Total synthesis of Le\textsuperscript{A}-LacNAc pentasaccharide as a ligand for \textit{Clostridium difficile} toxin A

Ping Zhang,\textsuperscript{a,b} Kenneth Ng\textsuperscript{b} and Chang-Chun Ling\textsuperscript{a} *

\textit{Alberta Ingenuity Center for Carbohydrate Science, \textsuperscript{a}Department of Chemistry and \textsuperscript{b}Department of Biological Science, University of Calgary, Calgary Alberta T2N 1N4 Canada.}

\textit{E-mail: ccling@ucalgary.ca}

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p-Chlorophenyl 2,3,4,6-tetra-O-acetyl-1-thio-β-D-galactopyranoside (34)

To a solution containing 1,2,3,4,6-penta-O-acetyl-β-D-galactopyranose 33 (20.0 g, 51.2 mmol) and p-chlorophenylthiol (11.1 g, 76.9 mmol, 1.5 equiv.) in anhydrous CH₂Cl₂ (250 mL), was added boron trifluoride etherate (9.7 mL, 76.9 mmol), and the mixture was stirred at room temperature overnight. The mixture was cooled to 0°C, Et₃N (10 mL) was added to quench the reaction. The unreacted thiol was acetylated by adding acetic anhydride (8.0 mL) to the mixture. After stirring at room temperature for 1 hour, the mixture was concentrated under reduced pressure. The residue was dissolved in EtOAc (300 mL), successively washed with H₂O (2 × 200 mL), 2N NaOH (1 × 100 mL), 2N HCl (1 × 100 mL), dried over anhydrous Na₂SO₄, and evaporated. Pure compound 34 was obtained by recrystallization from a mixture of AcOEt – hexane (21.0 g, 86.3% yield) as colorless crystals (Found: C, 50.63; H, 5.05%. C₂₀H₂₃O₉SCl requires C, 50.58; H, 4.88%); [α]D -1.3° (c 0.9, CHCl₃); δH (400 MHz, CDCl₃) 7.47 (d, 2H, J 8.6 Hz, SPhCl), 7.29 (d, 2H, J 8.6 Hz, SPhCl), 5.41 (dd, 1H, J 3.2, 0.7 Hz, H-4), 5.20 (1H, dd, J 9.9, 9.9 Hz, H-2), 5.05 (dd, 1H, J 9.9, 3.3 Hz, H-3), 4.66 (d, 1H, J 9.9 Hz, H-1), 4.18 (dd, 1H, J 11.4, 7.0 Hz, H-6a), 4.10 (dd, 1H, J 11.4, 6.1 Hz, H-6b), 3.93 (ddd, 1H, J 7.0, 6.3, 0.7, H-5), 2.11 (s, 3H, Ac), 2.10 (s, 3H, Ac), 2.05 (s, 3H, Ac), 1.98 (s, 3H, Ac); δC (100 MHz, CDCl₃) 170.33 (CO), 170.10 (CO), 170.01 (CO), 169.38 (CO), 137.45 C-1_SPhCl), 134.41 (C-3_SPhCl + C-5_SPhCl), 130.33 (C-4_SPhCl), 128.99 (C-2_SPhCl + C-6_SPhCl), 86.06 (C-1), 74.51 (C-5), 71.93 (C-3), 67.15 (C-4 or C-2), 67.12 (C-2 or C-4), 61.58 (C-6), 20.82 (Ac), 20.66 (Ac), 20.59 (Ac), 20.56 (Ac); m/z (ESI-HRMS) calcd for [C₂₀H₂₃O₉SCl + Na]⁺ 497.0644, found 497.0645.

p-Chlorophenyl 1-thio-β-D-galactopyranoside (35)

The per-acetate 34 (20.0 g, 42.1 mmol) was dissolved in anhydrous MeOH (170 mL), a solution of NaOMe in MeOH (1.5 M, 3 mL) was added, and the mixture was stirred at room temperature for 30 minutes. After neutralizing the reaction with Amberlite IR-120 (H⁺), the mixture was evaporated under reduced pressure to give pure tetraol 35 (12.9 g, 100% yield) as white solid (Found: C, 46.66; H, 5.28%. C₁₂H₁₅O₂SCl requires C, 46.98; H, 4.93%); [α]D -46.4° (c 1.0, CHCl₃); δH (400 MHz, CDCl₃) 7.54 (d, 2H, J 8.6 Hz, SPhCl), 7.29 (m, 2H, J 8.6 Hz, SPhCl), 4.57 (d, 1H, J 9.6 Hz, H-1), 3.90 (dd, 1H, J 3.2, 0.6 Hz, H-4), 3.77 (dd, 1H, J 11.5, 6.9 Hz, H-6a), 3.71 (dd, 1H, J 11.5, 5.1 Hz, H-6b), 3.60 (dd, 1H, J 9.3, 9.3 Hz, H-2),
3.57 (ddd, 1H, $J$ 0.9, 5.1, 6.9 Hz, H-5), 3.50 (dd, 1H, $J$ 9.2, 3.3 Hz, H-3); $\delta_C$ (100 MHz, CD$_3$OD) 133.29 (C-1_SPhCl), 132.66 (C-4_SPhCl), 132.33 (C-3_SPhCl + C-5_SPhCl), 128.43 (C-2_SPhCl + C-6_SPhCl), 88.51 (C-1), 79.27 (C-5), 74.88 (C-3), 69.45 (C-2), 69.01 (C-4), 61.25 (C-6); $m/z$ (ESI-HRMS) calcd for [C$_{12}$H$_{15}$O$_5$SCl + Na]$^+$ 329.0221, found 329.0224.

