.99 (1H, m), 1.16 (3H, t, J = 7.0 Hz); ^{13}C NMR (150 MHz, Acetone): δ 139.3, 138.9(2), 128.2, 128.1, 127.8, 127.7, 127.6(2), 127.4, 127.3(2), 102.7, 102.3, 81.7, 78.2, 73.7, 73.4, 72.9, 71.7, 69.4, 62.9, 41.7, 35.5, 14.8; ESI-HRMS: m/z calcd for $\text{C}_{31}\text{H}_{36}\text{NaO}_6$ $[\text{M}+\text{Na}]^+$: 527.2410; found: 527.2399.

(2*R*, 3*aR*, 4*R*, 5*S*, 6*R*, 7*aR*)-4,5-bis(benzyloxy)-6-((benzyloxy)methyl)-2-isopropoxyhexahydro-furo[2,3-*b*]pyran (10)

A suspension of glycosyl donor **1** (58.2 mg), and *i*-PrOH **9** (23.0 μL), containing activated 4 Å molecular sieves (50 mg) in dry CH_2Cl_2 (2.0 mL) was stirred under argon at room temperature for 30 minutes. After cooling to -30°C , NIS (33 mg) was added. The reaction mixture was then warmed slowly to room temperature, stirred for 2 h, and then quenched by the addition of NaS_2O_3 . The suspension was diluted with

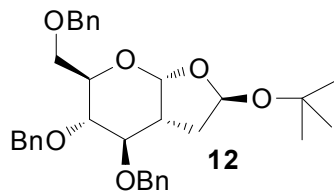
CH₂Cl₂ (5.0 mL), and filtered through Celite. The filtrate was washed successively with H₂O, saturated NaCl solution and dried with Na₂SO₄. The crude product was purified by flash column chromatography (petroleum ether/ethyl acetate, 5:1→4:1) to afford major product **10** (31.6 mg, 87%).



Colorless syrup; $[\alpha]_D^{20} + 33.1$ (*c* 0.14, Acetone); ¹H NMR (600 MHz, Acetone-*d*₆): δ 7.63–7.07 (m, 15H), 5.43 (d, *J* = 5.3 Hz, 1H), 5.20–5.16 (m, 1H), 4.82 (d, *J* = 11.6 Hz, 1H), 4.79 (d, *J* = 11.2 Hz, 1H), 4.71 (d, *J* = 11.6 Hz, 1H), 4.67 (d, *J* = 11.1 Hz, 1H), 4.61 (d, *J* = 12.0 Hz, 1H), 4.56 (d, *J* = 12.0 Hz, 1H), 4.14 (t, *J* = 7.7 Hz, 1H), 3.94 (ddd, *J* = 9.6, 4.0, 1.7 Hz, 1H), 3.86 (dt, *J* = 12.3, 6.1 Hz, 1H), 3.81 (dd, *J* = 10.8, 4.3 Hz, 1H), 3.72 (dd, *J* = 10.8, 2.0 Hz, 1H), 3.59 (dd, *J* = 9.6, 8.0 Hz, 1H), 2.28–2.25 (m, 1H), 2.22 (dd, *J* = 13.5, 7.7 Hz, 1H), 1.96 (d, *J* = 13.2 Hz, 1H), 1.18 (d, *J* = 6.2 Hz, 3H), 1.10 (d, *J* = 6.1 Hz, 3H). ¹³C NMR (150 MHz, Acetone): δ 139.3, 138.9 (2), 128.2, 128.1, 127.8, 127.7, 127.6, 127.4, 127.3, 102.6, 100.6, 81.4, 78.2, 73.8, 73.4, 72.9, 71.8, 69.4, 69.3, 41.8, 35.5, 23.2, 21.0; ESI-HRMS: *m/z* calcd for C₃₂H₃₈NaO₆ [M+Na]⁺: 541.2566; found: 541.2552.

(2*R*, 3*aR*, 4*R*, 5*S*, 6*R*, 7*aR*)-4,5-bis(benzyloxy)-6-[(benzyloxy)methyl]-2-(tert-butoxy)hexahydro-furo[2,3-*b*]pyran (12**)**

A suspension of glycosyl donor **1** (58.2 mg), and *t*-BuOH **11** (28.7 μL), containing activated 4 Å molecular sieves (50 mg) in dry CH₂Cl₂ (2.0 mL) was stirred under argon at room temperature for 30 minutes. After cooling to –30 °C, NIS (33 mg) was added. The reaction mixture was then warmed slowly to room temperature, stirred for 2 h, and then quenched by the addition of NaS₂O₃. The suspension was diluted with CH₂Cl₂ (5.0 mL), and filtered through Celite. The filtrate was washed successively with H₂O, saturated NaCl solution and dried with Na₂SO₄. The crude product was purified by flash column chromatography (petroleum ether/ethyl acetate, 5:1→4:1) to afford major product **12** (26.2 mg, 82%).

