## -Supporting Information-

# A Chondroitin Sulfate Small Molecule that Stimulates Neurite Outgrowth

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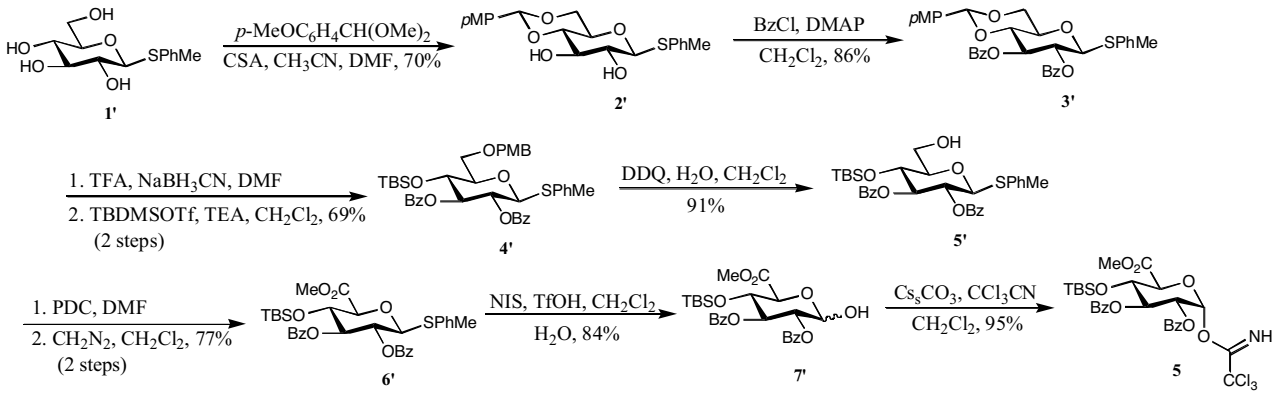
## General Methods

Unless stated otherwise, reactions were performed in flame-dried glassware under a nitrogen or an argon environment, using freshly distilled solvents. All other commercially obtained reagents were used as received. Thin-layer chromatography (TLC) was performed using E. Merck silica gel 60 F254 precoated plates (0.25 mm). Visualization of the developed chromatogram was performed by fluorescence quenching, cerium ammonium molybdate stain, or ninhydrin stain as necessary. ICN silica gel (particle size 0.032 - 0.063 mm) was used for flash chromatography. Gel filtration chromatography (Sephadex® G-10 and G-25 ultrafine) was used in order to achieve purification of the final products.

$^{1}$H NMR and proton decoupling experiments were recorded on Varian Mercury 300 (300 MHz) and Varian Mercury 600 (600 MHz) spectrometers and are reported in parts per million (δ) relative to $Me_4Si$ (0.0 ppm). Data for $^{1}$H are reported as follows: chemical shift (δ ppm), multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet), coupling constant in Hz, and integration. $^{13}$C NMR spectra were obtained on a Varian Mercury 300 (75 MHz) spectrometer and are reported in terms of chemical shift. IR spectra were recorded on a Perkin Elmer Paragon 1000 spectrometer and are reported in terms of frequency of absorption ($cm^{-1}$). A JASCO P-1010 was used to measure optical rotation. Mass spectra were obtained from the Protein/Peptide MicroAnalytical Laboratory and the Mass Spectrometry Facility at the California Institute of Technology.

## Experimental Details

**Scheme 1:** Synthesis of the Glucuronic Acid Monomer **5**




***p*-Methylphenyl 4,6-*O*-*p*-methoxybenzylidene-1-thio-β-D-glucopyranoside (2').** The procedure for the preparation of **2'** was adapted from Ye *et. al.*[1] *p*-Methylphenyl-1-thio-β-D-glucopyranoside[2] **1'** (36.7 g, 128 mmol) was dissolved in DMF (30.0 mL) and $CH_3CN$ (300 mL). *p*-Anisaldehyde dimethyl acetal (44.0 mL, 256 mmol) and DL-10-camphorsulfonic acid (6.00 g, 25.6 mmol) were added. The reaction was stirred at rt for 12 h. The reaction was quenched with TEA and concentrated to afford an orange syrup. The product was purified by flash chromatography (50% → 70% EtOAc:hexanes) to afford **2'** (36.3 g, 70%) as a white crystalline solid. $R_f$ 0.26 (50% EtOAc:hexanes). $[\alpha]_D^{21}$ = -38 (*c* = 1.0, $CH_2Cl_2$); IR (thin film on NaCl): υ = 3447, 2869, 1614, 1518, 1250, 1104, 1084, 1033 $cm^{-1}$; $^1H$ NMR (300 MHz, $CDCl_3$): δ = 7.43 (d, *J* = 8.1 Hz, 2H, $SC_6H_4Me$), 7.39 (d, *J* = 9.0 Hz, 2H, $C_6H_4OMe$), 7.15 (d, *J* = 7.5 Hz, 2H, $SC_6H_4Me$), 6.88 (d, *J* = 9.0 Hz, 2H, $C_6H_4OMe$), 5.48 (s, 1H, MeOPhC*H*), 4.56 (d, *J* = 9.9 Hz, 1H, H-1), 4.35 (dd, *J* = 3.9, 10.5 Hz, 1H), 3.85 – 3.72 (m, 5H), 3.50 – 3.39 (m, 3H), 2.80 (br s, 1H, O*H*), 2.67 (br s, 1H, O*H*), 2.36 (s, 3H, $SPhCH_3$); $^{13}C$ NMR (75 MHz, $CDCl_3$): δ = 138.8, 138.2, 133.6, 132.1, 129.9, 129.4, 127.7, 113.7, 101.8, 88.7, 80.2, 74.5, 72.5, 70.5, 68.6, 55.3, 21.2; FAB MS: *m/z*: calcd for $C_{21}H_{25}O_6S$: 405.1372; found: 405.1359 $[M + H]^+$.

***p*-Methylphenyl 2,3-di-*O*-benzoyl-4,6-*O*-*p*-methoxybenzylidene-1-thio-β-D-glucopyranoside (3'). 2'** (23.7 g, 58.6 mmol) was dissolved in $CH_2Cl_2$ (670 mL). In a separate flask, benzoyl chloride (17.0 mL, 146 mmol) was added dropwise to a solution of 4-(dimethylamino)pyridine (DMAP, 25.1 g, 205 mmol) in $CH_2Cl_2$ (225 mL). The benzoyl chloride/DMAP solution was then slowly added to the solution of **2'**. An additional volume of $CH_2Cl_2$ (19.0 mL) was used to complete the transfer of solution. The reaction was allowed to stir at rt for 25 min and then

quenched with saturated aqueous $NaHCO_3$. The aqueous layer was extracted with $CH_2Cl_2$ (2x). The combined organic layers were washed with brine, dried over $Na_2SO_4$, filtered, and concentrated to yield a pale yellow solid. This crude material was washed with MeOH and crystallization from EtOAc afforded **3'** as a white solid (30.8 g, 86%). $R_f$ 0.43 (30% EtOAc:hexanes). $[\alpha]_D^{22}$ = +25 (*c* = 0.42, $CH_2Cl_2$); IR (thin film on NaCl): $\upsilon$ = 2934, 1740, 1735, 1730, 1715, 1700, 1617, 1614, 1517, 1272, 1251, 1095 $cm^{-1}$; $^1H$ NMR (300 MHz, $CDCl_3$): $\delta$ = 7.98 – 7.90 (m, 4H, Ar*H*), 7.56 – 7.30 (m, 10H, Ar*H*), 7.12 (d, *J* = 8.1 Hz, 2H, $SC_6H_4Me$), 6.82 (d, *J* = 8.7 Hz, 2H, $C_6H_4OMe$), 5.76 (dd, *J* = 9.3, 9.3 Hz, 1H, H-3), 5.49 (s, 1H, MeOPhC*H*), 5.43 (dd, *J* = 9.3, 9.3 Hz, 1H, H-2), 4.95 (d, *J* = 10.5 Hz, 1H, H-1), 4.43 (dd, *J* = 4.5, 10.8 Hz, 1H), 3.90 – 3.82 (m, 2H), 3.76 – 3.67 (m, 4H), 2.35 (s, 3H, $SPhCH_3$); $^{13}C$ NMR (75 MHz, $CDCl_3$): $\delta$ = 165.6, 165.2, 160.1, 138.8, 133.8, 133.3, 133.1, 129.9, 129.8, 129.8, 129.4, 129.3, 129.2, 128.4, 128.3, 127.9, 127.5, 113.6, 101.5, 87.3, 78.5, 73.4, 71.1, 71.0, 68.5, 55.3, 21.3; FAB MS: *m/z*: calcd for $C_{35}H_{33}O_8S$: 613.1896; found: 613.1879 $[M + H]^+$.

***p*-Methylphenyl 2,3-di-*O*-benzoyl-4-*O*-*tert*-butyldimethylsilyl-6-*O*-*p*-methoxybenzyl-1-thio-$\beta$-D-glucopyranoside (4').** The procedure for the regioselective ring opening of **3'** was adapted from Johansson *et. al.*[3] **3'** (12.0 g, 19.6 mmol) was combined with sodium cyanoborohydride (6.15 g, 97.9 mmol), activated 3Å powdered molecular sieves (12.0 g), and dissolved in DMF (261 mL). The reaction was cooled to 0 °C. Trifluoroacetic acid (15.3 mL, 196 mmol) was added dropwise to the reaction. The reaction was stirred at 0 °C for 1 h, and then allowed to warm to rt. The reaction stirred at rt for 1 d. It was then filtered, diluted with $CH_2Cl_2$, and quenched with cold saturated aqueous $NaHCO_3$. The aqueous layer was separated and extracted with $CH_2Cl_2$ (2x). The combined organic layers were washed with saturated aqueous $NaHCO_3$ (1x) and brine (1x), dried over $Na_2SO_4$, filtered, and concentrated. To remove the remaining sodium cyanoborohydride, the crude material was re-dissolved in $CH_2Cl_2$ (250 mL) and washed with brine (3x). The organic layer was dried over $Na_2SO_4$, filtered, and concentrated to afford a white solid containing the desired alcohol. $R_f$ 0.23 (30% EtOAc:hexanes).

The crude alcohol was dissolved in $CH_2Cl_2$ (476 mL), TEA (8.20 mL, 58.6 mmol) was added, and the reaction cooled to 0 °C. *tert*-Butyldimethylsilyl trifluoromethanesulfonate (11.2 mL, 48.8 mmol) was added dropwise to the reaction. The reaction was allowed to warm to rt and stirred for 3 h. It was then quenched with saturated aqueous $NaHCO_3$ and diluted with $CH_2Cl_2$. The aqueous layer was separated and extracted with $CH_2Cl_2$ (3x). The combined

organic layers were washed with brine, dried over $Na_2SO_4$, filtered, and concentrated to afford an orange syrup. The product was purified by flash chromatography (10% → 12% EtOAc:hexanes) to afford **4'** (13.2 g, 94%) as a white foam. $R_f$ 0.64 (30% EtOAc:hexanes). $[\alpha]_D^{22}$ = +36 (*c* = 1.0, $CH_2Cl_2$); IR (thin film on NaCl): υ = 2953, 2928, 2856, 1734, 1612, 1602, 1513, 1451, 1272, 1251, 1106, 1089, 1069 $cm^{-1}$; $^1H$ NMR (300 MHz, $CDCl_3$): δ = 7.92 – 7.87 (m, 4H, Ar*H*), 7.51 – 7.27 (m, 10H, Ar*H*), 7.03 (d, *J* = 7.8 Hz, 2H, $SC_6H_4Me$), 6.94 – 6.91 (m, 2H, Ar*H*), 5.59 (dd, *J* = 9.2, 9.2 Hz, 1H, H-3), 5.30 (dd, *J* = 9.6, 9.6 Hz, 1H, H-2), 4.88 (d, *J* = 9.6 Hz, 1H, H-1), 4.60 (d, *J* = 11.4 Hz, 1H, C*H*$_2$PhOMe), 4.51 (d, *J* = 11.7 Hz, 1H, C*H*$_2$PhOMe), 4.01 (dd, *J* = 9.0, 9.0 Hz, 1H, H-4), 3.84 – 3.64 (m, 6H, H-5, H-6, H-6, PhOC*H*$_3$), 2.32 (s, 3H, SPhC*H*$_3$), 0.74 (s, 9H, (C*H*$_3$)$_3$CSi), 0.02 (s, 3H, C*H*$_3$Si), -0.22 (s, 3H, C*H*$_3$Si); $^{13}C$ NMR (75 MHz, $CDCl_3$): δ = 165.9, 165.3, 159.2, 138.2, 133.4, 133.1, 133.0, 130.5, 129.9, 129.9, 129.8, 129.7, 129.5, 129.3, 128.6, 128.4, 128.3, 113.9, 86.1, 81.0, 77.5, 73.3, 71.3, 69.4, 68.7, 55.5, 25.9, 21.5, 18.1, -3.9, -4.4; FAB MS: *m/z*: calcd for $C_{41}H_{47}O_8SSi$: 727.2785; found: 727.2761 $[M]^+$.