**p-Chlorophenyl 2,3-di-O-acetyl-4,6-O-benzylidene-1-thio-β-D-galactopyranoside (12)**

To a suspension of tetraol 35 (7.24 g, 23.6 mmol) and benzaldehyde dimethyl acet al (7.09 mL, 47.2 mmol) in anhydrous CH$_3$CN (100 mL) was added (±)-Camphor-10-sulfonic acid (500 mg), and the mixture was stirred for 30 minutes. Et$_3$N (2.0 mL) was added to quench the reaction. After removing the solvent under reduced pressure, the residue was acetylated with a mixture of acetic anhydride (25 mL) and anhydrous pyridine (30 mL) for 4 hours at room temperature. The reaction mixture was concentrated again and co-evaporated with toluene (3 × 50 mL). After a column chromatography on silica gel using a gradient of AcOEt – toluene (5% → 7%) as the eluent, compound 12 (10.2 g, 90% yield) was obtained in pure form (Found: C, 57.60; H, 5.35%. C$_{23}$H$_{23}$O$_7$SCl requires C, 57.68; H, 4.84%); $[\alpha]_D$-21.8° (c 0.6, CHCl$_3$); $\delta_H$ (400 MHz, CDCl$_3$) 7.58 (d, 2H, $J$ 8.4 Hz, SPhCl), 7.44 – 7.32 (m, 5H, Ph), 7.21 (d, 2H, $J$ 8.5, SPhCl), 5.46 (s, 1H, PhCH), 5.29 (dd, 1H, $J$ 9.8, 9.8 Hz, H-2), 5.01 (dd, 1H, $J$ 9.9, 3.3 Hz, H-3), 4.65 (d, 1H, $J$ 9.7 Hz, H-1), 4.38 – 4.29 (m, 2H, H-4 + H-6a), 3.98 (dd, 1H, $J$ 12.1, ~1 Hz, H-6b), 3.56 (m, 1H, H-5), 2.10 (s, 3H, Ac), 2.03 (s, 3H, Ac); $\delta_C$ (100 MHz, CDCl$_3$) 170.53 (CO), 169.03 (CO), 137.44, 135.58, 134.61, 129.25, 128.94, 128.90, 128.23, 126.43, 100.98 (PhCH), 84.22 (C-1), 73.34 (C-4), 73.03 (C-3), 69.66 (C-5), 68.99 (C-6), 66.59 (C-2), 20.89 (Ac), 20.85 (Ac); $m/z$ (ESI-HRMS) calcd for [C$_{23}$H$_{23}$O$_7$SCl + Na]$^+$ 501.0745, found 501.0749.

**Synthesis of compound 15**

![Synthesis of compound 15](image)

a. Ac$_2$O/pyridine; b. p-ClPhSH/BF$_3$.Et$_2$O/CH$_2$Cl$_2$; c. NaOMe/MeOH; d. BnBr/NaH/DMF;

**p-Chlorophenyl 2,3,4-tri-O-acetyl-1-thio-α,β-L-fucopyranoside (38)**

A solution of L-fucose (36, 20.34 g, 0.124 mol) in a mixture of acetic anhydride (70 mL) and anhydrous pyridine (80 mL) was stirred at 50° C overnight. The mixture was evaporated under vacuum and coevaporated with toluene (3 × 100 mL) to afford the crude 1,2,3,4-tetra-O-acetyl-α,β-L-fucopyranose (37, 40 g, quantitative). The crude α,β-mixture was dissolved in anhydrous CH$_2$Cl$_2$ (200 mL), and p-chlorophenylthiol (27.9 g, 192.6 mmol, 1.6 equiv.) was added. After the addition of boron trifluoride etherate (22.7 mL, 180.6 mmol, 1.5
equiv.), the mixture was stirred at room temperature overnight. The mixture was cooled to 0°C, Et₃N (20 mL) was added to quench the reaction. The unreacted thiol was acetylated by adding acetic anhydride (16.0 mL) to the mixture. After stirring at room temperature for 1 hour, the mixture was concentrated under reduced pressure. The residue was dissolved in EtOAc (600 mL), successively washed with H₂O (2 × 300 mL), 2N HCl (1 × 300 mL), and 5% NaHCO₃ (2 × 300 mL), dried over anhydrous Na₂SO₄, and evaporated. Compound 38 (41.15 g, 82% yield) was obtained as an α,β-mixture (1:9) by chromatography on silica gel using a mixture of 5% AcOEt – hexane as eluent (Found: C, 51.95; H, 5.09%. C₁₈H₂₁O₇SCl requires C, 51.86; H, 5.08%).