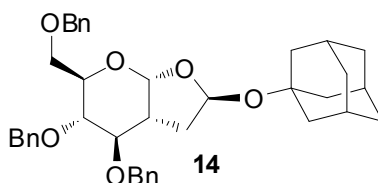


Colorless syrup; $[\alpha]_D^{20} + 59.0$ (*c* 0.23, Acetone); ¹H NMR (600 MHz, Acetone-*d*₆): δ 8.03–6.77 (m, 15H), 5.37 (d, *J* = 4.8 Hz, 1H), 5.35 (d, *J* = 5.5 Hz, 1H), 4.85–4.81 (m, 1H), 4.79 (d, *J* = 11.1 Hz, 1H), 4.73–4.70 (m, 1H), 4.70–4.67 (m, 1H), 4.62–4.55 (m, 2H), 4.18 (t, *J* = 7.7 Hz, 1H), 3.99 (ddd, *J* = 9.6, 4.3, 1.9 Hz, 1H), 3.82 (dd, *J* = 10.8,

4.3 Hz, 1H), 3.72 (dd, $J = 10.9, 1.9$ Hz, 1H), 3.59 (dd, $J = 9.6, 8.2$ Hz, 1H), 2.25–2.17 (m, 2H), 1.93–1.86 (m, 1H), 1.22 (s, 9H). ^{13}C NMR (150 MHz, Acetone): δ 139.4, 139.0, 128.9, 128.2, 128.1, 127.8, 127.7, 127.6 (2), 127.4 (2), 127.3, 102.4, 96.9, 81.3, 78.4, 73.9, 73.7, 73.5, 72.9, 71.7, 69.4, 42.0, 36.2, 29.5, 28.3, 28.0; ESI-HRMS: m/z calcd for $\text{C}_{33}\text{H}_{40}\text{NaO}_6$ $[\text{M}+\text{Na}]^+$: 555.2723; found: 555.2714.

(2*R*, 3*aR*, 4*R*, 5*S*, 6*R*, 7*aR*)-2-(adamantanyloxy)-4,5-bis(benzyloxy)-6-[(benzyloxy)methyl]hexahydro-furo[2,3-*b*]pyran (14)

A suspension of glycosyl donor **1** (58.2 mg), and adamantanol **13** (18.3 mg), containing activated 4 Å molecular sieves (50 mg) in dry CH_2Cl_2 (2.0 mL) was stirred under argon at room temperature for 30 minutes. After cooling to $-30\text{ }^\circ\text{C}$, NIS (33 mg) was added. The reaction mixture was then warmed slowly to room temperature, stirred for 3 h, and then quenched by the addition of NaS_2O_3 . The suspension was diluted with CH_2Cl_2 (5.0 mL), and filtered through Celite. The filtrate was washed successively with H_2O , saturated NaCl solution and dried with Na_2SO_4 . The crude product was purified by flash column chromatography. (petroleum ether/ethyl acetate, 5:1→4:1) to afford major product **14** (47.6 mg, 78%).

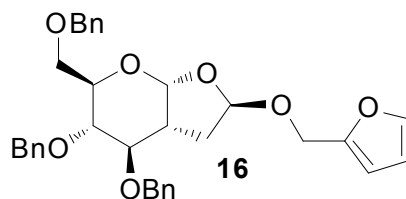


Colorless syrup; $[\alpha]_{\text{D}}^{20} + 17.5$ (c 0.23, Acetone); ^1H NMR (600 MHz, Acetone- d_6): δ 7.39–7.23 (m, 15H), 5.63 (dd, $J = 5.5, 3.8$ Hz, 1H), 5.45 (d, $J = 5.1$ Hz, 1H), 4.80 (d, $J = 11.7$ Hz, 1H), 4.74 (d, $J = 11.2$ Hz, 1H), 4.70 (d, $J = 11.7$ Hz, 1H), 4.61 (d, $J = 11.3$ Hz, 1H), 4.58 (d, $J = 12.0$ Hz, 1H), 4.53 (d, $J = 12.0$ Hz, 1H), 3.74 (dd, $J = 10.6, 4.5$ Hz, 2H), 3.66 (dd, $J = 10.3, 1.6$ Hz, 1H), 3.61 (dt, $J = 13.0, 6.3$ Hz, 2H), 2.44 (dd, $J = 12.2, 6.2$ Hz, 1H), 2.17–2.06 (m, 5H), 1.78 (dt, $J = 14.9, 11.6$ Hz, 6H), 1.62 (q, $J = 12.3$ Hz, 6H). ^{13}C NMR (150 MHz, Acetone): δ 139.1, 138.8, 138.7, 128.2, 128.2, 127.9, 127.8, 127.4, 127.3, 100.1, 95.3, 79.6, 77.6, 73.1, 73.0, 72.9, 71.6, 69.7, 42.7, 41.8, 36.2, 35.8, 30.6, 29.5; ESI-HRMS: m/z calcd for $\text{C}_{39}\text{H}_{46}\text{NaO}_6$ $[\text{M}+\text{Na}]^+$: 633.3192; found: 633.3185.