***p*-Methylphenyl 2,3-di-*O*-benzoyl-4-*O*-*tert*-butyldimethylsilyl-1-thio-β-D-glucopyranoside (5').** In a flask covered with aluminum foil, **4'** (13.2 g, 18.1 mmol) was dissolved in $CH_2Cl_2$ (440 mL). Water (23.0 mL) and 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (4.93 g, 21.7 mmol) were added. The reaction was stirred at rt for 13 h. The reaction was then quenched with aqueous $NaHCO_3$, and water was added to dissolve all solids. The aqueous layer was separated and extracted with $CH_2Cl_2$ (3x). The combined organic layers were washed with brine, dried over $Na_2SO_4$, filtered, and concentrated to yield a peach solid. The product was purified by flash chromatography (40% $CH_2Cl_2$:hexanes → 100% $CH_2Cl_2$ → 10% EtOAc: $CH_2Cl_2$) to afford **5'** (9.42 g, 86%) as a white foam. $R_f$ 0.41 (20% EtOAc:hexanes). $[\alpha]_D^{22}$ = +62 (*c* = 1.0, $CH_2Cl_2$); IR (thin film on NaCl): υ = 3442, 2951, 2928, 2856, 1733, 1602, 1493, 1451, 1273, 1088, 1070, 1027 $cm^{-1}$; $^1H$ NMR (300 MHz, $CDCl_3$): δ = 7.92 – 7.88 (m, 4H, Ar*H*), 7.52 – 7.45 (m, 2H, Ar*H*), 7.38 – 7.32 (m, 6H, Ar*H*), 7.12 (d, *J* = 8.1 Hz, 2H, $SC_6H_4Me$), 5.62 (dd, *J* = 9.3, 9.3 Hz, 1H, H-3), 5.29 (dd, *J* = 9.6, 9.6 Hz, 1H, H-2), 4.93 (d, *J* = 9.9 Hz, 1H, H-1), 4.02 – 3.92 (m, 2H), 3.81 – 3.73 (m, 1H), 3.60 – 3.55 (d, *J* = 11.4 Hz, 1H), 2.35 (s, 3H, SPhC*H*$_3$), 1.95 (br s, 1H, OH), 0.76 (s, 9H, (C*H*$_3$)$_3$CSi), 0.07 (s, 3H, C*H*$_3$Si), -0.20 (s, 3H, C*H*$_3$Si); $^{13}C$ NMR (75 MHz, $CDCl_3$): δ = 165.9, 165.4, 138.7, 133.5, 133.3, 133.2, 130.0, 130.0, 129.9, 129.8, 129.4, 128.5, 128.5, 128.4, 86.4, 81.1, 77.2, 71.3, 69.0, 62.0, 25.9, 21.6, 18.2, -3.9, -4.3; FAB MS: *m/z*: calcd for $C_{33}H_{41}O_7SSi$: 609.2342; found: 609.2321 $[M + H]^+$.

***p*-Methylphenyl (methyl 2,3-di-*O*-benzoyl-4-*O*-*tert*-butyldimethylsilyl-1-thio-β-D-glucopyranosyluronate (6').** **5'** (9.42 g, 15.5 mmol) was dissolved in DMF (115 mL). Pyridinium dichromate (34.9 g, 92.8 mmol) was added, and the reaction was stirred at rt for 3 d. To precipitate and remove the chromium salts, EtOAc was added, and the reaction was filtered and concentrated (3x). The remaining salts were removed by flash chromatography (100% EtOAc) to yield a white foam containing the desired carboxylic acid. $R_f$ 0.17 (30% EtOAc:hexanes).

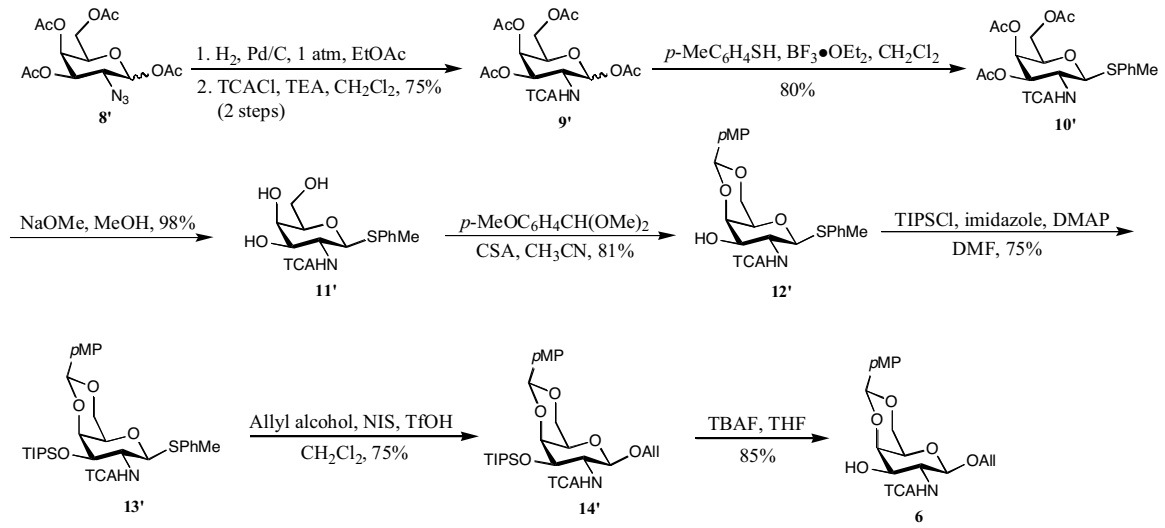
The crude acid was dissolved in $CH_2Cl_2$ (187 mL) and cooled to 0 °C. Diazomethane (93.0 mL, 0.2 M in diethyl ether, 18.6 mmol) was slowly added. The reaction stirred at 0 °C for 1 h. Glacial acetic acid was added to quench the reaction. It was then concentrated and purified by flash chromatography (10% → 15% EtOAc:hexanes) to yield **6'** (6.04 g, 61%) as a white solid. $R_f$ 0.67 (30% EtOAc:hexanes). $[\alpha]_D^{22}$ = +54 (*c* = 1.0, $CH_2Cl_2$); IR (thin film on NaCl): υ = 3443, 2953, 2928, 2857, 1732, 1601, 1493, 1451, 1437, 1269, 1085, 1069 $cm^{-1}$; $^1H$ NMR (300 MHz, $CDCl_3$): δ = 7.90 – 7.86 (m, 4H, Ar*H*), 7.52 – 7.46 (m, 2H, Ar*H*), 7.38 – 7.31 (m, 6H, Ar*H*), 7.10 (d, *J* = 8.1 Hz, 2H, $SC_6H_4Me$), 5.59 (dd, *J* = 9.3, 9.3 Hz, 1H, H-3), 5.30 (dd, *J* = 9.6, 9.6 Hz, 1H, H-2), 4.90 (d, *J* = 9.9 Hz, 1H, H-1), 4.26 (dd, *J* = 9.2, 9.2 Hz, 1H, H-4), 4.08 (d, *J* = 8.7 Hz, 1H, H-5), 3.82 (s, 3H, $CO_2CH_3$), 2.33 (s, 3H, $SPhCH_3$), 0.71 (s, 9H, $(CH_3)_3CSi$), -0.05 (s, 3H, $CH_3Si$), -0.22 (s, 3H, $CH_3Si$); $^{13}C$ NMR (75 MHz, $CDCl_3$): δ = 168.3, 168.3, 165.9, 165.3, 138.8, 133.7, 133.4, 133.4, 130.0, 130.0, 130.0, 129.7, 129.5, 128.5, 128.2, 87.2, 80.4, 76.6, 70.9, 70.7, 52.8, 25.6, 21.4, 18.0, -4.2, -4.9; FAB MS: *m/z*: calcd for $C_{34}H_{41}O_8SSi$: 637.2291; found: 637.2284 $[M + H]^+$.

**Methyl 2,3-di-*O*-benzoyl-4-*O*-*tert*-butyldimethylsilyl-α/β-D-glucopyranosyluronate (7'). 6'** (6.09 g, 9.56 mmol) was dissolved in $CH_2Cl_2$ (67.0 mL) and water (0.700 mL) was added. A solution was prepared containing 2.93 g *N*-iodosuccinimide, 127 mL $CH_2Cl_2$, 3.10 mL THF, and 78.0 μL triflic acid. 130 mL of this solution was added to the reaction mixture. The reaction stirred at rt for 5.5 h. It was then quenched with 1 M $Na_2S_2O_3$ and diluted with $CH_2Cl_2$. The aqueous layer was separated and extracted with $CH_2Cl_2$ (3x). The combined organic layers were washed with brine, dried over $Na_2SO_4$, filtered, and concentrated. The product was purified by flash chromatography (15% → 30% EtOAc:hexanes) to afford **7'** (4.27 g, 84%, 6.2β:1α) as a white foam. $R_f$ 0.30, 0.36 (30% EtOAc:hexanes). $[\alpha]_D^{22}$ = +99 (*c* = 1.0, $CH_2Cl_2$); IR (thin film on NaCl): υ = 3455, 2954, 2930, 2857, 1732, 1602, 1451, 1275, 1110, 1070 $cm^{-1}$; $^1H$ NMR (300 MHz, $CDCl_3$): δ = 8.18 – 8.07 (m, 4H, Ar*H*), 7.99 – 7.90 (m, 4H, Ar*H*), 7.69 – 7.31 (m, 12H, Ar*H*), 6.55 (d, *J* = 3.3 Hz, 1H, H-1, α), 5.94 (dd, *J* = 9.0, 9.9 Hz, 1H), 5.72 – 5.58

(m, 3H), 5.22 – 5.14 (m, 2H), 4.62 (d, *J* = 9.3 Hz, 1H, H-1, β), 4.40 – 4.27 (m, 2H), 4.13 (d, *J* = 9.3 Hz, 1H), 3.81 (s, 3H, $CO_2CH_3$), 3.80 (s, 3H, $CO_2CH_3$), 3.46 (d, *J* = 3.6 Hz, 1H), 0.76 (s, 9H, $(CH_3)_3CSi$), 0.75 (s, 9H, $(CH_3)_3CSi$), -0.01 (s, 6H, $CH_3Si$), -0.15 (s, 6H, $CH_3Si$); $^{13}C$ NMR (75 MHz, $CDCl_3$): δ = 169.8, 169.0, 168.7, 167.4, 167.3, 166.1, 165.9, 165.0, 134.2, 133.9, 133.8, 133.6, 133.4, 130.3, 130.2, 130.1, 129.9, 129.1, 129.0, 128.8, 128.6, 128.6, 92.2, 90.9, 75.8, 74.8, 74.6, 74.6, 72.5, 72.4, 72.3, 71.1, 70.5, 70.2, 52.9, 25.7, 25.6, 18.0, -4.2, -4.9; FAB MS: *m/z*: calcd for $C_{27}H_{35}O_9Si$: 531.2050; found: 531.2041 $[M + H]^+$.