δH (400 MHz, CDCl₃) for the β-anomer: 7.49 – 7.45 (m, 2H, SPhCl), 7.32 – 7.27 (m, 2H, SPhCl), 5.26 (dd, 1H, J₃.₄, 0.₈ Hz, H-4), 5.18 (dd, 1H, J₉.₈, 9.₈ Hz, H-2), 5.05 (dd, 1H, J₉.₉, 3.₃ Hz, H-3), 4.65 (d, 1H, J₉.₈ Hz, H-1), 3.83 (dq, 1H, J₆.₅, 1.₀ Hz, H-5), 2.13 (s, 3H, Ac), 2.09 (s, 3H, Ac), 1.97 (s, 3H, Ac), 1.23 (d, 1H, J₆.₄ Hz, H-6);

δC (100 MHz, CDCl₃) 170.43 (CO), 170.01 (CO), 169.35 (CO), 134.40 (Ar), 134.16 (Ar), 130.73 (Ar), 128.91 (Ar), 85.88 (C-1), 73.22 (C-5), 72.35 (C-3), 70.24 (C-4), 67.21 (C-2), 20.79 (Ac), 20.57 (Ac), 20.55 (Ac), 16.40 (C-6);

m/z (ESI-HRMS) calcd for \([\text{C}_{18}\text{H}_{21}\text{O}_{7}\text{SCl} + \text{Na}]^+\) 439.0589, found 439.0590.

**p-Chlorophenyl 2,3,4-tri-O-benzyl-1-thio-β-L-fucopyranoside (15)**

The triacetate 38 (1:9 α:β mixture, 21.5 g, 51.6 mmol) was dissolved in anhydrous MeOH (250 mL), and a solution of NaOMe in MeOH (1.5 M, 3.0 mL) was added. After stirring at room temperature for 2 hours, the mixture was neutralized with Amberlite IR-120 (H⁺). The resin was removed by filtration and the organic solution was concentrated under reduced pressure to give a syrup (~15 g). The crude triol was dissolved in anhydrous DMF (130 mL), NaH (60% in mineral oil, 10.0g, 250 mmol) was added portion wise, and the reaction mixture was stirred at room temperature for 1 hour. After cooling to 0°C, benzyl bromide (35 mL, 295.2 mmol) was added dropwise, and the mixture was allowed to warm-up to temperature. After stirring overnight, MeOH (15 mL) was added, and the mixture was concentrated under reduced pressure to remove most of the solvent. The mixture was dissolved in EtOAc (400 mL), washed with H₂O (1 × 200 mL), 2N HCl (1 × 200 mL), 10% NaHCO₃ (1 × 200 mL), dried over anhydrous Na₂SO₄, and evaporated. After a chromatography on silica gel using 3.5% AcOEt – hexane as eluent, the pure β-anomer 15 was obtained (23.6 g, 85.5 yield%) as a white solid (Found: C, 70.70; H, 5.83%. C₃₃H₃₃O₄SCl requires C, 70.63; H, 5.93%). [α]D +3.₈° (c 0.₇, CHCl₃);

δH (400 MHz, CDCl₃) 7.54 (d, 2H, J 8.₆ Hz, SPhCl), 7.47 – 7.28 (m, 15H, 3 × Bn), 7.15 (d, 2H, J 8.₆ Hz, SPhCl), 5.03 (d, 1H, J 11.₄ Hz, Bn), 4.77 (s, 4H, Bn), 4.68 (d, 1H, J 11.₄ Hz, Bn), 4.58 (d, 1H, J 9.₆ Hz, H-1), 3.92 (dd, 1H, J 9.₄, 9.₄ Hz, H-2), 3.67 (dd, 1H, J 2.₃, ~1 Hz, H-4), 3.62 (dd, 1H, J 2.₇, 9.₂ Hz, H-3), 3.56 (dq, 1H, J 6.₃, ~1 Hz, H-5), 1.30 (d, 3H, J 6.₄ Hz, H-6);

δC (100 MHz, CDCl₃) 138.62, 138.29, 133.12, 132.94, 132.57, 128.85, 128.44, 128.33, 128.25, 128.22, 127.98, 127.74, 127.71, 127.59, 127.55 (Ar), 87.12 (C-1), 84.50 (C-3), 76.87 (C-2), 76.55 (C-4), 75.55 (Bn), 74.68 (C-5), 74.67 (Bn), 72.82 (Bn), 17.29 (C-6);

m/z (ESI-HRMS) calcd for [C₃₃H₃₃O₄SCl + Na]⁺ 583.1680, found 583.1678.
p-Chlorophenyl 3,4,6-tri-O-acetyl-2-deoxy-2-phthalimido-1-thio-β-D-glucopyranoside (17)