(2*R*, 3*aR*, 4*R*, 5*S*, 6*R*, 7*aR*)-4,5-bis(benzyloxy)-6-[(benzyloxy)methyl]-2-(furan-2-ylmethoxy)hexahydro-furo[2,3-*b*]pyran (16)

A suspension of glycosyl donor **1** (58.2 mg), and 2-Furanmethanol **15** (10.4 μL), containing activated 4 Å molecular sieves (50 mg) in dry CH_2Cl_2 (2.0 mL) was stirred under argon at room temperature for 30 minutes. After cooling to $-30\text{ }^\circ\text{C}$, NIS (33 mg) was added. The reaction mixture was then warmed slowly to room temperature, stirred for 3 h, and then quenched by the addition of NaS_2O_3 . The suspension was diluted with CH_2Cl_2 (5.0 mL), and filtered through Celite. The filtrate was washed successively with H_2O , saturated NaCl solution and dried with Na_2SO_4 . The crude product was purified by flash column chromatography (petroleum ether/ethyl acetate,

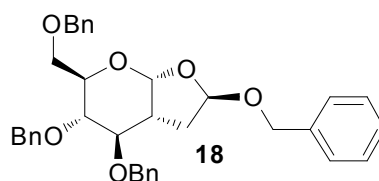
5:1) to afford major product **16** (39.5 mg, 71%).



$[\alpha]_D^{20}$ -11.6 (*c* 0.24, Acetone); ^1H NMR (600 MHz, Acetone- d_6): δ 7.51 (dd, J = 1.6, 0.8 Hz, 1H), 7.39–7.25 (m, 15H), 6.38 (dt, J = 6.9, 2.5 Hz, 2H), 5.52 (d, J = 5.4 Hz, 1H), 5.30 (dd, J = 5.6, 2.7 Hz, 1H), 4.78 (d, J = 11.8 Hz, 1H), 4.72 (d, J = 11.3 Hz, 1H), 4.69 (d, J = 11.8 Hz, 1H), 4.61–4.53 (m, 4H), 4.46 (d, J = 12.8 Hz, 1H), 3.81–3.77 (m, 1H), 3.73 (dd, J = 10.8, 4.7 Hz, 1H), 3.68 (dd, J = 10.9, 2.2 Hz, 1H), 3.66–3.64 (m, 2H), 2.57 (d, J = 5.8 Hz, 1H), 2.22 (dt, J = 13.6, 5.9 Hz, 1H), 1.89 (ddd, J = 13.6, 8.0, 2.7 Hz, 1H). ^{13}C NMR (150 MHz, Acetone): δ 151.9, 142.8, 139.0, 138.8, 138.6, 128.2, 128.1, 128.0, 127.9(2), 127.6, 127.5, 127.4, 127.3, 110.2, 110.1, 100.9, 100.5, 79.5, 77.2, 72.9, 72.8, 72.6, 71.5, 69.8, 60.7, 40.8, 34.4; ESI-HRMS: m/z calcd for $\text{C}_{34}\text{H}_{36}\text{NaO}_7$ $[\text{M}+\text{Na}]^+$: 579.2359; found: 579.2362.

(2*R*, 3*aR*, 4*R*, 5*S*, 6*R*, 7*aR*)-2,4,5-tris(benzyloxy)-6-[(benzyloxy)methyl]hexahydro-furo[2,3-*b*]pyran (18**)**

A suspension of glycosyl donor **1** (58.2 mg), and BnOH **17** (12.5 μL), containing activated 4 Å molecular sieves (50 mg) in dry CH_2Cl_2 (2.0 mL) was stirred under argon at room temperature for 30 minutes. After cooling to $-30\text{ }^\circ\text{C}$, NIS (33 mg) was added. The reaction mixture was then warmed slowly to room temperature, stirred for 2.5 h, and then quenched by the addition of NaS_2O_3 . The suspension was diluted with CH_2Cl_2 (5.0 mL), and filtered through Celite. The filtrate was washed successively with H_2O , saturated NaCl solution and dried with Na_2SO_4 . The crude product was purified by flash column chromatography (petroleum ether/ethyl acetate, 5:1→4:1) to afford major product **18** (39.1 mg, 69%).