**Methyl 2,3-di-*O*-benzoyl-4-*O*-*tert*-butyldimethylsilyl-α-D-glucopyranosyluronate trichloroacetimidate (5).** The preparation of **5** was performed by using a procedure modified from Driguez *et. al.*[4] **7'** (3.32 g, 6.26 mmol) was coevaporated with toluene (2 x 20 mL) and dried under vacuum overnight. It was then dissolved in $CH_2Cl_2$ (49.0 mL). Trichloroacetonitrile (3.80 mL, 37.5 mmol) and $Cs_2CO_3$ (0.820 g, 2.50 mmol) were added. After stirring at rt for 4 h, additional trichloroacetonitrile (0.950 mL, 9.50 mmol) and $Cs_2CO_3$ (0.200 g, 0.600 mmol) were added. The reaction was allowed to stir an additional 4 h and then concentrated. The product was purified by flash chromatography (10% EtOAc:hexanes + 0.1% TEA) to afford **5** (3.77 g, 89%), with a trace amount of the β anomer, as a white foam. $R_f$ 0.57 (30% EtOAc:hexanes). $[\alpha]_D^{22}$ = +99 (*c* = 1.0, $CH_2Cl_2$); IR (thin film on NaCl): υ = 3343, 2954, 2930, 2858, 1757, 1735, 1676, 1602, 1451, 1315, 1267, 1111, 1095 $cm^{-1}$; $^1H$ NMR (300 MHz, $CDCl_3$): δ = 8.60 (s, 1H, C=N*H*), 7.96 – 7.87 (m, 4H, Ar*H*), 7.53 – 7.29 (m, 6H, Ar*H*), 6.74 (d, *J* = 3.9 Hz, 1H, H-1), 5.99 (dd, *J* = 9.0, 10.2 Hz, 1H, H-3), 5.43 (dd, *J* = 3.9, 10.5 Hz, 1H, H-2), 4.51 (d, *J* = 9.3 Hz, 1H, H-5), 4.38 (dd, *J* = 9.3, 9.3 Hz, 1H, H-4), 3.81 (s, 3H, $CO_2CH_3$), 0.74 (s, 9H, $(CH_3)_3CSi$), -0.01 (s, 3H, $CH_3Si$), -0.15 (s, 3H, $CH_3Si$); $^{13}C$ NMR (75 MHz, $CDCl_3$): δ = 168.7, 165.7, 165.7, 160.8, 133.7, 133.5, 130.1, 129.9, 129.7, 128.7, 128.6, 128.6, 93.4, 74.6, 72.5, 70.9, 70.8, 53.0, 53.0, 25.7, 18.0, -4.1, -4.9; ESI MS: *m/z*: calcd for $C_{29}H_{34}Cl_3NNaO_9Si$: 696.1; found: 696.2 $[M + Na]^+$.

**Scheme 2:** Synthesis of the Galactosamine Monomer **6**




**1,3,4,6-tetra-*O*-acetyl-2-deoxy-2-trichloroacetamido-α/*β*-D-galactopyranoside (9').** 1,3,4,6-tetra-*O*-acetyl-2-azido-2-deoxy-D-galactopyranoside[5] **8'** (0.100 g, 0.268 mmol) in THF (5.00 mL), was added *p*-tosic acid monohydrate (0.051 g, 0.27 mmol) followed by Pd/C (0.017 g, 6 mol%). The reaction was then placed under an atmosphere of $H_2$ and stirred at rt for 18 h. The Pd/C was removed by filtration through Celite and the solvent concentrated to afford an anomeric mixture of crude amines as a pale yellow foam. The crude mixture was used for the next step without purification. To a solution of crude amines in THF (5 mL), cooled to 0 °C was added trichloroacetylchloride (0.220 g, 1.21 mmol, 0.130 mL) followed by TEA (0.180 g, 1.79 mmol, 0.250 mL). The reaction mixture was stirred at 0 °C for 15 min and then quenched with saturated aqueous $NaHCO_3$. The water layer was separated and extracted with $CH_2Cl_2$ (2x) and the combined organics dried over $Na_2SO_4$ and the solvent removed *in vacuo* to afford a yellow oil. Purification of this oil by flash chromatography (30% → 40% EtOAc:hexanes) afforded **9'** (0.099 g, 75%, 3.1β:1α) as a white solid $R_f$ 0.61 and 0.53 (60% EtOAc:hexanes). $^1$H NMR (300 MHz, $CDCl_3$): δ = 6.73 (d, *J* = 9.0 Hz, 2H, N*H*), 6.30 (d, *J* = 3.9 Hz, 1H, H-1, α), 5.45 (d, *J* = 3.3 Hz, 3H), 5.32 (dd, *J* = 3.5 Hz and 11.3 Hz, 2H), 4.58 (m, 2H), 4.26 (dd, *J* = 6.6 Hz, 6.6 Hz, 2H), 4.20 – 4.03 (m, 4H), 2.17 (s, 6H), 2.15 (s, 6H), 2.02 (s, 6H), 2.00 (s, 6H); $^{13}$C NMR (75 MHz, $CDCl_3$): δ = 171.2, 170.5, 170.2, 168.7, 162.2, 90.5, 69.0, 67.8, 66.8, 61.5, 49.6, 21.2, 21.0; ESI MS: *m/z*: calcd for $C_{16}H_{19}C_{l3}NO_{10}$: 490.0075; found: 490 [*M* - H]$^-$.

***p*-Methylphenyl 2-deoxy-2-trichloroacetamido-3,4,6-tri-*O*-acetyl-1-thio-β-D-galactopyranoside (10').** To a solution of **9'** (0.050 g, 0.10 mmol) in dry $CH_2Cl_2$ (0.35 mL) was added *p*-toluenethiol (0.042 g, 0.34 mmol) followed by $BF_3$•$OEt_2$ (0.043 g, 0.30 mmol, 38 μL) and the reaction mixture stirred at rt. After 2 h, a further addition of *p*-toluenethiol (0.012 g, 0.10 mmol) and $BF_3$•$OEt_2$ (0.014 g, 0.10 mmol, 13 μL) was made followed by stirring at rt for 1 h. The reaction mixture was quenched with saturated aqueous $NaHCO_3$ and the organic phase washed twice with saturated aqueous $NaHCO_3$ and water. The aqueous layers were back extracted with $CH_2Cl_2$ (3x) and the combined organics washed with brine and dried over $Na_2SO_4$ to afford an amber oil. Purification of this oil by flash chromatography (20% → 25% EtOAc:hexanes) afforded **10'** (0.044 g, 80%) as a white solid. $R_f$ 0.51 (50% EtOAc:hexanes). $[\alpha]_D^{23}$ = -2.4 (*c* = 0.5, $CH_2Cl_2$); IR (thin film on NaCl): υ = 3450, 1752, 1655, 1529, 1493, 1370, 1230, 1082, 1045 $cm^{-1}$; $^1H$ NMR (300 MHz, $CDCl_3$): δ = 7.42 (d, *J* = 8.3 Hz, 2H, $SC_6H_4Me$), 7.12 (d, *J* = 8.3 Hz, 2H, $SC_6H_4Me$), 6.77 (d, *J* = 8.7 Hz, 1H, N*H*), 5.39 (d, *J* = 3.3 Hz, 1H, H-4), 5.29 (dd, *J* = 3.3, 11.1 Hz, 1H, H-3), 4.89 (d, *J* = 10.5 Hz, 1H, H-1), 4.22 – 4.09 (m, 3H, H-2, H-6), 3.94 (dd, *J* = 6.6, 6.6 Hz, 1H, H-5), 2.34 (s, 3H, SPhC$H_3$), 2.13 (s, 3H, OC(O)C$H_3$), 2.04 (s, 3H, OC(O)C$H_3$), 1.97 (s, 3H, OC(O)C$H_3$); $^{13}C$ NMR (75 MHz, $CDCl_3$): δ = 170.6, 170.5, 170.2, 161.9, 138.8, 133.5, 129.9, 128.5, 92.5, 87.2, 74.9, 70.9, 67.1, 62.0, 51.7, 21.6, 21.1, 21.0, 20.9; FAB MS: *m/z*: calcd for $C_{21}H_{25}Cl_3NO_8S$: 556.0367; found: 556.0369 $[M + H]^+$.

***p*-Methylphenyl 2-deoxy-2-trichloroacetamido-3-*O*-triisopropylsilyl-4,6-*O*-*p*-methoxybenzylidene-1-thio-β-D-galactopyranoside (11').** A solution of **10'** (17.9 g, 0.0320 mol) in dry $CH_2Cl_2$ (85 mL) and MeOH (435 mL) was stirred at rt for 30 min and NaOMe (25 wt% solution in MeOH, 0.517 g, 9.58 mmol, 2.07 mL) was then added. The mixture was stirred for 2 h and DOWEX 50X8-200 added and stirring continued for a further 30 min. The DOWEX was removed by filtration and the solvent removed *in vacuo* to afford **11'** (13.5 g, 98%) as a yellow solid. This compound was suitable for the next step without purification.

***p*-Methylphenyl 2-deoxy-2-trichloroacetamido-4,6-*O*-*p*-methoxybenzylidene-1-thio-β-D-galactopyranoside (12').** To a solution of **11'** (13.5 g, 0.0310 mol) in acetonitrile (800 mL, minimum amount) was added *p*-anisaldehyde dimethyl acetal (11 g, 0.063 mol, 12 mL) and DL-10-camphorsulfonic acid (10 mol%) and the mixture stirred at rt for 12 h. The reaction mixture was quenched with TEA and the solvent concentrated to afford a yellow solid. Purification of this solid by flash chromatography (40% → 80% EtOAc:hexanes) afforded **12'** (13 g, 76%) as

a white solid. $R_f$ 0.25 (50% EtOAc:hexanes). $[\alpha]_D^{24}$ = -14.6 (*c* = 0.5, $CH_2Cl_2$); IR (thin film on NaCl): υ = 3333, 1687, 1615, 1519, 1492, 1403, 1364, 1301, 1248, 1167, 1095, 1055 $cm^{-1}$; $^1H$ NMR (300 MHz, $CDCl_3$): δ = 7.55 (d, *J* = 8.4 Hz, 2H, $SC_6H_4Me$), 7.34 (d, *J* = 8.7 Hz, 2H, $C_6H_4OMe$), 7.12 (d, *J* = 8.4 Hz, 2H, $SC_6H_4Me$), 6.88 (d, *J* = 8.7 Hz, 2H, $C_6H_4OMe$), 6.81 (d, *J* = 7.5 Hz, 1H, N*H*), 5.48 (s, 1H, MeOPhC*H*), 5.03 (d, *J* = 9.9 Hz, 1H, H-1), 4.37 (dd, *J* = 1.5, 12.6 Hz, 1H, H-6), 4.20 – 4.10 (m, 2H, H-3, H-4), 4.01 (dd, *J* = 1.5, 12.6 Hz, 1H, H-6), 3.83 (s, 3H, PhOC$H_3$), 3.69 (m, 1H, H-2), 3.57 (s, 1H, H-5), 2.58 (d, *J* = 10.5 Hz, 1H, O*H*), 2.37 (s, 3H, SPhC$H_3$); $^{13}C$ NMR, (75 MHz, $CDCl_3$): δ = 162.1, 160.5, 139.0, 134.7, 130.2, 130.0, 128.1, 126.9, 113.8, 101.4, 84.0, 75.2, 70.7, 70.3, 69.5, 55.7, 54.4, 21.7; FAB MS: *m/z*: calcd for $C_{23}H_{25}Cl_3NO_6S$: 548.0469; found: 548.0448 $[M + H]^+$.