To a solution of 1,3,4,6-tetra-O-acetyl-2-deoxy-2-phthalimido-α,β-D-glucopyranose 16 (40.0 g, 89.4 mmol) and p-chlorophenylthiol (20.6 g, 142.4 mmol) in anhydrous CH2Cl2 (200 mL), was added BF3·Et2O (16.8 mL, 134 mmol) dropwise. After stirring for 3 days at rt, the reaction was cooled to 0°, and Et3N (35 mL) was added to quench the reaction. The unreacted thiol was then acetylated by the addition of excess Ac2O (15 mL). After 1 h at rt, the mixture was concentrated under reduced pressure; the residue was dissolved in EtOAc (600 mL), and the organic solution was washed successively with H2O (2 × 300 mL), a solution of 2 N HCl (1 × 300 mL) and a 5% solution of aqueous NaHCO3 (1 × 150 mL), dried over anhydrous Na2SO4, and concentrated to give a syrup which was recrystallized from a mixture of AcOEt–hexane. The desired thioglycoside 17 (38 g, yield 76%) was obtained in pure form as a white solid (Found: C, 55.47; H, 4.69; N, 2.41%. C26H24NO9ClS requires C, 55.57; H, 4.30; N, 2.49%); [α]D +39.7° (c 1.2, CHCl3); δH (400 MHz, CDCl3) 7.88 (m, 2H, Phth), 7.77 (m, 2H, Phth), 7.37 (m, 2H, SPhCl), 7.26 (m, 2H, SPhCl), 5.79 (dd, 1H, J 9.7 Hz, H-3), 5.67 (d, 1H, J 10.5 Hz, H-1), 5.12 (dd, 1H, J 9.7 Hz, H-4), 4.32 (dd, 1H, J 10.4, 10.4 Hz, H-2), 4.29 (dd, 1H, J 4.9, 12.4 Hz, H-6a), 4.21 (dd, 1H, J 2.3, 12.3 Hz, H-6b), 3.90 (ddd, 1H, J 2.3, 4.9, 10.2 Hz, H-5), 2.11 (s, 1H, Ac), 2.03 (s, 3H, Ac), 1.84 (s, 3H, Ac); δC (100 MHz, CDCl3) 170.53 (CO), 170.05 (CO), 169.38 (CO), 167.82 (CO), 166.91 (CO), 135.01, 134.99, 129.04, 123.74, 82.70 (C-1), 75.98 (C-5), 71.52 (C-3), 68.59 (C-4), 62.11 (C-6), 53.55 (C-2), 20.75 (Ac), 20.59 (Ac), 20.37 (Ac); m/z (ESI-HRMS) calc'd for [C26H24NO9ClS + Na]+ 584.0725, found 584.0754.

p-Chlorophenyl 2-deoxy-2-phthalimido-1-thio-β-D-glucopyranoside (18)

The peracetylated thioglycoside 17 (20.0 g, 35.6 mmol) was added to a solution of ~0.1 M guanidine/guanidinium chloride (400 mL); the starting material was observed to gradually dissolve to give a clear solution followed by the precipitation of desired deacetylated thioglycoside from the reaction mixture. The solid was filtered off under vacuum and washed with MeOH to afford pure 18 (14.53 g); after concentration of the mother liquor, more 18 (0.62 g) was crystallized out from the mixture. The total amount of 18 is 15.15 g (yield: 97.7%) (Found: C, 53.27; H, 4.50; N, 3.04%. C20H18NO6ClS.H2O requires C, 52.92; H, 4.44; N, 3.09%); [α]D +59.5° (c 0.34, CHCl3); δH (400 MHz, CDCl3) 7.93 – 7.81 (m, 4H, Phth), 7.40 (d, 2H, J 8.6 Hz, SPhCl), 7.25 (d, 2H, J 8.6 Hz, SPhCl), 5.57 (d, 1H, J 10.4 Hz, H-1), 4.24 (dd, 1H, J 10.2, 8.5 Hz, H-3), 4.08 (dd, 1H, J 10.3, 10.3 Hz, H-2), 3.95 (dd, 1H, J 12.1, 2.1 Hz, H-6a), 3.75 (dd, 1H, J 12.1, 1.9 Hz, H-6b), 3.49 (dd, 1H, J 9.9, 5.5, 2.0 Hz, H-5), 3.43 (dd, 1H, J 9.8, 8.6 Hz, H-4); δC (100 MHz, CDCl3) 135.84, 135.79, 135.06, 134.65, 133.12, 130.16, 124.64, 124.34 (Ar), 85.14 (C-1), 82.92 (C-5), 73.96 (C-3), 72.36 (C-4), 62.97 (C-6), 57.84 (C-2); m/z (ESI-HRMS) calc'd for [C20H18NO6ClS + Na]+ 458.0436, found 458.0435.
To a suspension containing the triol 18 (3.56 g, 8.2 mmol) and benzaldehyde dimethyl acetal (2.38 mL, 15.8 mmol) in anhydrous CH$_3$CN (20 mL), was added (±)-camphor-10-sulfonic acid (350 mg); the mixture was stirred at rt for 2 hrs. Et$_3$N (1.0 mL) was added to quench the reaction, and the mixture was concentrated under reduced pressure. The residue was dissolved in EtOAc (100 mL) and the organic solution was washed with H$_2$O (2 x 50 mL), dried over anhydrous Na$_2$SO$_4$ and evaporated under vacuum. The desired compound 14 (4.0 g, yield: 93%) was obtained by column chromatography on silica gel using 5% EtOAc – toluene as eluent. [$\alpha$]$_D$ +29.2° (c 0.65, CHCl$_3$); $\delta$H (400 MHz, CDCl$_3$) 7.96 – 7.83 (m, 2H, Phth), 7.81 – 7.72 (m, 2H, Phth), 7.53 – 7.45 (m, 2H, Ph), 7.43 – 7.32 (m, 5H, 3 x Ph + 2 x SPhCl), 7.30 – 7.23 (m, 2H, SPhCl), 5.65 (d, 1H, $J$ 10.5 Hz, H-1), 5.57 (s, 1H, PhCH), 4.63 (dd, 1H, $J$ 9.5, 9.5 Hz, H-2), 3.81 (dd, 1H, $J$ 10.2, 10.2 Hz, H-6b), 3.70 (ddd, 1H, $J$ 9.6, 9.6, 4.8 Hz, H-5), 3.58 (dd, 1H, $J$ 9.2, 9.2 Hz, H-4), 2.57 (s, 1H, OH-3); $\delta$C (100 MHz, CDCl$_3$) 168.20 (CO), 167.45 (CO), 136.81, 134.64, 134.42, 134.31, 131.50, 129.79, 129.40, 129.10, 129.01, 128.38, 128.20, 126.28, 101.97 (PhCH), 83.92 (C-1), 81.79 (C-4), 70.33 (C-3), 69.69 (C-5), 68.49 (C-6), 55.47 (C-2); m/z (ESI-HRMS) calcd for [C$_{27}$H$_{22}$NO$_6$ClS + Na]$^+$ 546.0749, found 546.0751.