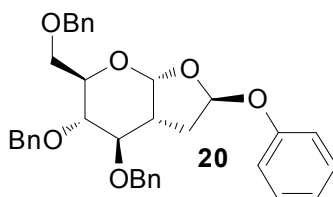


$[\alpha]_D^{20}$ + 1.1 (*c* 0.27, Acetone); ^1H NMR (600 MHz, Acetone- d_6): δ 7.42–7.22 (m, 20H), 5.54 (d, J = 5.4 Hz, 1H), 5.32 (dd, J = 5.6, 2.7 Hz, 1H), 4.78 (d, J = 11.8 Hz, 1H), 4.73 (d, J = 12.1 Hz, 2H), 4.69 (d, J = 11.8 Hz, 1H), 4.61–4.57 (m, 2H), 4.54 (d, J = 12.0 Hz, 1H), 4.49 (d, J = 12.0 Hz, 1H), 3.81–3.77 (m, 1H), 3.73 (dd, J = 10.8, 4.7 Hz, 1H), 3.70–3.64 (m, 2H), 2.64–2.55 (m, 1H), 2.24 (ddd, J = 11.0, 8.5, 4.1 Hz, 2H), 1.96 (ddd, J = 13.1, 8.0, 2.8 Hz, 1H); ^{13}C NMR (150 MHz, Acetone): δ 139.0, 138.8, 138.6 (2), 128.2 (2), 127.8 (2), 127.6 (2), 127.5, 127.4, 127.3 (2), 101.4, 100.5, 79.1,

77.3, 72.9, 72.8, 72.6, 71.5, 69.8, 69.1, 41.0, 34.5; ESI-HRMS: m/z calcd for $C_{38}H_{38}NaO_6 [M+Na]^+$: 589.2566; found: 589.2557.

(2*R*, 3*aR*, 4*R*, 5*S*, 6*R*, 7*aR*)-4,5-bis(benzyloxy)-6-[(benzyloxy)methyl]-2-phenoxyhexahydro-furo[2,3-*b*]pyran (20)

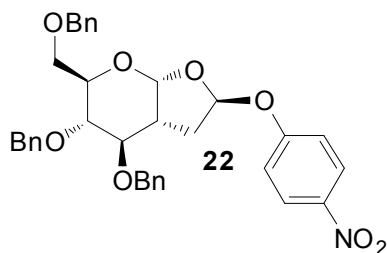
A suspension of glycosyl donor **1** (58.2 mg), and PhOH **19** (11.3 mg), containing activated 4 Å molecular sieves (50 mg) in dry CH_2Cl_2 (2.0 mL) was stirred under argon at room temperature for 30 minutes. After cooling to $-30\text{ }^\circ\text{C}$, NIS (33 mg) was added. The reaction mixture was then warmed slowly to room temperature, stirred for 3 h, and then quenched by the addition of NaS_2O_3 . The suspension was diluted with CH_2Cl_2 (5.0 mL), and filtered through Celite. The filtrate was washed successively with H_2O , saturated NaCl solution and dried with Na_2SO_4 . The crude product was purified by flash column chromatography (petroleum ether/ethyl acetate, 5:1→4:1) to afford major product **20** (37.6 mg, 68%).



$[\alpha]_D^{20}$ -17.1 (c 0.06, Acetone); 1H NMR (600 MHz, Acetone- d_6): δ 7.42–7.25 (m, 16H), 7.14 (d, J = 2.8 Hz, 1H), 7.04 (dd, J = 12.6, 8.3 Hz, 2H), 6.97 (t, J = 7.8 Hz, 1H), 5.96 (dd, J = 5.6, 2.9 Hz, 1H), 5.62 (dd, J = 5.2, 3.3 Hz, 1H), 4.83 (dd, J = 11.6, 3.1 Hz, 1H), 4.75 (ddd, J = 12.0, 8.6, 3.2 Hz, 2H), 4.64–4.53 (m, 3H), 3.88–3.84 (m, 1H), 3.78–3.73 (m, 2H), 3.72–3.67 (m, 2H), 2.48 (dt, J = 13.5, 5.8 Hz, 1H), 2.29 (s, 1H), 2.21 (ddd, J = 13.9, 7.9, 3.0 Hz, 1H). ^{13}C NMR (150 MHz, Acetone): δ 139.0, 138.8, 138.6, 133.8, 129.8, 129.6, 129.3, 128.2 (2), 127.8, 127.7, 127.5 (2), 127.3, 121.6, 116.6, 101.1, 100.4, 78.9, 77.2, 72.9 (2), 72.8, 71.7, 69.7, 40.9, 34.6. ESI-HRMS: m/z calcd for $C_{35}H_{36}NaO_6 [M+Na]^+$: 575.2410; found: 575.2391.