***p*-Methylphenyl 2-deoxy-2-trichloroacetamido-3-*O*-triisopropylsilyl-4,6-*O*-*p*-methoxybenzylidene-β-D-galactopyranoside (13').** To a solution of **12'** (5.6 g, 0.010 mol) in dry DMF (50 mL) at rt was added triisopropylsilyl chloride (6.3 g, 0.033 mol, 7.0 mL), imidazole (2.7 g, 0.040 mol) and DMAP (0.49 g, 40 mol%). The reaction mixture was stirred for 4 h whereupon further addition of triisopropylsilyl chloride (3.2 g, 0.016 mol, 3.5 mL), imidazole (1.4 g, 0.020 mol) and DMAP (0.25 g, 20 mol%) were added. The reaction mixture was stirred for 12 h and quenched with saturated aqueous $NaHCO_3$. The aqueous layer was extracted with EtOAc (3x) and the combined organics washed with brine and dried over $MgSO_4$ to afford a pale yellow oil. Purification of this oil by flash chromatography (10% → 15% EtOAc:hexanes) afforded **13'** (5.3 g, 75%) as a white solid. $R_f$ 0.57 (30% EtOAc:hexanes). $[\alpha]_D^{23}$ = +5.9 (*c* = 0.5, $CH_2Cl_2$); IR (thin film on NaCl): υ = 2943, 2866, 1705, 1616, 1519, 1493, 1464, 1365, 1249, 1170, 1139, 1083, 1051 $cm^{-1}$; $^1H$ NMR (300 MHz, $CDCl_3$): δ = 7.57 (d, *J* = 8.1 Hz, 2H, $SC_6H_4Me$), 7.38 (d, *J* = 8.7 Hz, 2H, $C_6H_4OMe$), 7.07 (d, *J* = 8.1 Hz, 2H, $SC_6H_4Me$), 6.87 (d, *J* = 8.7 Hz, 2H, $C_6H_4OMe$), 6.85 (m, 1H, N*H*), 5.45 (s, 1H, MeOPhC*H*), 5.39 (d, *J* = 9.9 Hz, 1H, H-1), 4.62 (dd, *J* = 3.2, 10.2 Hz, 1H, H-3), 4.37 (dd, *J* = 1.7, 12.5 Hz, 1H, H-6), 4.13 (d, *J* = 3.2 Hz, 1H, H-4), 4.01 (dd, *J* = 1.7, 12.5 Hz, 1H, H-6), 3.83 (s, 3H, PhOC$H_3$), 3.71 (m, 1H, H-2), 3.55 (s, 1H, H-5), 2.34 (s, 3H, SPhC$H_3$), 1.01 (s, 21H, $[(CH_3)_2CH]_3$), $^{13}C$ NMR (75 MHz, $CDCl_3$): δ = 161.3, 160.1, 138.5, 134.1, 130.7, 130.0, 128.0, 127.9, 113.5, 101.1, 83.4, 76.7, 71.0, 70.3, 69.7, 55.6, 54.8, 21.7, 18.5, 18.4, 13.1; FAB MS: *m/z*: calcd for $C_{32}H_{45}Cl_3NO_6SSi$: 704.1621; found: 704.1623 $[M + H]^+$.

**Allyl 2-deoxy-2-trichloroacetamido-3-*O*-triisopropylsilyl-4,6-*O*-*p*-methoxybenzylidene-β-D-galactopyranoside (14').** To a solution of **13'** (11 g, 0.016 mol) in dry $CH_2Cl_2$ (675 mL) was added 4Å powdered molecular sieves and the mixture stirred for 1 h. Allyl alcohol (9.3 g, 0.16 mol, 11 mL) and *N*-iodosuccinimide (5.3 g, 0.023 mol) was added and the mixture cooled to 0 °C. Triflic acid (0.5 *N* solution in $CH_2Cl_2$, 1.44 g, 9.60 mmol, 19.2 mL) was added and the reaction stirred at 0 °C for 10 min. The mixture was quenched with TEA, washed with brine and dried over $MgSO_4$. The solvent was removed *in vacuo* to afford a yellow oil. Purification of this oil by flash chromatography (5% → 15% EtOAc:hexanes) afforded **14'** (8.1 g, 79%) as a white solid. $R_f$ 0.41 (30% EtOAc:hexanes). $[\alpha]_D^{24}$ = +38.1 (*c* = 0.5, $CH_2Cl_2$); IR (thin film on NaCl): υ = 3445, 1644, 1520, 1463, 1368, 1249, 1171, 1123, 1060 $cm^{-1}$; 1H NMR (300 MHz, $CDCl_3$): δ = 7.45 (d, *J* = 8.9 Hz, 2H, $C_6H_4OMe$), 6.97 (d, *J* = 7.2 Hz, 1H, N*H*), 6.87 (d, *J* = 8.9 Hz, 2H, $C_6H_4OMe$), 5.96 – 5.83 (m, 1H, $OCH_2CH=CH_2$), 5.49 (s, 1H, MeOPhC*H*), 5.26 (dd, *J* = 1.4, 17.3 Hz, 1H, $OCH_2CH=CH_2$), 5.17 (dd, *J* = 1.4, 10.5 Hz, 1H, $OCH_2CH=CH_2$), 5.16 (d, *J* = 8.1 Hz, 1H, H-1), 4.65 (dd, *J* = 3.3, 10.5 Hz, 1H, H-3), 4.37 (m, 2H, $OCH_2CH=CH_2$, H-6), 4.13 – 4.05 (3H, m, $OCH_2CH=CH_2$, H-4, H-6), 3.81 (s, 3H, $PhOCH_3$), 3.75 (m, 1H, H-2), 3.48 (s, 1H, H-5), 1.05 (s, 21H, $[(CH_3)_2CH]_3$); $^{13}C$ NMR (75 MHz, $CDCl_3$): δ = 161.7, 160.1, 134.0, 130.5, 127.8, 118.2, 113.6, 101.2, 97.8, 76.6, 70.6, 69.9, 69.5, 66.7, 64.2, 57.6, 55.6, 18.5, 18.4, 13.1; FAB MS: *m/z*: calcd for $C_{25}H_{37}Cl_3NO_6Si$: 580.1456; found: 580.1474 [$M^+$ - OAll].

**Allyl 2-deoxy-2-trichloroacetamido-4,6-*O*-*p*-methoxybenzylidene-β-D-galactopyranoside (6).** To a solution of **14'** (8.00 g, 12.5 mmol) in THF (290 mL) was added tetrabutylammonium fluoride (1 *N* solution in THF, 4.91 g, 18.8 mmol, 18.8 mL) and the mixture stirred at rt for 8 h. At this time a second addition of tetrabutylammonium fluoride (2.5 g, 9.4 mmol, 9.4 mL) was made and the reaction stirred for a further 12 h. The solvent was removed *in vacuo* to afford a yellow oil. Purification of this oil by flash chromatography (40% → 80% EtOAc:hexanes) afforded **6** (5.14 g, 85%) as a white solid. $R_f$ 0.17 (50% EtOAc:hexanes). $[\alpha]_D^{24}$ = +0.62 (*c* = 0.5, $CH_2Cl_2$); IR (thin film on NaCl): υ = 3423, 1686, 1616, 1531, 1402, 1366, 1303, 1249, 1170, 1097, 1060 $cm^{-1}$; $^1H$ NMR (300 MHz, $CDCl_3$): δ = 7.43 (d, *J* = 8.7 Hz, 2H, $C_6H_4OMe$), 6.89 (d, *J* = 8.7 Hz, 2H, $C_6H_4OMe$), 6.87 (m, 1H, N*H*), 5.95 – 5.82 (m, 1H, $OCH_2CH=CH_2$), 5.54 (s, 1H, MeOPhC*H*), 5.29 (dd, *J* = 1.4, 17.7 Hz, 1H, $OCH_2CH=CH_2$), 5.19 (dd, *J* = 1.4, 10.5 Hz, 1H, $OCH_2CH=CH_2$), 4.84 (d, *J* = 8.4Hz, 1H, H-1), 4.44 – 4.32 (m, 2H, H-3, H-6), 4.26 – 4.07 (m, 4H, $OCH_2CH=CH_2$, H-4, H-6), 3.81 (m, 1H, H-2), 3.81 (s, 3H, $PhOCH_3$), 3.53 (s, 1H, H-5), 2.71 (d, *J* = 9.9 Hz, 1H,

O*H*); $^{13}$C NMR (75 MHz, $CDCl_3$): δ = 162.5, 160.4, 153.6, 133.7, 130.0, 127.9, 118.3, 113.8, 101.6, 98.7, 75.2, 70.4, 69.4, 69.3, 67.0, 57.2, 55.7; FAB MS: *m/z*: calcd for $C_{19}H_{23}Cl_3NO_7$: 482.0540; found: 482.0531 $[M + H]^+$.

**Allyl (methyl 2,3-di-*O*-benzoyl-4-*O*-*tert*-butyldimethylsilyl-β-D-glucopyranosyluronate)-(1 → 3)-4,6-*O*-*p*-methoxybenzylidene-2-deoxy-2-trichloroacetamido-β-D-galactopyranoside (4).** A mixture of donor **5** (0.50 g, 0.74 mmol) and acceptor **6** (0.30 g, 0.62 mmol) was coevaporated with toluene (3 x 3 mL) and dried under vacuum overnight. The mixture was dissolved in $CH_2Cl_2$ (16 mL), and activated 4Å powdered molecular sieves were added. The reaction was stirred at rt for 1.5 h. The reaction was then cooled to -40 °C and stirred for an additional 30 min. Trimethylsilyl trifluoromethanesulfonate (1 M in $CH_2Cl_2$, 125 μL, 0.123 mmol) at -40 °C was added to the reaction dropwise. The reaction was allowed to stir an additional 30 min. It was then warmed to -10 °C over a period of 30 min,[6] quenched with TEA, and allowed to warm to rt. The reaction was filtered and concentrated to afford a yellow syrup. The product was purified by flash chromatography (30% EtOAc:hexanes) to afford **4** (0.46 g, 74%) as a white solid. $R_f$ 0.12 (30% EtOAc:hexanes). $^1$H NMR (300 MHz, $CDCl_3$): δ = 7.87 – 7.82 (m, 4H, Ar*H*), 7.48 – 7.39 (m, 4H, Ar*H*), 7.35 – 7.26 (m, 4H, Ph Ar*H*), 6.86 (d, *J* = 8.7 Hz, 2H, $C_6H_4$OMe), 6.82 (d, *J* = 7.2 Hz, 1H, N*H*), 5.89 – 5.76 (m, 1H, $OCH_2CH{=}CH_2$), 5.45 (s, 1H, MeOPhC*H*), 5.52 – 5.39 (m, 2H, H-2', H-3'), 5.22 (dd, *J* = 1.6, 17.6 Hz, 1H, $OCH_2CH{=}CH_2$), 5.13 (dd, *J* = 1.0, 10.4 Hz, 1H, $OCH_2CH{=}CH_2$), 5.08 (d, *J* = 7.5 Hz, 1H, H-1'), 5.05 (d, *J* = 8.1 Hz, 1H, H-1), 4.67 (dd, *J* = 3.3, 10.8 Hz, 1H, H-3), 4.36 – 4.27 (m, 4H, $OCH_2CH{=}CH_2$, H-4, H-4' H-6), 4.10 (d, *J* = 9.3 Hz, 1H, H-5'), 4.07 – 4.01 (m, 2H, $OCH_2CH{=}CH_2$, H-6), 3.79 (s, 6H, $CO_2CH_3$, $PhOCH_3$), 3.77 – 3.68 (m, 1H, H-2), 3.48 (s, 1H, H-5), 0.72 (s, 9H, $(CH_3)_3CSi$), -0.08 (s, 3H, $CH_3Si$), -0.23 (s, 3H, $CH_3Si$); $^{13}$C NMR (75 MHz, $CDCl_3$): δ = 168.7, 165.7, 165.2, 162.3, 160.0, 133.8, 133.4, 133.4, 130.5, 130.0, 129.9, 129.5, 129.2, 128.5, 127.7, 118.2, 113.6, 100.7, 100.6, 97.8, 92.3, 76.4, 75.8, 75.6, 73.6, 72.0, 70.9, 70.6, 69.2, 66.8, 55.6, 55.4, 52.9, 25.7, 18.1, -4.0, -4.7; FAB MS: *m/z*: calcd for $C_{46}H_{53}Cl_3NO_{15}Si$: 992.2250; found: 992.2255 $[M]^+$.