Synthesis of compound 21

\[
\text{HO} \quad \begin{array}{c} \text{a} \end{array} \quad \text{a, NaN$_3$/DMF, 80° C.} \quad \text{N$_3$} \\
\text{HO} \quad \begin{array}{c} \text{R} \end{array} \\
\text{39} \quad \begin{array}{c} \text{21} \end{array}
\]

6-Azido-1-hexanol (21)

Compound was prepared from 6-chloro-1-hexanol (39) according to identical procedure published before (93% yield). The NMR data is identical to the literature. $^1$ $\delta$H (400 MHz, CDCl$_3$) 3.63 (t, 2H, $J$ 6.5 Hz, H-1), 3.26 (t, 2H, $J$ 6.9 Hz, H-6), 1.67 – 1.52 (m, 4H, H-2 + H-5), 1.45 – 1.34 (m, 4H, H-3 + H-4). $\delta$C (100 MHz, CDCl$_3$) 62.70, 51.37, 32.52, 28.79, 26.51, 25.32.

Attempt to synthesize p-chlorophenyl 2,3,4,6-tetra-O-acetyl-β-D-galactopyranosyl–(1→3)-6-O-benzyl-2-deoxy-4-O-p-methoxybenzyl-2-phthalimido-1-thio-β-D-glucopyranoside (6)

A mixture of imidate 10 (63.8 mg, 0.129 mmol, 3.0 eq), alcohol 13 (27.9 mg, 0.043 mmol) and 4 Å molecular sieves (100 mg) in anhydrous CH$_2$Cl$_2$ (0.8 mL) was stirred under Ar for 1
h. The mixture was cooled to 0° C, and TMSOTf (3.0 µL) was added. After 1 h, the reaction was neutralized with Et$_3$N (5 drops). The mixture was filtered off and concentrated. The residue was purified by chromatography on silica gel using a gradient of AcOEt – hexane (7% → 15%) to obtain the recovered acceptor 13 (19 mg) and rearranged imidate 25 (12 mg). No desired disaccharide 6 was formed. Data for 2,3,4,6-Tetra-O-acetyl-1-N-trichloroacetyl-β-D-galactopyranosylamine (25): [α]$_D$ +23.7° (c 0.5, CHCl$_3$; δ$_H$ (400 MHz, CDCl$_3$) 7.47 (d, 1H, $J$ 8.6 Hz, NH), 5.48 (dd, 1H, $J$ 3.1, 0.9 Hz, H-4), 5.24 (dd, 1H, $J$ 10.1, 9.0 Hz, H-2), 5.18 (dd, 1H, $J$ 9.9, 3.2 Hz, H-3), 5.14 (dd, 1H, $J$ 8.9, 8.9 Hz, H-1), 4.18 – 4.11 (m, 2H, H-6a + H-6b), 4.09 (ddd, 1H, $J$ 7.0, 5.7, 0.9 Hz, H-5), 2.18 (s, 3H, Ac), 2.08 (s, 3H, Ac), 2.06 (s, 3H, Ac), 2.02 (s, 3H, Ac); δ$_C$ (100 MHz, CDCl$_3$) 171.38 (CO), 170.36 (CO), 169.93 (CO), 169.72 (CO), 162.03 (CO), 80.42 (C-1), 72.86 (C-5), 70.43 (C-3), 68.01 (C-2), 66.97 (C-4), 60.95 (C-6), 20.65 (Ac), 20.64 (Ac), 20.59 (Ac), 20.52 (Ac); m/z (ESI-MS) calcd for [C$_{16}$H$_{20}$NO$_{10}$Cl$_3$ + Na]$^+$ 514.0, 516.0, 518.0, found 514.2, 516.1, 518.0.

Attempt to synthesize $p$-chlorophenyl 2,3-di-O-acetyl-4,6-O-benzylidene-β-D-galactopyranosyl–(1→3)-6-O-benzyl-2-deoxy-4-O-p-methoxybenzyl-2-phthalimido-1-thio-β-D-glucopyranoside (24)