(2*R*, 3*aR*, 4*R*, 5*S*, 6*R*, 7*aR*)-4,5-bis(benzyloxy)-6-[(benzyloxy)methyl]-2-(4-nitrophenoxy)hexahydro-furo[2,3-*b*]pyran (22)

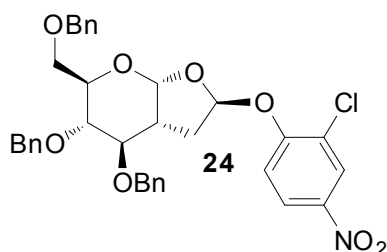
A suspension of glycosyl donor **1** (58.2 mg), and *p*-NO₂-PhOH **21** (16.7 mg), containing activated 4 Å molecular sieves (50 mg) in dry CH_2Cl_2 (2.0 mL) was stirred under argon at room temperature for 30 minutes. After cooling to $-30\text{ }^\circ\text{C}$, NIS (33 mg) was added. The reaction mixture was then warmed slowly to room temperature, stirred for 3 h, and then quenched by the addition of NaS_2O_3 . The suspension was diluted with CH_2Cl_2 (5.0 mL), and filtered through Celite. The filtrate was washed successively with H_2O , saturated NaCl solution and dried with Na_2SO_4 . The crude product was purified by flash column chromatography (petroleum ether/ethyl acetate, 5:1→4:1) to afford major product **22** (47.2 mg, 79%).



$[\alpha]_D^{20}$ -8.3 (c 0.30, Acetone); ^1H NMR (600 MHz, Acetone- d_6): δ 8.26–8.18 (m, 2H), 7.47–7.12 (m, 17H), 6.17 (dd, J = 5.5, 2.6 Hz, 1H), 5.66 (d, J = 5.5 Hz, 1H), 4.82 (d, J = 11.8 Hz, 1H), 4.75 (dd, J = 11.5, 9.3 Hz, 2H), 4.64–4.52 (m, 3H), 3.87 (ddd, J = 8.9, 4.7, 2.3 Hz, 1H), 3.80 (t, J = 5.7 Hz, 1H), 3.77–3.68 (m, 3H), 2.77 (d, J = 6.1 Hz, 1H), 2.56 (dt, J = 13.9, 6.0 Hz, 1H), 2.30 (ddd, J = 14.0, 8.1, 2.6 Hz, 1H); ^{13}C NMR (150 MHz, Acetone): δ 162.4, 142.1, 138.9, 138.7, 138.5, 128.2 (3), 127.9, 127.8, 127.7, 127.6, 127.5, 127.4, 125.5, 116.6, 101.6, 100.6, 78.4, 76.9 (2), 72.8, 72.6, 71.7, 69.8, 40.4, 34.4; ESI-HRMS: m/z calcd for $\text{C}_{35}\text{H}_{35}\text{NNaO}_8$ $[\text{M}+\text{Na}]^+$: 620.2260; found: 620.2267.

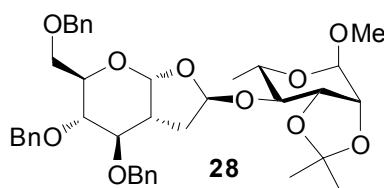
(2*R*, 3*aR*, 4*R*, 5*S*, 6*R*, 7*aR*)-4,5-bis(benzyloxy)-6-[(benzyloxy)methyl]-2-(2-chloro-4-nitrophenoxy)hexahydro-furo[2,3-*b*]pyran (24)

A suspension of glycosyl donor **1** (58.2 mg), and 2-Cl-4-NO₂-PhOH **23** (20.8 mg), containing activated 4 Å molecular sieves (50 mg) in dry CH₂Cl₂ (2.0 mL) was stirred under argon at room temperature for 30 minutes. After cooling to -30 °C, NIS (33 mg) was added. The reaction mixture was then warmed slowly to room temperature, stirred for 3 h, and then quenched by the addition of NaS₂O₃. The suspension was diluted with CH₂Cl₂ (5.0 mL), and filtered through Celite. The filtrate was washed successively with H₂O, saturated NaCl solution and dried with Na₂SO₄. The crude product was purified by flash column chromatography (petroleum ether/ethyl acetate, 5:1→4:1) to afford major product **24** (46.1 mg, 73%).