**Methyl (2,3-di-*O*-benzoyl-4-*O*-*tert*-butyldimethylsilyl-β-D-glucopyranosyluronate)-(1 → 3)-4,6-*O*-*p*-methoxybenzylidene-2-deoxy-2-trichloroacetamido-α-D-galactopyranoside trichloroacetimidate (7).** To a solution of **4** (2.5 g, 2.5 mmol) in dry $CH_2Cl_2$ (40 mL) was added Grubbs' second generation catalyst[7] (0.43 g, 20 mol%) and the mixture stirred at rt for 2 h. The solvent was removed *in vacuo* to afford a brown oil. Purification of this oil by flash chromatography (15% → 20% EtOAc:hexanes) afforded *E/Z*-prop-2-enyl (methyl 2,3-di-*O*-

benzoyl-4-*O*-*tert*-butyldimethylsilyl-*β*-D-glucopyranosyluronate)-(1 → 3)-4,6-*O*-*p*-methoxybenzylidene-2-deoxy-2-trichloroacetamido-*β*-D-galactopyranoside (1.92 g, 77%) as a white solid. $R_f$ (E and Z) 0.68 (60% EtOAc:hexanes). $[\alpha]_D^{25}$ = +29.1 (*c* = 1.0, $CH_2Cl_2$); IR (thin film on NaCl): υ = 3308, 2954, 2858, 1755, 1734, 1717, 1694, 1617, 1602, 1540, 1520, 1452, 1371, 1268, 1221, 1176, 1147, 1089, 1069, 1040, 1026, 1001 $cm^{-1}$; $^1H$ NMR (300 MHz, $CDCl_3$): δ = 7.85 (m, 3H, Ar*H*), 7.48 – 7.28 (m, 10H, Ar*H*, OC*H*=CHCH$_3$), 6.87 (d, *J* = 8.7 Hz, 2H, $C_6H_4$OMe), 6.82 (d, *J* = 6.6 Hz, 1H, N*H*), 6.17 (m, 1H, CH=C*H*CH$_3$), 5.52 – 5.40 (m, 3H, MeOPhC*H*, H-2', H-3'), 5.19 (d, *J* = 8.1 Hz, 1H, H-1), 5.08 (d, *J* = 7.2 Hz, 1H, H-1'), 4.68 (dd, *J* = 3.8, 11.0 Hz, 1H, H-3), 4.39 – 4.28 (m, 3H, H-4, H-4', H-6), 4.16 – 4.02 (m, 2H, H-5', H-6), 3.87 (m, 1H, H-2), 3.81 (s, 3H, PhOC$H_3$), 3.80 (s, 3H, $CO_2CH_3$), 3.54 (s, 1H, H-5), 1.51 (m, 3H, OCH=CHC$H_3$), 0.72 (s, 9H, ($CH_3$)$_3$CSi), -0.07 (s, 3H, C$H_3$Si), -0.22 (s, 3H, C$H_3$Si); $^{13}C$ NMR (75 MHz, $CDCl_3$): δ = 168.7, 165.7, 165.3, 162.4, 162.3, 160.0, 143.5, 142.1, 133.5, 133.4, 130.4, 130.1, 129.9, 129.5, 129.1, 128.5, 127.7, 113.6, 105.7, 104.8, 100.8, 100.6, 100.5, 98.4, 98.0, 76.5, 75.6, 75.5, 73.5, 73.4, 72.0, 70.9, 69.0, 67.2, 67.1, 55.6, 55.1, 55.0, 52.9, 25.7, 18.1, 12.6, 9.7, -4.0, -4.7.

To a solution of *E*/*Z*-prop-2-enyl (methyl 2,3-di-*O*-benzoyl-4-*O*-*tert*-butyldimethylsilyl-*β*-D-glucopyranosyluronate)-(1 → 3)-4,6-*O*-*p*-methoxybenzylidene-2-deoxy-2-trichloroacetamido-*β*-D-galactopyranoside (6.2 g, 6.3 mmol) in dry THF (118 mL), water (24 mL) and pyridine (1.9 mL) was added iodine (3.1 g) and the mixture stirred at ambient temperature for 30 min. The solvent was removed *in vacuo* to afford a yellow oil. The oil was taken up in EtOAc and washed with 5% aqueous $Na_2SO_3$, saturated aqueous $NaHCO_3$, brine and dried over $MgSO_4$. The solvent was removed *in vacuo* to afford a pale yellow oil. Purification of this oil by flash chromatography (40% → 60% EtOAc:hexanes) afforded an anomeric mixture of methyl (2,3-di-*O*-benzoyl-4-*O*-*tert*-butyldimethylsilyl-*β*-D-glucopyranosyluronate)-(1→3)-4,6-*O*-*p*-methoxybenzylidene-2-deoxy-2-trichloro-acetamido-*α*/*β*-D-galactopyranoside (4.8 g, 81%) as a pale yellow solid. $R_f$ 0.28 and 0.18 (50% EtOAc:hexanes). $[\alpha]_D^{25}$ = +79.0 (*c* = 1.0, $CH_2Cl_2$); IR (thin film on NaCl): υ = 3521, 2930, 1738, 1682, 1615, 1519, 1452, 1394, 1251, 1172, 1093, 1069, 1031 $cm^{-1}$; $^1H$ NMR (300 MHz, $CDCl_3$): δ = 7.92 – 7.85 (m, 3H, Ar*H*), 7.54 – 7.45 (m, 3H, Ar*H*), 7.40 – 7.27 (m, 4H, Ar*H*), 7.12 (d, *J* = 9.0 Hz, 2H, $C_6H_4$OMe), 6.96 (d, *J* = 6.3Hz, 1H, N*H*), 6.72 (d, *J* = 9.0 Hz, 2H, $C_6H_4$OMe), 5.60 (m, 1H, H-1), 5.50 (dd, *J* = 8.2, 8.2 Hz, 1H, H-3'), 5.42 (dd, *J* = 8.2, 8.2 Hz, 1H, H-2'), 5.24 (s, 1H, MeOPhC*H*), 5.21 (d, *J* = 7.5 Hz, 1H, H-1'), 4.39 – 4.35 (m, 4H, H-3, H-4, H-4'), 4.23 – 4.02 (m, 3H, H-2, H-5', H-6), 3.96 (s, 1H, H-5), 3.79 (s, 3H, PhOC$H_3$), 3.75 (s, 3H, $CO_2CH_3$), 3.03 (d, *J* = 3.3 Hz, 1H, O*H*), 0.73 (s,

9H, ($CH_3$)$_3$CSi), -0.08 (s, 3H, C$H_3$Si), -0.22 (s, 3H, C$H_3$Si); ESI MS: *m/z*: calcd for $C_{43}H_{50}Cl_3NO_{15}Si$: 954.2914; found: 954 $[M - H]^-$.

To a solution of methyl (2,3-di-*O*-benzoyl-4-*O*-*tert*-butyldimethylsilyl-*β*-D-glucopyranosyluronate)-(1 → 3)-4,6-*O*-*p*-methoxybenzylidene-2-deoxy-2-trichloroacetamido-*α*/*β*-D-galactopyranoside (4.6 g, 4.8 mmol) in dry $CH_2Cl_2$ (190 mL) cooled to 0 °C was added 1,8-diazabicyclo[5.4.0]undec-7-ene (0.29 g, 1.9 mmol, 0.29 mL) and trichloroacetonitrile (10 g, 71 mmol, 7.2 mL) and the mixture stirred for 15 min. The mixture was quenched with TEA and concentrated *in vacuo* to afford a yellow oil. Purification of this oil by flash chromatography (35% EtOAc:hexanes, + 2% TEA) afforded **7** (4.7 g, 90%) as a pale yellow foam. $R_f$ 0.74, (50% EtOAc:hexanes). $[\alpha]_D^{24}$ = +12.0 (*c* = 0.5, $CH_2Cl_2$); IR (thin film on NaCl): υ = 3422, 2956, 2991, 2361, 1731, 1676, 1616, 1519, 1452, 1373, 1271, 1177, 1147, 1094, 1070, 1028 $cm^{-1}$; $^1$H NMR (300 MHz, $CDCl_3$): δ = 8.69 (s, 1H, C=N*H*), 7.90 (m, 4H, Ar*H*), 7.51 (m, 2H, Ar*H*), 7.42 – 7.26 (m, 4H, Ar*H*), 7.00 (d, *J* = 8.9 Hz, 2H, $C_6H_4$OMe), 6.93 (d, *J* = 5.4 Hz, 1H, N*H*TCA), 6.77 (d, *J* = 2.1 Hz, 1H, H-1), 6.68 (d, *J* = 8.9 Hz, 2H, $C_6H_4$OMe), 5.52 (dd, *J* = 8.7, 8.7 Hz, 1H, H-3'), 5.45 (dd, *J* = 8.7, 8.7 Hz, 1H, H-2'), 5.27 (d, *J* = 7.8 Hz, 1H, H-1'), 5.17 (s, 1H, MeOPhC*H*), 4.62 (m, 2H, H-4, H-4'), 4.49 (m, 1H, H-3), 4.31 (m, 2H, H-2, H-6), 4.18 (d, *J* = 9.0 Hz, 1H, H-5'), 4.00 (d, *J* = 12.6 Hz, 1H, H-6), 3.94 (s, 1H, H-5), 3.75 (s, 3H, PhOC$H_3$), 3.74 (s, 3H, $CO_2CH_3$), 0.73 (s, 9H, ($CH_3$)$_3$CSi), -0.06 (s, 3H, C$H_3$Si), -0.19 (s, 3H, C$H_3$Si); $^{13}$C NMR (75 MHz, $CDCl_3$): δ = 168.1, 165.9, 165.6, 162.0, 160.4, 133.9, 133.6, 130.1, 129.9, 129.4, 128.7, 128.6, 127.6, 113.6, 101.1, 98.4, 95.3, 77.2, 75.5, 74.4, 71.2, 70.9, 69.2, 69.0, 65.5, 55.6, 53.0, 50.5, 46.5, 25.7, -4.0, -4.8.

**Allyl (methyl 2,3-di-*O*-benzoyl-*β*-D-glucopyranosyluronate)-(1 → 3)-4,6-*O*-*p*-methoxybenzylidene-2-deoxy-2-trichloroacetamido-*β*-D-galactopyranoside (8).** To a solution of **4** (2.5 g, 2.5 mmol) in dry THF (40 mL) and pyridine (40 mL) cooled to 0 °C was added HF•pyridine (13 mL). The reaction mixture was warmed to rt and stirred for 18 h. The mixture was then diluted with EtOAc and washed with 10% aqueous $CuSO_4$. The aqueous phase was extracted with EtOAc (3x) and the combined organics washed with saturated aqueous $NaHCO_3$ and dried over $MgSO_4$. The solvent was removed *in vacuo* to afford a yellow oil. Purification of this oil by flash chromatography (30 → 60% EtOAc:hexanes) afforded **8** (1.9 g, 85%) as a white solid. $R_f$ 0.35 (60% EtOAc:hexanes). $[\alpha]_D^{25}$ = +32.8 (*c* = 1.0, $CH_2Cl_2$); IR (thin film on NaCl): υ = 3422, 1731, 1616, 1519, 1452, 1369, 1251, 1173, 1093, 1069 $cm^{-1}$;

$^1$H NMR (300 MHz, $CDCl_3$): δ = 7.93 – 7.87 (m, 4H, A*rH*), 7.50 – 7.42 (m, 4H, Ar*H*, $C_6H_4$OMe), 7.36 – 7.26 (m, 4H, ArH), 7.01 (d, *J* = 6.6 Hz, 1H, NH), 6.89 (d, *J* = 8.7 Hz, 2H, $C_6H_4$OMe), 5.89 – 5.77 (m, 1H, $OCH_2CH$=$CH_2$), 5.47 (m, 3H, MeOPhC*H*, H-2', H-3'), 5.26 – 5.12 (m, 4H, $OCH_2CH$=$CH_2$, H-1, H-1'), 4.73 (dd, *J* = 3.6, 11.4 Hz, 1H, H-3), 4.41 – 4.28 (m, 3H, $OCH_2CH$=$CH_2$, H-4, H-6), 4.19 (m, 1H, H-4'), 4.12 – 4.02 (m, 3H, $OCH_2CH$=$CH_2$, H-5', H-6), 3.83 (s, 3H, $PhOCH_3$), 3.81 (s, 3H, $CO_2CH_3$), 3.72 (m, 1H, H-2), 3.48 (s, 1H, H-5), 3.45 (d, *J* = 3.3 Hz, 1H, O*H*); $^{13}$C NMR (75 MHz, $CDCl_3$): δ = 169.3, 166.6, 165.2, 162.3, 160.1, 133.8, 133.6, 133.5, 130.4, 130.1, 130.0, 129.2, 129.1, 128.7, 128.6, 127.5, 118.2, 113.7, 100.8, 100.7, 97.7, 76.1, 75.4, 74.3, 74.1, 71.4, 70.7, 69.3, 66.8, 55.7, 53.4; ESI MS: *m/z*: calcd for $C_{40}H_{39}Cl_3NO_{15}$; 880.1; found: 880.2 $[M - H]^-$.