A mixture of imidate 11 (31 mg, 0.062 mmol, 2.0 eq), alcohol 13 (20 mg, 0.031 mmol) and 4 Å molecular sieves (100 mg) in anhydrous CH$_2$Cl$_2$ (0.8 mL) was stirred under argon for 1 h. The mixture was cooled to 0° C, and TMSOTf (3.0 µL) was added. After 1 h, the reaction was neutralized with Et$_3$N (5 drops). The mixture was filtered off and concentrated. The residue was purified by chromatography on silica gel using a gradient of AcOEt – hexane (7% → 15%) to obtain the recovered acceptor 13 (14 mg) and rearranged imidate 26 (21 mg). No desired disaccharide 24 was formed. Data for 2,3-Di-O-acetyl-4,6-O-benzylidene-β-D-galactopyranosylamine trichloroacetate (26) (Found: C, 46.21; H, 4.43; N, 2.75%. C$_{19}$H$_{20}$NO$_8$Cl$_3$ requires C, 45.94; H, 4.06; N, 2.82%); [α]$_D$ +50.2° (c 0.6, CHCl$_3$; δ$_H$ (400 MHz, CDCl$_3$) 7.61 (d, 1H, $J$ 8.9 Hz, NH), 7.55 – 7.49 (m, 2H, Ph), 7.43 – 7.34 (m, 3H, Ph), 5.55 (s, 1H, PhCH), 5.44 (dd, 1H, $J$ 10.2, 9.4 Hz, H-2), 5.18 (dd, 1H, $J$ 9.1, 9.1 Hz, H-1), 5.13 (dd, 1H, $J$ 10.3, 3.6 Hz, H-3), 4.50 (dd, 1H, $J$ 3.6, 0.8 Hz, H-4), 4.36 (dd, 1H, $J$ 12.6, 1.5 Hz, H-6a), 4.09 (dd, 1H, $J$ 12.7, 1.8 Hz, H-6b), 3.71 (dd, 1H, $J$ 1.7, 1.7, 1.1 Hz, H-5), 2.13 (s, 3H, Ac), 2.07 (s, 3H, Ac); δ$_C$ (100 MHz, CDCl$_3$) 171.19 (CO), 170.38 (CO), 162.21 (CO), 137.15, 129.15, 128.26, 126.07 (Ar), 100.75 (PhCH), 80.32 (C-1), 73.21 (C-4), 71.57 (C-3), 68.83 (C-6), 68.29 (C-5), 67.89 (C-2), 20.84 (Ac), 20.66 (Ac); m/z (ESI-MS) calcd for [C$_{16}$H$_{20}$NO$_{10}$Cl$_3$ + Na]$^+$ 514.0, 520.0, 522.0, found 518.2, 520.1, 522.0.

2,3,4-tri-O-acetyl-1-thio-α,β-L-fucopyranosyl trichloroacetimidate (28)

Thioglycoside 15 (5.16 g, 9.20 mmol) was dissolved in a mixture of CH$_3$CN (30 mL) – H$_2$O (2.8 mL); N-iodosuccinimide (4.36 g, 18.39 mmol) was added and the mixture was stirred for 30 minutes at rt. Et$_3$N (3 mL) was added to quench the reaction. The mixture was diluted with EtOAc (200 mL), and washed with 10% aqueous Na$_2$S$_2$O$_3$ solution (2 × 100 mL), dried
over anhydrous Na$_2$SO$_4$ and evaporated. The residue was purified by chromatography on silica gel using 20% AcOEt – toluene as eluent to afford the hemiacetal 27 (3.29 g, 82.3% yield). Part of the hemiacetal (3.0 g, 8.90 mmol) and CCl$_3$CN (6.3 mL, 62.8 mmol) were dissolved in anhydrous CH$_2$Cl$_2$ (20 mL), anhydrous K$_2$CO$_3$ (3.3 g, 23.9 mmol) was added; the mixture was stirred at rt overnight. The reaction was diluted with EtOAc (150 mL), washed with H$_2$O (2 × 50 mL), and evaporated to dryness. NMR showed that the mixture contained 28 as a mixture (α/β 1:2) which was pure enough for use in next step, no further purification was performed.

δ$_H$ (300 MHz, CDCl$_3$) for α-anomer: 8.49 (s, 1H, C=NH), 7.44 – 7.11 (m, 15H, Ar), 6.51 (d, 1H, $J_{3.4}$ Hz, H-1), 5.06 – 4.61 (m, 6H, Ar), 1.14 (d, 3H, $J_{6.0}$ Hz, H-6). For β-anomer 8.59 (s, 1H, C=NH), 7.44 – 7.11 (m, 15H), 5.71 (d, 1H, $J_{8.1}$ Hz, H-1), 5.06 – 4.61 (m, 6H, Ar), 1.21 (d, 3H, $J_{6.4}$ Hz, H-6).

**p-Chlorophenyl 2,3,4-tri-O-benzyl-α-L-fucopyranosyl–(1$→$3)-6-O-benzyl-2-deoxy-2-phthalimido-1-thio-β-D-glucopyranoside (29) and p-Chlorophenyl 2,3,4-tri-O-benzyl-α-L-fucopyranosyl–(1$→$4)-6-O-benzyl-2-deoxy-2-phthalimido-1-thio-β-D-glucopyranoside (30)**

A mixture of imidate 28 (1.57 g, 2.7 mmol), diol 19 (1.10 g, 2.09 mmol) and 4 Å molecular sieves (1.5 g) in anhydrous CH$_2$Cl$_2$ (10 mL) were stirred under Ar for 1 h. The mixture was cooled to -78° C, and TMSOTf (15 µL) was added dropwise. After 30 mins, the reaction was neutralized with Et$_3$N (0.5 mL). The mixture was diluted with EtOAc (100 mL) and the insoluble molecular sieves were removed by filtration. After concentration, the residue was purified by chromatography on silica gel using a gradient of AcOEt – hexane (15% → 20%) to afford 29 (1.46 g, 52% yield) and 30 (0.760 g, 27% yield).

