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Solid-Phase Synthesis of 2-Aminoethyl Glucosamine Sulfoforms

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Abstract

Mono- and disaccharides of sulfonated glucosamines (GlcN sulfoforms) conjugated to 2-aminoethyl linkers were generated by solid-phase synthesis. Orthogonally protected intermediates were tethered onto tritylated polystyrene resin beads, subjected to a modular sequence of deprotection and sulfonation steps, then cleaved from solid support without degradation of *N*- or *O*-sulfate esters using solvolytic conditions, and finally purified by reverse-phase HPLC to afford the title compounds.

Introduction

Heparan sulfate proteoglycans (HSPGs) are well known for their many important roles in cellular function.^{1,2} HSPGs are recognized by a diverse range of heparin-binding proteins in key biological processes, such as angiogenesis (fibroblast growth factors, or FGFs),³ pathogenic infection (herpes simplex virus glycoprotein D),⁴ and inflammation (L-selectin).⁵ However, so far only a handful of HSPG sequences have been elucidated, due to the heterogeneity of structures that exist within heparin. Many studies have shown that the specificity of HS binding is defined in large part by sulfonation patterns, or sulfoforms. For example, FGF1 binding requires glucosamine-2,6-disulfate (GlcN_{2,6S}), whereas FGF2 binding requires GlcN₅ and also iduronate-2-sulfate (IdoA-2_S).^{6,7,8}

The relevance of sulfoforms within HS and particularly glucosamine (GlcN) to protein binding suggests that even relatively simple sulfoforms are likely to exhibit sufficient binding avidity to serve as potential antagonists in HS-mediated signaling. Recent examples in the scientific literature supports this notion: a disaccharide sulfoform containing GlcN has been found to have significant binding to FGF2,⁶ and a clinical study showed that dendrimers presenting multiple GlcNAc-6_S units can prevent scar tissue formation.⁹ However, structure–affinity relationships between HS-like compounds and heparin-binding proteins remain rare, and are limited by challenges in identifying or producing structurally well-characterized ligands in sufficient quantities for study.

To address this bottleneck, we have introduced a method of generating GlcN sulfoforms using solid-phase synthesis.¹⁰ Performing deprotections and sulfonations on resin-immobilized intermediates greatly simplifies the purification process, and reduces the attrition in yield caused by multiple extraction and chromatography steps. Our previous study established proof of concept, but the glycol linker associated with these sulfoforms was not amenable to further conjugation. Here we further optimize the solid-phase synthesis approach in order to generate a number of mono- and disaccharide GlcN sulfoforms bearing

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Supporting Information

¹H and ¹³C NMR spectra of all compounds are available directly from the corresponding author.

a 2'-aminoethyl linker (Figure 1), and to facilitate the preparation of glycoconjugates for subsequent protein binding studies.

Results and Discussion

Synthesis of orthogonally protected GlcN monosaccharide and disaccharide

The preparation of orthogonally protected α -GlcN monosaccharides with ethanolamine linkers is described in Scheme 1. Phthalimide-protected GlcN derivative **5** was converted in 85% yield over three steps to 2-azido-2-deoxyglucoside,¹⁰ followed by reductive ring opening of the 4,6-benzylidene acetal using $\text{BH}_3/\text{Bu}_2\text{BOTf}^{11}$ and formation of 6-*O*-TBDPS ether to afford **6** in 62% yield over two steps. Glycoside **6** was subjected to glycosylation with 9-fluorenylmethoxycarbonyl (Fmoc)-protected ethanolamine to yield **7** as a mixture of anomers (4.2:1 α : β ratio) in 99% yield. The major and minor isomers were carefully separated by silica gel chromatography, then treated with 20% piperidine in DMF to provide amine-terminated GlcN derivatives **8a** and **8b** respectively, each in 99% isolated yield. The selective cleavage of Fmoc in the presence of other protecting groups was essential for conducting our orthogonal deprotection/sulfonation strategy on a solid-phase support.

In order to prepare β -aminoethyl-linked GlcN($\beta 1 \rightarrow 4$)Glc derivative **12**, the trichloroethoxycarbonyl (Troc) group was installed at the C2 position of GlcN to provide anchimeric assistance during glycosyl coupling (Scheme 2). Troc-protected GlcN derivative **9** was prepared from **6** in 94% overall yield, then subjected to NIS/TfOH-promoted glycosylation with **15** to yield β -linked disaccharide **10** in 90% yield, followed by selective deprotection with indium powder in aqueous $\text{NH}_4\text{Cl}^{12}$ and Cu^{2+} -mediated diazo transfer to yield **11** in 91% yield over 2 steps. Selective Fmoc deprotection with 20% piperidine in DMF gave 2'-aminoethyl GlcN derivative **12** in 99% isolated yield.