**Allyl (methyl 2,3-di-*O*-benzoyl-4-*O*-*tert*-butyldimethylsilyl-β-D-glucopyranosyluronate)-(1 → 3)-2-deoxy-2-acetamido-β-D-galactopyranoside (10). 10** was prepared using a procedure modified from Bélot *et. al.*[8] **4** (250 mg, 0.251 mmol) was dissolved in benzene (7.80 mL). Tributylstannane (305 µL, 1.51 mmol) and 2,2'-azobisisobutyronitrile (80.0 mg) were added. The reaction was stirred at rt for 45 min. It was then heated to 80 °C and stirred an additional 1.5 h. The reaction was cooled to rt and concentrated to afford a white solid. The product was purified by flash chromatography (50% EtOAc:hexanes) to afford allyl (methyl 2,3-di-*O*-benzoyl-4-*O*-*tert*-butyldimethylsilyl-β-D-glucopyranosyluronate)-(1 → 3)-4,6-*O*-*p*-methoxybenzylidene-2-deoxy-2-acetamido-β-D-galactopyranoside (190 mg, 85%) as a white solid. $R_f$ 0.19 (50% EtOAc:hexanes). $^1$H NMR (300 MHz, $CDCl_3$): δ = 7.89 – 7.86 (m, 4H, Ar*H*), 7.51 – 7.42 (m, 4H, Ar*H*), 7.37 – 7.31 (m, 4H, Ar*H*), 6.88 (d, *J* = 8.7 Hz, 2H, $C_6H_4$OMe), 5.91 – 5.75 (m, 1H, $OCH_2CH$=$CH_2$), 5.55 (dd, *J* = 8.9, 8.9 Hz, 1H, H-3'), 5.46 (s, 1H, MeOPhC*H*), 5.40 – 5.35 (m, 2H, N*H*, H-2'), 5.20 (dd, *J* = 1.4, 17.3 Hz, 1H, $OCH_2CH$=$CH_2$), 5.14 – 5.11 (m, 2H, $OCH_2CH$=$CH_2$, H-1), 4.97 (d, *J* = 7.5 Hz, 1H, H-1'), 4.77 (dd, *J* = 3.9, 11.1 Hz, 1H, H-3), 4.37 – 4.25 (m, 4H, $OCH_2CH$=$CH_2$, H-4, H-4', H-6), 4.10 (d, *J* = 9.6 Hz, 1H, H-5'), 4.10 – 3.98 (m, 2H, $OCH_2CH$=$CH_2$, H-6), 3.81 (s, 3H, $CO_2CH_3$), 3.78 (s, 3H, $PhOCH_3$), 3.47 (s, 1H, H-5), 3.34 – 3.26 (m, 1H, H-2), 1.53 (s, 3H, $HNC(O)CH_3$), 0.72 (s, 9H, $(CH_3)_3CSi$), -0.07 (s, 3H, $CH_3Si$), -0.23 (s, 3H, $CH_3Si$); $^{13}$C NMR (75 MHz, $CDCl_3$): δ = 171.4, 168.7, 165.8, 165.0, 160.0, 134.1, 133.5, 133.4, 130.7, 129.9, 129.8, 129.6, 129.5, 128.6, 128.5, 127.8, 118.0, 113.6, 101.6, 100.8, 98.0, 76.3, 76.1, 75.6, 72.4, 70.9, 70.4, 69.4, 66.7, 55.6, 55.1, 52.9, 25.8, 23.6, 18.1, -4.0, -4.7; ESI MS: $[M + Na]^+$ calcd for $C_{46}H_{57}NNaO_{15}Si$: 914.3, found 914.4.

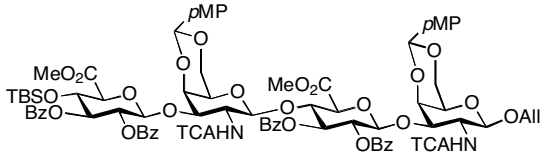
Allyl (methyl 2,3-di-*O*-benzoyl-4-*O*-*tert*-butyldimethylsilyl-*β*-D-glucopyranosyluronate)-(1 → 3)-4,6-*O*-*p*-methoxybenzylidene-2-deoxy-2-acetamido-*β*-D-galactopyranoside (190 mg, 0.213 mmol) was dissolved in $CH_2Cl_2$ (2.40 mL) and $H_2O$ (0.560 mL). 2,3-Dichloro-5,6-dicyano-1,4-benzoquinone (73.0 mg, 0.320 mmol) was added. The reaction was stirred at rt for 3 h, quenched with MeOH, and concentrated to yield a red solid. The product was purified on Sephadex LH-20 (50% $CH_2Cl_2$:MeOH), followed by silica gel chromatography (100% EtOAc), to afford an orange solid containing the desired diol **10** (102 mg, 62%). $R_f$ 0.23 (100% EtOAc). $^1$H NMR (300 MHz, $CD_3OD$): δ = 7.90 – 7.86 (m, 4H, Ar*H*), 7.49 – 7.44 (m, 2H, Ar*H*), 7.37 – 7.29 (m, 4H, Ar*H*), 5.83 – 5.74 (m, 1H, $OCH_2CH{=}CH_2$), 5.61 (dd, *J* = 9.0, 8.7 Hz, 1H, H-3'), 5.35 (dd, *J* = 8.1, 9.0 Hz, 1H, H-2'), 5.18 (dd, *J* = 1.7, 17.6 Hz, 1H, $OCH_2CH{=}CH_2$), 5.10 (d, *J* = 9.9 Hz, 1H, $OCH_2CH{=}CH_2$), 4.97 (d, *J* = 7.5 Hz, 1H, H-1'), 4.90 (d, *J* = 7.5 Hz, 1H, H-1), 4.552 (m, 1H, N*H*), 4.29 – 4.17 (m, 3H, H-1, H-4, H-6), 4.03 – 3.93 (m, 4H, $OCH_2CH{=}CH_2$, H-3, H-4', H-6), 3.89 – 3.86 (m, 2H, $OCH_2CH{=}CH_2$, H-5, H-5'), 3.65 (m, 1H, H-2), 3.78 (s, 3H, $CO_2CH_3$), 1.26 (s, 3H, $HNC(O)CH_3$), 0.73 (s, 9H, $(CH_3)_3CSi$), -0.07 (s, 3H, $CH_3Si$), -0.20 (s, 3H, $CH_3Si$); ESI MS: *m/z*: calcd for $C_{38}H_{52}NO_{14}Si$ 774.9; found 774.2 $[M + H]^+$.

**Allyl (sodium *β*-D-glucopyranosyluronate)-(1 → 3)-4,6-di-*O*-sodium sulfonato-2-deoxy-2-acetamido-*β*-D-galactopyranoside (1).** The crude diol **10** (102 mg, 0.132 mmol) was dissolved in DMF (5 mL). $SO_3 \bullet$ TMA (0.550 g, 3.96 mmol) was added. The reaction was stirred at 50 °C overnight. It was cooled to rt, quenched with MeOH, and concentrated to afford a yellow solid. The product was purified on Sephadex LH-20 (50% $CH_2Cl_2$:MeOH), followed by silica gel chromatography (10% → 20% MeOH:$CH_2Cl_2$), to afford allyl (methyl 2,3-di-*O*-benzoyl-4-*O*-*tert*-butyldimethylsilyl-*β*-D-glucopyranosyluronate)-(1 → 3)-4,6-di-*O*-sodium sulfonato-2-deoxy-2-acetamido-*β*-D-galactopyranoside (115 mg, 93%) as a white solid. $R_f$ 0.125 (15% MeOH:$CH_2Cl_2$). $^1$H NMR (300 MHz, $CD_3OD$): δ = 7.88 – 7.85 (m, 4H, Ar*H*), 7.54 – 7.47 (m, 2H, Ar*H*), 7.38 – 7.32 (m, 4H, Ar*H*), 5.86 – 5.73 (m, 1H, $OCH_2CH{=}CH_2$), 5.67 (dd, *J* = 9.3, 9.3 Hz, 1H, H-3'), 5.48 (dd, *J* = 8.1, 9.2 Hz, 1H, H-2'), 5.18 (dd, *J* = 1.7, 17.6 Hz, 1H, $OCH_2CH{=}CH_2$), 5.11 (d, *J* = 7.5 Hz, 1H, H-1'), 5.05 (dd, *J* = 1.8, 10.5 Hz, 1H, $OCH_2CH{=}CH_2$), 4.44 – 4.35 (m, 3H, H-1, H-4, H-6), 4.30 – 4.22 (m, 4H, $OCH_2CH{=}CH_2$, H-3, H-4', H-6), 4.09 – 3.98 (m, 2H, $OCH_2CH{=}CH_2$, H-5), 3.95 – 3.91 (m, 2H, H-2, H-5'), 3.86 (s, 3H, $CO_2CH_3$), 1.30 (s, 3H, $HNC(O)CH_3$), 0.74 (s, 9H, $(CH_3)_3CSi$), -0.02 (s, 3H, $CH_3Si$), -0.18 (s, 3H, $CH_3Si$); $^{13}$C NMR (75 MHz, $CD_3OD$): δ = 172.3, 170.0, 166.2, 165.8, 134.1, 133.5, 133.4, 130.0, 129.5, 129.4, 129.0, 128.3, 128.2, 115.9, 102.5, 100.8, 79.2, 76.3, 75.9, 75.4, 72.8, 72.6, 70.9,

69.7, 67.6, 54.2, 52.6, 25.0, 21.4, 17.6, -4.9, -5.6; FAB MS: *m/z*: calcd for $C_{38}H_{49}NNa_3O_{20}S_2Si$: 1000.175; found: 1000.175 $[M + Na]^+$.

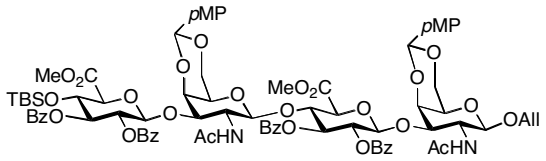
Allyl (methyl 2,3-di-*O*-benzoyl-4-*O*-*tert*-butyldimethylsilyl-*β*-D-glucopyranosyluronate)-(1 → 3)-4,6-di-*O*-sodium sulfonato-2-deoxy-2-acetamido-*β*-D-galactopyranoside (115 mg, 0.123 mmol) was dissolved in pyridine (1.7 mL) and THF (1.7 mL). The reaction was cooled to 0 °C, HF • pyridine (0.60 mL) was added, and it slowly warmed to rt overnight. After 12 h, the mixture was flowed through a Sephadex LH-20 column (50% $CH_2Cl_2$:MeOH) and the concentrated residue was purified by silica gel chromatography (10% → 20% MeOH:$CH_2Cl_2$) to afford a white solid (90.0 mg). $R_f$ 0.50 (EtOAc:pyr:$H_2O$:AcOH, 8:5:3:1).

The crude alcohol (90 mg, 0.11 mmol) was dissolved in THF (1.8 mL) and $H_2O$ (1.8 mL) and to this was added 2 M NaOH (0.72 mL). After 12 h at rt, the reaction was neutralized with Amberlyst IR-120 resin, filtered, and lyophilized to afford an orange solid. The product was purified on Sephadex G-10 (100% $H_2O$) and Sephadex SP C25 (100% $H_2O$) and lyophilized to afford **1** (45 mg, 55%, 2 steps) as a white solid. $R_f$ 0.12 (EtOAc:pyr:$H_2O$:AcOH, 8:5:3:1). $^1$H NMR (300 MHz, $D_2O$): δ = 5.79 – 5.66 (m, 1H, $OCH_2CH$=$CH_2$), 5.17 – 5.07 (m, 2H, $OCH_2CH$=$CH_2$), 4.42 – 4.39 (m, 1H), 4.31 (d, *J* = 7.8 Hz, 1H, H-1'), 4.16 – 4.10 (m, 2H), 4.05 – 3.98 (m, 3H), 3.90 – 3.87 (m, 3H), 3.53 (dd, *J* = 9.0, 9.0 Hz, 1H), 3.36 – 3.29 (m, 2H), 3.21 – 3.16 (m, 1H), 1.84 (s, 3H, HNC(O)$CH_3$); $^{13}$C NMR (75 MHz, $D_2O$): δ = 118.7, 103.4, 100.0, 175.6, 174.8, 133.2, 76.4, 75.2, 75.1, 72.6, 72.4, 71.9, 70.8, 68.0, 51.8, 22.5; FAB MS: *m/z*: calcd for $C_{17}H_{24}NNa_2O_{18}S_2$: 640.0230; found: 640.0202 $[M - Na]^-$.