$[\alpha]_D^{20}$ -5.9 (c 0.35, Acetone); ^1H NMR (600 MHz, Acetone- d_6): δ 8.26 (d, J = 2.7 Hz, 1H), 8.21 (dd, J = 9.2, 2.8 Hz, 1H), 7.52 (d, J = 9.2 Hz, 1H), 7.42–7.23 (m, 15H), 6.24 (dd, J = 5.4, 2.3 Hz, 1H), 5.70 (d, J = 5.6 Hz, 1H), 4.81 (d, J = 11.7 Hz, 1H), 4.74 (dd, J = 11.3, 10.0 Hz, 2H), 4.60 (d, J = 11.4 Hz, 1H), 4.58–4.51 (m, 2H), 3.86 (ddd, J = 8.8, 4.7, 2.4 Hz, 1H), 3.82 (t, J = 5.5 Hz, 1H), 3.76–3.66 (m, 3H), 2.84 (dd, J = 13.6, 6.7 Hz, 1H), 2.65–2.57 (m, 1H), 2.39 (ddd, J = 14.0, 8.1, 2.4 Hz, 1H). ^{13}C NMR (150 MHz, Acetone): δ 158.0, 142.0, 138.9, 138.7, 138.5, 128.3 (2), 128.2, 127.9, 127.8,

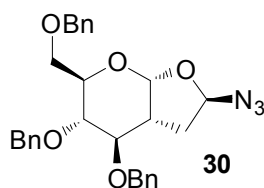
was washed successively with H₂O, saturated NaCl solution and dried with Na₂SO₄. The crude product was purified by flash column chromatography (petroleum ether/ethyl acetate, 5:1→4:1) to afford major product **28** (57.5 mg, 85%).



Colorless syrup; $[\alpha]_D^{20} + 8.7$ (*c* 1.83, Acetone); ¹H NMR (600 MHz, CDCl₃): δ 7.36–7.22 (m, 13H), 7.16 (d, *J* = 6.5 Hz, 2H), 5.63 (dd, *J* = 5.4, 2.3 Hz, 1H), 5.57 (d, *J* = 5.3 Hz, 1H), 4.84 (s, 1H), 4.76 (d, *J* = 11.8 Hz, 1H), 4.65–4.60 (m, 3H), 4.53 (d, *J* = 12.1 Hz, 1H), 4.47 (d, *J* = 11.1 Hz, 1H), 4.10 (t, *J* = 6.1 Hz, 1H), 4.07 (d, *J* = 5.7 Hz, 1H), 3.85–3.80 (m, 1H), 3.75–3.66 (m, 3H), 3.57–3.53 (m, 3H), 3.35 (s, 3H), 2.57–2.50 (m, 1H), 2.27–2.18 (m, 1H), 1.90 (ddd, *J* = 13.6, 7.9, 2.3 Hz, 1H), 1.54 (s, 3H), 1.34 (s, 3H), 1.24 (d, *J* = 5.6 Hz, 3H); ¹³C NMR (150 MHz, CDCl₃): δ 138.4, 138.1, 138.0, 128.5, 128.4, 128.3, 127.9, 127.8 (3), 127.7, 127.6, 109.3, 101.4, 100.5, 98.0, 79.4, 78.8, 77.7, 77.0, 76.0, 73.5, 73.4, 73.3, 71.5, 69.3, 64.3, 54.8, 41.1, 35.1, 28.0, 26.4, 17.5; ESI-HRMS: *m/z* calcd for C₃₉H₄₈NaO₁₀ [M+Na]⁺: 699.3145; found 699.3140.

(2*R*, 3*aR*, 4*R*, 5*S*, 6*R*, 7*aR*)-2-azido-4,5-bis(benzyloxy)-6-[(benzyloxy)methyl]hexahydro-furo[2,3-*b*]pyran (30)