Data for 29 (Found: C, 68.51; H, 5.56; N, 1.54%. C$_{54}$H$_{52}$NO$_{10}$SCl requires C, 68.81; H, 5.56; N, 1.49%): [$\alpha$]$_D$ +32.1° (c 0.5, CHCl$_3$); δ$_H$ (400 MHz, CDCl$_3$) 7.88 (dd, 1H, $J_{7.4}$ Hz, Phth), 7.73 – 7.66 (m, 2H, 2 × Phth), 7.58 (ddd, 1H, $J_{7.4}$, 7.4, ~1 Hz, Phth), 7.47 – 7.15 (m, 22H, Ar), 6.99 – 6.93 (m, 2H, Ar), 5.68 (d, 1H, $J_{10.3}$ Hz, H-1_GlcN), 4.86 (d, 1H, $J_{11.4}$ Hz, Bn), 4.65 (d, 1H, J 12.0, Bn), 4.61 (d, 1H, J 12.1 Hz, Bn, overlapped), 4.61 (d, 1H, J 3.5 Hz, H-1_Fuc), 4.61 (d, 1H, J 12.1 Hz, Bn, overlapped) 4.54 (d, 1H, J 11.4 Hz, Bn), 4.53 (d, 1H, J 10.9 Hz, Bn), 4.30 (dd, 1H, J 10.3, 10.3 Hz, H-2_GlcN), 4.26 (d, 1H, J 1.2, OH-4_GlcN), 4.21 (dd, 1H, J 10.3, 8.2 Hz, H-3_GlcN), 4.10 (d, 1H, J 13.4 Hz, Bn), 4.07 (dq, 1H, J 6.6, ~1 Hz, H-5_Fuc), 3.93 (dd, 1H, J 10.6, 1.4 Hz, H-6a_GlcN), 3.82 – 3.68 (m, 4H, H-3_Fuc + H-5_GlcN + H-2_Fuc + H-6b_GlcN), 3.57 – 3.49 (m, 2H, H-4_GlcN + H-4_Fuc), 3.39 (d, 1H, J 13.0 Hz, Bn), 1.07 (d, 3H, J 6.5 Hz, H-6_Fuc); δ$_C$ (100 MHz, CDCl$_3$) 168.61 (CO), 167.64 (CO), 138.70, 138.43, 138.26, 138.03, 134.33, 134.24, 133.77, 132.38, 131.95, 130.27, 128.95, 128.42, 128.34, 128.25, 128.15, 128.61, 127.59, 127.54, 123.19, 123.00, 100.87 (C-1_Fuc), 84.11 (C-3_GlcN), 82.82 (C-1_GlcN), 79.35 (C-5_GlcN or C-3_Fuc), 78.90 (C-3_Fuc or C-5_GlcN), 77.86 (C-4_Fuc), 74.74 (Bn), 73.85 (C-2_Fuc), 73.42 (CH$_2$Ph), 73.41 (CH$_2$Ph), 72.41 (CH$_2$Ph), 70.99 (C-4_GlcN), 69.37 (C-6_GlcN), 68.52 (C-5_Fuc), 53.52 (C-2_GlcN), 16.43 (C-6_Fuc); m/z (ESI-HRMS) calcd for [C$_{54}$H$_{52}$NO$_{10}$SCl + Na]$^+$ 964.2893, found 964.2891.
Data for 30 (Found: C, 68.61; H, 5.59; N, 1.52%. $C_{54}H_{52}NO_{10}SCl$ requires C, 68.81; H, 5.56; N, 1.49%): $[\alpha]_D$ -14.1° (c 0.5, CHCl$_3$); $\delta$H (400 MHz, CDCl$_3$) 7.92 (m, 1H, Phth), 7.83 (m, 1H, Phth), 7.80 – 7.69 (m, 2H, Phth), 7.45 – 7.20 (m, 22H, 5 × Ph + 2 × SPhCl), 7.13 (d, 2H, J 8.3, SPhCl), 5.55 (d, 1H, J 10.3, H-1_GlcN), 4.96 (d, 1H, J 3.9 Hz, H-1_Fuc), 4.96 (d, 1H, J 11.4 Hz, Bn), 4.84 (d, 1H, J 12.1 Hz, Bn), 4.80 (d, 1H, J 11.7 Hz, Bn), 4.74 (d, 1H, J 11.8 Hz, Bn), 4.66 (d, 1H, J 11.6 Hz, Bn), 4.61 (d, 1H, J 11.5 Hz, Bn), 4.38 (d, 1H, J 11.6 Hz, Hz), 4.35 (d, 1H, J 11.9 Hz, Bn), 4.31 (m, 1H, H-3_GlcN), 4.22 (dd, 1H, J 9.9, 9.9 Hz, H-2_GlcN), 4.07 (dd, 1H, J 10.2, 3.7 Hz, H-2_Fuc), 4.02 (dq, 1H, J 6.4, ~1 Hz, H-5_Fuc), 3.95 (high order m, 1H, H-6a_GlcN), 3.87 (dd, 1H, J 10.0, 2.9 Hz, H-3_Fuc), 3.81 – 3.72 (m, 2H, H-5_GlcN + H-6b_GlcN), 3.65 (br, 1H, H-4_Fuc), 3.49 (t, 2H, J 8.7 Hz, CH$_2$N$_3$), 1.57 (s, 1H, OH-3_GlcN), 1.07 (d, 3H, J 6.5 Hz, H-6_Fuc); m/z (ESI-HRMS) calcd for $[C_{54}H_{52}NO_{10}SCl + Na]^+$ 964.2893, found 964.2900.