**Allyl (methyl 2,3-di-*O*-benzoyl-4-*O*-*tert*-butyldimethylsilyl-*β*-D-glucopyranosyluronate)-(1 → 3)-(4,6-*O*-*p*-methoxybenzylidene-2-deoxy-2-trichloroacetamido-*β*-D-galactopyranosyl)-(1 → 4)-(methyl 2,3-di-*O*-benzoyl-*β*-D-glucopyranosyluronate)-(1 → 3)-4,6-*O*-*p*-methoxybenzylidene-2-deoxy-2-trichloroacetamido-*β*-D-galactopyranoside (15').** **7** (0.20 g, 0.182 mmol) and **8** (0.13 g, 0.15 mmol) were combined and coevaporated with

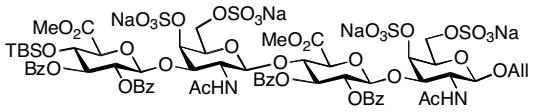
toluene (3x) and put under high vacuum overnight to dry. The mixture was dissolved in $CH_2Cl_2$ (3.0 mL) and 4Å powdered molecular sieves added. The mixture was stirred for 1 h at rt and then cooled to –15 °C. Trimethylsilyl trifluoromethanesulfonate (0.*5 N* solution in $CH_2Cl_2$, 0.0068 g, 0.031 mmol, 61 μL) was added and the reaction was stirred at –15 °C for 30 min and then quenched with TEA. The mixture was filtered and concentrated to afford a yellow oil. Purification of this oil by flash chromatography (30 → 40% EtOAc:hexanes containing 0.1% TEA) afforded **15'** (85 mg, 31%) as a white solid. $R_f$ 0.43 (60% EtOAc:hexanes). $[\alpha]_D^{25}$ = +13.4 (*c* = 0.5, $CH_2Cl_2$); IR (thin film on NaCl): υ = 3424, 2956, 2361, 1732, 1638, 1519, 1452, 1368, 1251, 1173, 1093, 1173, 1093, 1070, 1028; $^1$H NMR (600 MHz, $CDCl_3$): δ = 7.88 – 7.80 (m, 8H, Ar*H*), 7.49 – 7.45 (m, 4H, Ar*H*), 7.38 – 7.28 (m, 8H, Ar*H*), 7.22 – 7.20 (m, 2H, Ar*H*), 7.06 (d, *J* = 8.4 Hz, 2H, $C_6H_4$OMe), 6.93 (d, *J* = 8.4 Hz, 2H, $C_6H_4$OMe), 6.85 (d, *J* = 6.6 Hz, 1H, N*H*''), 6.74 (d, *J* = 8.4 Hz, 2H, Ph), 6.66 (d, *J* = 7.2 Hz, 1H, N*H*), 5.87 – 5.81 (m, 1H, $OCH_2CH$=$CH_2$), 5.58 (dd, *J* = 7.8, 7.8 Hz, 1H, H-3'), 5.49 (s, 1H, MeOPhC*H*), 5.44 (dd, *J* = 8.7, 8.7 Hz, 1H, H-3'''), 5.35 (m, 2H, H-2', H-2'''), 5.23 (d, *J* = 18.0 Hz, 1H, $OCH_2CH$=C$H_2$), 5.20 (s, 1H, MeOPhC*H*), 5.15 (m, 2H, $OCH_2CH$=C$H_2$, H-1'), 5.11 (d, *J* = 7.8 Hz, 1H, H-1''), 5.03 (d, *J* = 7.2 Hz, 1H, H-1'''), 5.00 (d, *J* = 8.4 Hz, 1H, H-1), 4.68 (dd, *J* = 3.6, 10.8 Hz, 1H, H-3''), 4.58 (dd, *J* = 9.0, 9.0 Hz, 1H, H-4'), 4.39 – 4.30 (m, 5H, O$CH_2$CH=$CH_2$, H-3, H-4'', H-4''', H-6''), 4.14 (m, 2H, H-4, H-5'), 4.06 (m, 3H, O$CH_2$CH=$CH_2$, H-5''', H-6''), 3.83 (s, 3H, PhO$CH_3$), 3.81 – 3.68 (m, 4H, H-2, H-2'', H-6, H-6), 3.80 (s, 3H, PhO$CH_3$), 3.80 (s, 3H, $CO_2CH_3$), 3.79 (s, 3H, $CO_2CH_3$), 3.48 (s, 1H, H-5''), 3.10 (s, 1H, H-5), 0.72 (s, 9H, $(CH_3)_3$CSi), -0.09 (s, 3H, $CH_3$Si), -0.24 (s, 3H, $CH_3$Si); $^{13}$C NMR (75 MHz, $CDCl_3$): δ = 168.8, 168.4, 165.7, 165.4, 165.2, 165.1, 162.2, 161.9, 160.0, 159.8, 133.8, 133.4, 133.3, 133.1, 130.5, 130.4, 130.2, 130.1, 130.0, 129.9, 129.6, 129.5, 129.2, 129.1, 128.6, 128.5, 128.4, 127.9, 127.8, 118.2, 113.7, 113.4, 100.8, 100.5, 100.4, 100.2, 98.6, 97.7, 77.4, 76.4, 75.9, 75.8, 75.3, 75.0, 74.2, 74.1, 73.5, 73.4, 72.1, 71.9, 70.8, 70.6, 69.3, 68.4, 66.9, 55.7, 55.6, 54.8, 53.5, 52.8, 25.7, 18.1, -4.1, -4.8. ESI MS: *m/z*: calcd for $C_{83}H_{89}Cl_6N_2O_{29}Si$: 1819.4; found 1820.4 $[M + H]^+$.




**Allyl (methyl 2,3-di-*O*-benzoyl-4-*O*-*tert*-butyldimethylsilyl-β-D-glucopyranosyluronate)-(1 → 3)-(4,6-*O*-*p*-methoxybenzylidene-2-deoxy-2-acetamido-β-D-galactopyranosyl)-(1 → 4)-(methyl 2,3-di-*O*-benzoyl-β-D-glucopyranosyluronate)-(1 → 3)-4,6-*O*-*p*-methoxybenzylidene-2-deoxy-2-acetamido-β-D-galactopyranoside (16'). 15'** (50 mg, 0.027 mmol) was dissolved in benzene (0.88 mL) and *N*,*N*-dimethylacetamide (0.22 mL) and to this were added tributylstannane (0.10 mL, 0.49 mmol) and 2,2'-azobisisobutyronitrile (2.0 mg). The reaction was stirred at rt for 30 min and then was heated at 80 °C for 5 h. It was cooled to rt, concentrated to afford a yellow-white solid, and purified by silica gel chromatography (80% → 100% EtOAc:hexanes) to yield **16'** as a white solid (37 mg, 85%). $R_f$ 0.69 (100% EtOAc). $^1$H NMR (300 MHz, $CDCl_3$): δ = 7.95 – 7.84 (m, 8H, Ar*H*), 7.52 – 7.43 (m, 6H, Ar*H*), 7.38 – 7.27 (m, 8H, Ar*H*), 7.21 (d, *J* = 9.0 Hz, 2H, $C_6H_4$OMe), 6.86 (d, *J* = 8.7 Hz, 2H, $C_6H_4$OMe), 6.80 (d, *J* = 9.0 Hz, 2H, Ph $C_6H_4$OMe), 5.89 – 5.76 (m, 1H, $OCH_2CH$=$CH_2$), 5.61 (dd, *J* = 7.2, 8.1 Hz, 1H, H-3'), 5.51 (s, 1H, MeOPhC*H*), 5.44 (dd, *J* = 8.7, 9.0 Hz, 1H, H-3'''), 5.42 (d, *J* = 6.6 Hz, 1H, N*H*''), 5.31 (dd, *J* = 6.6, 7.2 Hz, 1H, H-2'), 5.28 (dd, *J* = 7.2, 8.7 Hz, 1H, H-2'''), 5.20 (dd, *J* = 0.9, 17.3 Hz, 1H, $OCH_2CH$=C$H_2$), 5.18 (s, 1H, MeOPhC*H*), 5.13 (d, *J* = 11.4 Hz, 1H, $OCH_2CH$=C$H_2$), 5.11 (d, *J* = 8.1 Hz, 1H, H-1'), 5.05 (d, *J* = 7.2 Hz, 1H, H-1''), 4.98 (d, *J* = 6.6 Hz, 1H, N*H*), 4.89 (d, *J* = 7.5 Hz, 1H, H-1), 4.86 (d, *J* = 9.0 Hz, 1H, H-1'''), 4.75 (dd, *J* = 3.3, 10.8 Hz, 1H, H-3''), 4.51 (dd, *J* = 8.1, 9.3 Hz, 1H, H-4'), 4.37 – 4.25 (m, 5H, O$CH_2$CH=$CH_2$, H-3, H-4'', H-4''', H-6''), 4.16 (d, *J* = 9.3 Hz, 1H, H-5'''), 4.06 – 3.98 (m, 4H, O$CH_2$CH=$CH_2$, H-4, H-5', H-6''), 3.77 – 3.73 (m, 1H, H-6), 3.80 (s, 3H, PhOC$H_3$), 3.79 (s, 3H, PhOC$H_3$), 3.73 (s, 3H, $CO_2CH_3$), 3.70 (s, 3H, $CO_2CH_3$), 3.56 – 3.52 (m, 1H, H-6), 3.46 (s, 1H, H-5''), 3.35 – 3.26 (m, 2H, H-2, H-2''), 2.84 (s, 1H, H-5), 1.54 (s, 3H, HNC(O)C$H_3$), 1.50 (s, 3H, HNC(O)C$H_3$), 0.70 (s, 9H, $(CH_3)_3$CSi), -0.10 (s, 3H, C$H_3$Si), -0.25 (s, 3H, C$H_3$Si). ESI MS: *m/z*: calcd for $C_{83}H_{94}N_2O_{29}Si$: 1647.2; found 1648.0 [*M* + Cl]$^-$.

**Allyl (methyl 2,3-di-*O*-benzoyl-4-*O*-*tert*-butyldimethylsilyl-β-D-glucopyranosyluronate)-(1 → 3)-(2-deoxy-2-acetamido-β-D-galactopyranosyl)-(1 → 4)-(methyl 2,3-di-*O*-benzoyl-β-D-glucopyranosyluronate)-(1 → 3)-2-deoxy-2-acetamido-β-D-galactopyranoside (9). 16'** (13 mg, 0.0083 mmol) was dissolved in $CH_2Cl_2$ (200 μL) and $H_2O$ (24 μL) and the reaction was covered with aluminum foil and stirred in the dark. 2,3-Dichloro-5,6-dicyano-1,4-

benzoquinone (6.0 mg, 0.025 mmol) was added and the reaction stirred for 2 h at rt. The reaction was quenched with MeOH and concentrated to afford a red solid. The crude product was subjected to Sephadex LH-20 (50% $CH_2Cl_2$:MeOH) to afford **9** as a yellow solid (8.5 mg, 75%). $R_f$ 0.2 (100% EtOAc). $^1$H NMR (300 MHz, $CD_3OD$): δ = 7.85 – 7.76 (m, 8H, Ar*H*), 7.47 – 7.42 (m, 4H, Ar*H*), 7.36 – 7.27 (m, 8H, Ar*H*), 5.79 – 5.66 (m, 1H, $OCH_2CH$=$CH_2$), 5.52 (dd, *J* = 8.4, 8.4 Hz, 1H, H-3'), 5.51 (dd, *J* = 8.4, 9.9 Hz, 1H, H-3'''), 5.27 – 5.19 (m, 3H), 5.12 (dd, *J* = 1.6 Hz, 17.3 Hz, 1H, $OCH_2CH$=$CH_2$), 5.00 – 4.96 (m, 4H), 4.43 – 4.42 (m, 1H), 4.32 – 4.26 (m, 2H), 4.20 – 4.10 (m, 5H), 4.00 (d, *J* = 2.4 Hz, 1H), 3.96 – 3.88 (m, 3H), 3.70 (s, 3H, $CO_2CH_3$), 3.69 (s, 3H, $CO_2CH_3$), 3.41 – 3.35 (m, 2H), 3.17 – 3.10 (m, 3H), 3.04 –3.00 (m, 1H), 1.20 (s, 3H, HNC(O)$CH_3$), 1.18 (s, 3H, HNC(O)$CH_3$), 0.66 (s, 9H, $(CH_3)_3$CSi), -0.10 (s, 3H, $CH_3$Si), -0.26 (s, 3H, $CH_3$Si). ESI MS: *m/z*: calcd for $C_{67}H_{82}N_2NaO_{27}Si$: 1398.4; found 1397.6 $[M + Na]^+$.