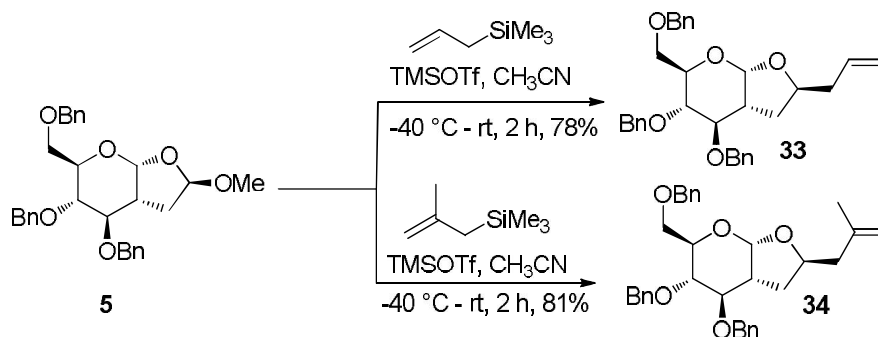
A suspension of glycosyl donor **1** (58.2 mg), and TMSN₃ **29** (18.4 μL), containing activated 4 Å molecular sieves (50 mg) in dry CH₂Cl₂ (2.0 mL) was stirred under argon at room temperature for 30 minutes. After cooling to –30 °C, NIS (33 mg) was added. The reaction mixture was then warmed slowly to room temperature, stirred for 2 h, and then quenched by the addition of NaS₂O₃. The suspension was diluted with CH₂Cl₂ (5.0 mL), and filtered through Celite. The filtrate was washed successively with H₂O, saturated NaCl solution and dried with Na₂SO₄. The crude product was purified by flash column chromatography (petroleum ether/ethyl acetate, 6:1) to afford major product **30** (39.1 mg, 78%).



$[\alpha]_D^{20} + 12.0$ (*c* 0.27, Acetone); ¹H NMR (600 MHz, Acetone-*d*₆): δ 7.31 (m, 15H), 5.72 (dd, *J* = 6.1, 3.5 Hz, 1H), 5.62 (d, *J* = 5.5 Hz, 1H), 4.78 (d, *J* = 11.8 Hz, 1H), 4.70 (t, *J* = 12.2 Hz, 2H), 4.59 (d, *J* = 3.3 Hz, 1H), 4.57 (d, *J* = 4.2 Hz, 1H), 4.53 (d, *J* = 12.0 Hz, 1H), 3.78 (ddd, *J* = 8.6, 4.5, 2.2 Hz, 1H), 3.74–3.65 (m, 4H), 2.65–2.58 (m,

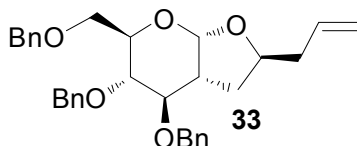
1H), 2.35–2.27 (m, 1H), 1.86 (ddd, $J = 13.6, 7.8, 3.5$ Hz, 1H). ^{13}C NMR (150 MHz, Acetone): δ 138.9, 138.8, 138.5, 128.2 (3), 127.8 (2), 127.6, 127.5 (2), 127.3, 101.5, 90.4, 78.2, 76.9 (2), 72.9, 72.8, 72.6, 71.7, 69.7, 40.6, 34.0; ESI-HRMS: m/z calcd for $\text{C}_{29}\text{H}_{31}\text{N}_3\text{NaO}_5$ $[\text{M}+\text{Na}]^+$: 524.2161; found: 524.2156.

2.5 Allylation of 5 – Experimental Procedures and Spectral Data



(2*R*, 3*aR*, 4*R*, 5*S*, 6*R*, 7*aR*)-2-allyl-4,5-bis(benzyloxy)-6-[(benzyloxy)methyl]hexahydro-furo[2,3-*b*]pyran (33)

To a stirring solution of 5 (49.0 mg.) in anhydrous CH_3CN (1 mL) at $-40\text{ }^\circ\text{C}$ and under N_2 was added allyltrimethylsilane (32 μL). Then trimethylsilyl triflate (14.8 μL) was added dropwise. The reaction mixture was stirred at $-40\text{ }^\circ\text{C}$ for 1.5 h, then for 0.5 h at room temperature. The yellow mixture was diluted with CH_2Cl_2 (10 mL), and neutralised with saturated NaHCO_3 solution ($2 \times 10\text{ mL}$). The organic layer was collected, and the aqueous layer was reextracted with further CH_2Cl_2 ($2 \times 10\text{ mL}$). The combined organic phases were dried over anhydrous Na_2SO_4 and concentrated. The crude material was slightly diluted with CH_2Cl_2 (0.2 mL) and purified by silica gel flash column chromatography (petroleum ether/ethyl acetate, 8:1) to afford product 33 as a colorless syrup (39.2 mg, 78%).