II. $^1$H and $^{13}$C spectra of all synthesized compounds

The $^1$H and $^{13}$C spectra of all synthesized compounds and the $^1$H-$^1$H GCOSY and $^1$H-$^{13}$C GHSQC of the final products.

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$^1$H NMR in CDCl$_3$, 400 MHz
$^{13}$C NMR in CDCl$_3$, 100 MHz
$^{1}$H NMR in CDCl$_3$, 400 MHz
$^{13}$C NMR in CDCl$_3$, 100 MHz
$^1$H NMR in CDCl$_3$, 400 MHz
$^{13}$C NMR in CDCl$_3$, 100 MHz

[Chemical structure image]

0 10 20 30 40 50 60 70 80 90 100 110 120 130 140 150 160 170 180 190 200 0 2000 4000 6000 8000 10000 12000 14000 16000 18000 20000 22000 24000 26000
$\text{H NMR in CDCl}_3$, 400 MHz
$^{13}$C NMR in CDCl$_3$, 100 MHz

![NMR Spectrum Diagram]
$^{1}H$ NMR in CD$_3$OD, 400 MHz
$^{13}$C NMR in CDCl$_3$, 100 MHz

![Chemical structure and NMR spectrum](image_url)
$^1$H NMR in CDCl$_3$, 400 MHz
$^{13}$C NMR in CDCl$_3$, 100 MHz
$^1$H NMR in CDCl$_3$, 400 MHz
$^{13}$C NMR in CDCl$_3$, 100 MHz
$^1$H NMR in CDCl$_3$, 400 MHz
$^{13}$C NMR in CDCl$_3$, 100 MHz
$^1$H NMR in CDCl$_3$, 400 MHz
$^{13}$C NMR in CDCl$_3$, 100 MHz
$^1$H NMR in CDCl$_3$, 400 MHz
$^{13}$C NMR in CDCl$_3$, 100 MHz

$\text{+ } \alpha$-anomer

![Chemical structure and NMR spectrum](image)
$^{1}\text{H NMR in CDCl}_3, 400 MHz$
$^{13}$C NMR in CDCl$_3$, 100 MHz
$^1$H NMR in CDCl$_3$, 400 MHz
$^1\text{H NMR in CDCl}_3$, 400 MHz
$^{13}$C NMR in CDCl$_3$, 100 MHz

S35
$^{13}$C NMR in CDCl$_3$, 100 MHz

![Carbon NMR spectrum](image-url)
$^1$H NMR in CDCl$_3$, 400 MHz
$^{13}$C NMR in CDCl$_3$, 100 MHz
$^{1}H$ NMR in CDCl$_3$, 400 MHz
$^{13}$C NMR in CDCl$_3$, 100 MHz
$^1$H NMR in CDCl$_3$, 400 MHz
$^{13}$C NMR in CDCl$_3$, 100 MHz
$^1\text{H NMR in } \text{CDCl}_3, 400 \text{ MHz}$

![NMR Spectrogram](image)
$^{1}H$ NMR in CDCl$_3$, 400 MHz
$^1$H NMR in CDCl$_3$, 400 MHz
$^{13}$C NMR in CDCl$_3$, 100 MHz
$^1$H NMR in CDCl$_3$, 400 MHz

![Chemical structure with NMR spectrum](image)
$^1$H NMR in CDCl$_3$, 400 MHz
$\text{C NMR in CDCl}_3, 100 \text{ MHz}$

$\text{S50}$
$^1\text{H NMR in CDCl}_3, 400 \text{ MHz}$
$^{13}$C NMR in CDCl$_3$, 100 MHz

\begin{center}
\includegraphics[width=\textwidth]{image}
\end{center}
$^1$H NMR in CDCl$_3$, 400 MHz
$^1$H NMR in CDCl$_3$, 400 MHz
1D $^1$H TOCSY Experiments on 31. – Green arrows indicate the selective excitation frequencies

Section of the original spectrum
$^1$H-$^1$H COSY NMR (CDCl$_3$, 600 MHz) combined with a 1D TOCSY trace (OH-2' was excited)
$^{1}H$ NMR in $D_2O$, 400 MHz

S59
$^{13}$C NMR in D$_2$O, 100 MHz
$^{1}H-^{1}H$ 2D GCOSY NMR in D$_2$O, 400 MHz
$^{1}H-^{13}C$ GHSQC NMR in D$_2$O, 400 MHz
High Resolution ESI Mass Spectra

Marinor Spec /5:9 ASC=>SM5[BP = 848.4, 481]

Mass (m/z)

847.81576 848.24331 848.67066 849.09841 849.52596 849.95351

% Intensity

849.38706

849.39260

P. Zhang 02.142 pos es
C1_00010008.dat
Acquired: 15:47, January 06, 2009

S63
$^1$H NMR in CDCl$_3$, 400 MHz
$^{1}H-^{13}C$ GHSQC NMR in CDCl$_3$, 400 MHz
$^{13}$C NMR in D$_2$O, 100 MHz
$^1$H-$^1$H 2D GCOSY NMR in D$_2$O, 400 MHz
$^1$H-$^{13}$C GHSQC NMR in D$_2$O, 400 MHz
High Resolution ESI Mass Spectra

Mariner Spec/7:11 ASC MC=>SM5[BP = 994.4, 256]

Mass (m/z)

% Intensity

994.44509

995.44982

993.8924 994.3570 994.6216 995.2862 995.7508 996.2154

P. Zhang 2008060519.dat
Acquired: 19:53, June 05, 2008

S70