**Allyl (methyl 2,3-di-*O*-benzoyl-4-*O*-*tert*-butyldimethylsilyl-β-D-glucopyranosyluronate)-(1 → 3)-(4,6-di-*O*-sodium sulfonato-2-deoxy-2-acetamido-β-D-galactopyranosyl)-(1 → 4)-(methyl 2,3-di-*O*-benzoyl-β-D-glucopyranosyluronate)-(1 → 3)-4,6-di-*O*-sodium sulfonato-2-deoxy-2-acetamido-β-D-galactopyranoside (17').** **9** (13 mg, 0.0095 mmol) was dissolved in DMF (315 μL) and to this was added $SO_3$ • TMA (50 mg, 0.36 mmol) and the reaction stirred at 50 °C for 2 d. It was quenched with MeOH, concentrated to afford a yellow solid, and purified on Sephadex LH-20 (50% $CH_2Cl_2$:MeOH) and Sephadex SP C25 (50% $H_2O$:MeOH) to afford **17'** as a white solid (11 mg, 67%). $R_f$ 0.29 (EtOAc:pyr:$H_2O$:AcOH, 8:5:3:1). $^1$H NMR (300 MHz, $CD_3OD$): δ = 7.92 – 7.81 (m, 8H, Ar*H*), 7.55 – 7.45 (m, 4H, Ar*H*), 7.43 – 7.33 (m, 8H, Ar*H*), 5.87 – 5.73 (m, 1H, $OCH_2CH$=$CH_2$), 5.67 (dd, *J* = 9.0, 9.0 Hz, 1H, H-3'), 5.61 (dd, *J* = 9.3, 9.3 Hz, 1H, H-3'''), 5.42 – 5.32 (m, 3H), 5.19 (dd, *J* = 1.6, 17.3 Hz, 1H, $OCH_2CH$=$CH_2$), 4.93 – 4.79 (m, 4H, H-4, H-4''), 4.54 – 4.52 (m, 1H), 4.49 (dd, *J* = 9.0, 9.6 Hz, 1H, H-4'), 4.40 – 4.33 (m, 5H), 4.28 –4.22 (m, 3H), 4.18 (d, *J* = 9.3 Hz, 1H, H-5'''), 4.08 – 3.98 (m, 4H), 3.90 – 3.89 (m, 1H), 3.87 (s, 3H, $CO_2CH_3$), 3.86 – 3.85 (m, 2H), 3.83 (s, 3H, $CO_2CH_3$), 1.20 (s, 3H, HNC(O)$CH_3$), 1.18 (s, 3H, HNC(O)$CH_3$), 0.73 (s, 9H, $(CH_3)_3$CSi), -0.03 (s, 3H, $CH_3$Si), -0.19 (s, 3H, $CH_3$Si). ESI MS: *m/z*: calcd for $C_{67}H_{78}N_2Na_3O_{39}S_4Si$: 1760.6; found 1759.8 $[M - Na]^-$.

**Allyl (sodium β-D-glucopyranosyluronate)-(1 → 3)-(4,6-di-*O*-sodium sulfonato-2-deoxy-2-acetamido-β-D-galactopyranosyl)-(1 → 4)-(sodium β-D-glucopyranosyluronate)-(1 → 3)-4,6-di-*O*-sodium sulfonato-2-deoxy-2-acetamido-β-D-galactopyranoside (2). 17'** (11 mg, 0.0062 mmol) was dissolved in pyridine (150 μL), THF (150 μL), and $H_2O$ (35 μL). The reaction was cooled to 0 °C and to this was added HF • pyridine (41 μL). It stirred at 0 °C for 1 h and at rt overnight, and following this, was loaded onto a Sephadex LH-20 (50% $CH_2Cl_2$:MeOH) column. The product was concentrated, taken up in $H_2O$, and lyophilized to afford a white solid (4.9 mg) that was immediately used in the next reaction.

The alcohol was deprotected in a manner similar to a procedure from Lucas *et. al*.[9] The alcohol (4.9 mg, 0.0033 mmol) was dissolved in THF (190 μL) and $H_2O$ (94 μL) and cooled to 0 °C. To this were added 1 M aq. LiOH (75 μL) and 30% $H_2O_2$ (38 μL). The reaction stirred at 0 °C for 1 h and at rt for 12 h. At this time, 4 M NaOH (56 μL) and MeOH (280 μL) were added and the reaction stirred for another 12 h. It was then neutralized with Amberlyst IR-120 resin, filtered, and lyophilized to afford an orange solid. The product was purified by Sephadex G-25 UF (0.9 % NaCl in $H_2O$) and desalted with Sephadex G-25 UF (100% $H_2O$) to afford **2** as a white solid upon lyophilization (1.9 mg, 25% from **17'**). $^1$H NMR (600 MHz, $D_2O$): δ = 5.93 – 5.89 (m, 1H, $OCH_2CH$=$CH_2$), 5.32 (d, *J* = 17.4 Hz, 1H, $OCH_2CH$=C$H_2$), 5.13 (d, *J* = 10.2 Hz, 1H, $OCH_2CH$=C$H_2$), 4.80 – 4.73 (m, 2H, H-4, H-4''), 4.62 – 4.55 (m, 2H), 4.50 – 4.46 (m, 2H), 4.34 (dd, *J* = 4.8, 12.6 Hz, 1H, $OCH_2CH$=$CH_2$), 4.29 (d, *J* = 10.2 Hz, 1H), 4.24 – 4.18 (m, 2H), 4.13 (d, *J* = 7.8 Hz, 1H), 4.06 (d, *J* = 10.8 Hz, 4H), 3.83 – 3.75 (m, 2H), 3.70 – 3.63 (m, 3H), 3.60 (dd, *J* = 7.8, 9.6 Hz, 1H, H-3'), 3.57 – 3.51 (m, 2H), 3.47 (dd, *J* = 9.0, 9.6 Hz, 1H, H-3'''), 3.41 (dd, *J* = 8.4, 8.4 Hz, 1H, H-2'), 3.34 (dd, *J* = 8.4, 8.4 Hz, 1H, H-2'''), 2.04 (s, 3H, HNC(O)C$H_3$), 2.01 (s, 3H, HNC(O)C$H_3$). ESI MS: *m/z*: calcd for $C_{31}H_{42}N_2Na_5O_{35}S_4$: 1245.9; found 1245.0 [*M* - Na]$^-$.

**Allyl (sodium β-D-glucopyranosyluronate)-(1 → 3)-(2-deoxy-2-acetamido-β-D-galactopyranosyl)-(1 → 4)-(sodium β-D-glucopyranosyluronate)-(1 → 3)-2-deoxy-2-acetamido-β-D-galactopyranoside (3). 9** (8.5 mg, 0.0062 mmol) was dissolved in pyridine (110 μL) and THF (110 μL). The reaction was cooled to 0 °C and to this was added HF • pyridine (30 μL). The reaction stirred at 0 °C for 1 h and at rt overnight. Following this, the mixture

was loaded onto a Sephadex LH-20 (50% $CH_2Cl_2$:MeOH) column and the product was a yellow solid (5.3 mg) that was immediately used in the next reaction.

The alcohol (5.3 mg, 0.0042 mmol) was dissolved in THF (120 μL) and $H_2O$ (60 μL) and cooled to 0 °C. To this were added 1 M aq. LiOH (47 μL) and 30% $H_2O_2$ (23 μL). The reaction stirred at 0 °C for 1 h and at rt for 12 h. At this time, 4 M NaOH (35 μL) and MeOH (173 μL) were added and the reaction stirred for another 12 h. It was neutralized with Amberlyst IR-120 resin, filtered, and lyophilized to afford an orange solid. The product was purified by Sephadex G-25 UF (100% $H_2O$) and lyophilized to afford **3** as a white solid (2.6 mg, 52% from **9**). $^1$H NMR (600 MHz, $D_2O$): δ = 5.91 – 5.84 (m, 1H, $OCH_2CH$=$CH_2$), 5.28 (d, *J* = 17.4 Hz, 1H, $OCH_2CH$=C$H_2$), 5.23 (d, *J* = 10.2 Hz, 1H, $OCH_2CH$=C$H_2$), 4.51 – 4.45 (m, 4H), 4.31 (dd, *J* = 4.8, 12.9 Hz, 1H, O$CH_2$CH=$CH_2$), 4.16 – 4.09 (m, 3H), 4.01 – 3.96 (m, 2H), 3.78 – 3.71 (m, 5H), 3.67 – 3.64 (m, 5H), 3.55 (dd, *J* = 9.0, 9.0 Hz, 1H, H-3’’’), 3.48 – 3.42 (m, 3H), 3.34 (dd, *J* = 8.4, 9.0 Hz, 1H, H-2’), 3.29 (dd, *J* =7.2, 8.4 Hz, 1H, H-2’’’), 1.99 (s, 3H, HNC(O)C$H_3$), 1.98 (s, 3H, HNC(O)C$H_3$). ESI MS: *m/z*: calcd for $C_{31}H_{47}N_2O_{23}$: 815.7; found 815.4 [*M* - H]$^-$.

**Hippocampal Neuronal Cultures.** Hippocampal neuronal cultures were prepared using a modified version of the Goslin and Banker protocol.[10] Embryos at the E18 stage were obtained from timed-pregnant Sprague-Dawley rats, and the hippocampus from each embryo was dissected. All the hippocampi from one preparation were transferred to a 15 mL conical tube containing 4.5 mL of ice-cold Calcium and Magnesium Free-Hank’s Balanced Salt Solution (CMF-HBSS) (GIBCO). Trypsin (2.5%, no EDTA; GIBCO) was added to 5 mL, and the tissue was digested for 15 min at 37 °C. The trypsin solution was removed and the tissue rinsed with 5 mL of CMF-HBSS three times. The tissue was then dissociated in 1 mL of CMF-HBSS by passing through a P1000 pipet tip twenty times. The cells were counted with a hemacytometer and plated on glass coverslips at 80 cells/mm$^2$ and cultivated in minimal Eagle’s Medium (MEM) (GIBCO) supplemented with the N2 mixture (GIBCO) and 0.1 mM pyruvate. The cultures were maintained in 5% $CO_2$ at 37 °C. Glass coverslips were coated as described by Clement *et. al.*[11] Briefly, coverslips were precoated with 0.015 mg/mL poly-DL-ornithine (SIGMA) for 1 h at 37 °C/5% $CO_2$, washed three times with double distilled $H_2O$ (500 μL), and coated with 0.5 mg/mL of compounds **1**-**3** in PBS (100 μL) overnight at 37 °C/ 5% $CO_2$. The coverslips were then washed three times with PBS (500 μL) and flooded with MEM + N2 media (500 μL). Notably, the use of adhered compounds to glass coverslips has been reported to simulate the

extracellular matrix, and the procedure by Clement *et al.* was used previously to implicate heterogeneous polysaccharides containing the CS-E motif in neuronal outgrowth.

**Immunocytochemistry of Hippocampal Neuronal Cultures.** After 48 h in culture, hippocampal neurons on coverslips were used for immunostaining. Cells were rinsed one time with PBS, fixed in 4% paraformaldehyde for 20 min at rt, washed twice with PBS, permeabilized in 0.3% Triton X-100 for 5 min at rt, and washed twice with PBS. Non-specific binding was blocked with 3% BSA for 1 h at rt. The blocking solution was rinsed off one time with PBS. Cells were then incubated with anti-tau antibodies (rabbit polyclonal, 1:600; SIGMA) in 3% BSA for 2 h at rt. Excess antibody was rinsed away 5 times with PBS. Fluorophore-conjugated secondary antibodies were purchased from Molecular Probes and added for 1 h at 37 °C in 3% BSA. The secondary antibody used was anti-rabbit IgG AlexaFluor 488 (1:600). Excess secondary antibody was washed off 5 times with PBS. The coverslips were mounted onto glass slides using Vectashield mounting medium (Vector Labs) and sealed with clear nail polish. Cells were then subjected to confocal laser microscopy.

**Confocal Laser Microscopy.** All cells were imaged on a Zeiss Axiovert 100M inverted confocal laser microscope in the Biological Imaging Center in the Beckman Institute at Caltech. The images were captured with LSM Pascal software using a 40X plan-neofluar oil objective. All cells were excited with 488nm light.

**Morphometric Analysis.** For quantitative analysis, 50 cells were analyzed per coverslip. Only cells with neurites longer than one cell body diameter were counted. The length of the longest neurite from stained cells was measured using NIH Image 1.52 software. The mean neurite lengths were compared among the different substrate conditions by the ANOVA test using the statistical analysis program StatView (SAS Institute Inc., Cary, NC).

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