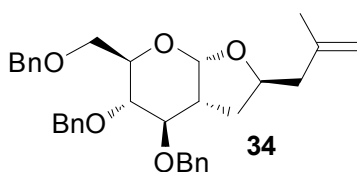


$[\alpha]_{\text{D}}^{20} + 70.6$ (c 0.30, CHCl_3); ^1H NMR (600 MHz, CDCl_3): δ 7.38–7.19 (m, 15H), 5.80–5.67 (m, 1H), 5.45 (d, $J = 4.5$ Hz, 1H), 5.12–5.01 (m, 2H), 4.88 (d, $J = 11.5$ Hz, 1H), 4.78 (d, $J = 10.9$ Hz, 1H), 4.70–4.66 (m, 1H), 4.65 (d, $J = 9.7$ Hz, 1H), 4.63 (d, $J = 8.5$ Hz, 1H), 4.55 (d, $J = 12.1$ Hz, 1H), 4.15 (dq, $J = 12.0, 6.1$ Hz, 1H), 3.82 (dd, $J = 18.8, 7.9$ Hz, 2H), 3.74 (t, $J = 8.9$ Hz, 1H), 3.70 (dd, $J = 10.4, 1.4$ Hz, 1H), 3.54 (t, $J = 8.6$ Hz, 1H), 2.32 (dt, $J = 12.8, 6.4$ Hz, 2H), 2.21 (dt, $J = 13.4, 6.5$ Hz, 1H), 1.88 (dd, $J = 12.5, 5.8$ Hz, 1H), 1.71–1.64 (m, 1H); ^{13}C NMR (150 MHz, CDCl_3): δ 138.5, 138.3, 138.1, 133.9, 128.5, 128.4, 128.4, 128.1, 127.9, 127.8, 127.7, 127.6, 117.5, 101.5, 80.7, 77.9, 76.6, 74.6, 74.4, 73.6, 72.2, 68.8, 44.3, 40.7, 33.8. ESI-HRMS: m/z

calcd for $C_{32}H_{36}NaO_5$ $[M+Na]^+$: 523.2460; found: 523.2455.

(2*R*, 3*aR*, 4*R*, 5*S*, 6*R*, 7*aR*)-4,5-bis(benzyloxy)-6-[(benzyloxy)methyl]-2-(2-methylallyl)hexahydro-furo[2,3-*b*]pyran (34**)**

To a stirring solution of **5** (49.0 mg,) in anhydrous CH_3CN (1 mL) at $-40\text{ }^\circ\text{C}$ and under N_2 was added 2-methylallyltrimethylsiane (35 μL). Then trimethylsilyl triflate (14.8 μL) was added dropwise. The reaction mixture was stir at $-40\text{ }^\circ\text{C}$ for 1.5 h, then for 0.5 h at room temperature. The yellow mixture was diluted with CH_2Cl_2 (10 mL), and neutralised with saturated $NaHCO_3$ solution ($2 \times 10\text{ mL}$). The organic layer was collected, and the aqueous layer was reextracted with further CH_2Cl_2 ($2 \times 10\text{ mL}$). The combined organic phases were dried over anhydrous Na_2SO_4 and concentrated. The crude material was slightly diluted with CH_2Cl_2 (0.2 mL) and purified by silica gel flash column chromatography (petroleum ether/ethyl acetate, 8:1) to afford product **34** as a colorless syrup (41.9 mg, 81%).



$[\alpha]_D^{20} + 74.6$ (c 0.30, $CHCl_3$); 1H NMR (600 MHz, $CDCl_3$): δ 7.37–7.20 (m, 15H), 5.46 (d, $J = 4.6\text{ Hz}$, 1H), 4.88 (d, $J = 11.6\text{ Hz}$, 1H), 4.79 (d, $J = 11.2\text{ Hz}$, 2H), 4.69 (d, $J = 11.2\text{ Hz}$, 2H), 4.65 (d, $J = 8.9\text{ Hz}$, 1H), 4.64 (d, $J = 7.6\text{ Hz}$, 1H), 4.54 (d, $J = 12.1\text{ Hz}$, 1H), 4.23 (dq, $J = 12.6, 6.3\text{ Hz}$, 1H), 3.82 (dd, $J = 15.5, 6.4\text{ Hz}$, 2H), 3.75 (t, $J = 8.9\text{ Hz}$, 1H), 3.70 (d, $J = 8.8\text{ Hz}$, 1H), 3.54 (t, $J = 8.6\text{ Hz}$, 1H), 2.33 (dd, $J = 13.9, 6.5\text{ Hz}$, 2H), 2.08 (dd, $J = 14.0, 6.4\text{ Hz}$, 1H), 1.88 (dd, $J = 12.8, 5.9\text{ Hz}$, 1H), 1.70 (s, 3H), 1.68–1.62 (m, 1H). ^{13}C NMR (150 MHz, $CDCl_3$): δ 142.0, 138.5, 138.3, 138.1, 128.4, 128.4, 128.4, 128.1, 127.9, 127.8, 127.7, 127.6, 112.6, 101.3, 80.6, 77.9, 75.8, 74.4, 74.4, 73.6, 72.2, 68.8, 44.8, 44.3, 34.4, 22.9; ESI-HRMS: m/z calcd for $C_{33}H_{38}NaO_5$ $[M+Na]^+$: 537.2617; found: 537.2621.