The β -aminoethyl-linked GlcN($\alpha 1 \rightarrow 4$)Glc β derivative **17** was synthesized as described in Scheme 3. 2'-Azidoethyl β -glucoside tetraacetate **13** was prepared in 46% yield from glucose pentaacetate by glycosylation with 2-bromoethanol and azide substitution. Saponification, 4,6-*O*-benzylidene acetal formation, benzylation of the C2 and C3 hydroxyls, and regioselective reductive ring opening with Et_3SiH and TfOH yielded glycosyl acceptor **14** in 56% yield over 4 steps.¹³ The azide of **14** was converted into Fmoc derivative **15** in 54% yield over 3 steps, and NIS/TfOH-promoted glycosyl coupling of **15** and thioglucoside **6** yielded α -1,4-linked disaccharide **16** in 60% yield. The Fmoc group was efficiently cleaved to produce 2'-aminoethyl derivative **17** in 99% yield.

Loading of orthogonally protected GlcN derivatives onto resins

The loading of 2'-aminoethyl GlcN derivatives onto trityl-PS resins was initially accompanied by multiple side reactions, presumably because of the nucleophilicity of the terminal amine. Moreover, the recovery and purification of excess aminoethyl-linked GlcNs from the reaction mixture was problematic. Using a lower concentration of 2'-aminoethyl GlcN derivatives in dry pyridine at 60 °C produced much cleaner results, but the resin loadings were commensurately lower.

Aminoethyl-linked GlcN derivatives **8a** (GlcN- α), **8b** (GlcN- β), **12** (GlcN($\beta 1 \rightarrow 4$)Glc- β), and **17** (GlcN($\alpha 1 \rightarrow 4$)Glc- β) were each loaded onto trityl-PS resin in the presence of 0.4 equivalents of DMAP (Table 1). Introducing the amine-terminated derivatives **8a**, **8b**, and **12** at 50% loading capacity (0.75 mmol/g) and **17** at 33% loading capacity (0.5 mmol/g) produced resin-immobilized GlcN **18a**, **18b**, **19**, and **20**, with loading ratios of 0.38, 0.27, 0.18, and 0.18 mmol/g, respectively.

Generation of GlcN sulfoforms

We first investigated conditions for cleaving 2'-aminoethyl-linked glycosides from the trityl-PS resins. No detectable cleavage was found when using 0.3 M $\text{BF}_3 \cdot \text{Et}_2\text{O}$ in CH_2Cl_2 at -20°C , the condition used to cleave glycol-linked GlcNs, and higher temperatures (above 0°C) would result in the significant decomposition of *N*-sulfate esters.¹⁰ Fortunately, 30% hexafluoroisopropanol (HFIP) in CH_2Cl_2 at room temperature provided an ideal alternative: the cleavage was remarkably efficient and selective, yet mild enough to leave both *O* and *N*-sulfate esters unaffected.¹⁴ This condition was also found to be effective for cleaving glycol-linked sulfoforms (trityl ethers).

The solid-phase deprotection and sulfonation conditions developed in our earlier protocol¹⁰ was applied toward resin-immobilized monosaccharide **18a**, to produce fully deprotected α -linked GlcN **1a** in 87% yield after 6 operations, and sulfoforms **1b–1h** in overall yields ranging from 76% (**1b**) to 44% (**1f**) after 8 operations (Table 2). This method was also used to generate GlcN sulfoforms **2(b,f)**, **3(b,f)**, and **4(b,f)** in comparable yields from **18b**, **19**, and **20**, respectively. The relatively low yields obtained for GlcN S_3S_6S sulfoforms **1f–4f** may be due to the premature removal of the 3-*O*-acetate or acetyl transfer from O3 to N2, with subsequent sulfonation of the C3 alcohol. This problem may be circumvented by protecting the C3 alcohol as a SEM ether, which previously demonstrated excellent orthogonality with several other protecting groups in solution-phase synthesis.¹⁵

It is worth mentioning that in our earlier studies, we performed ion exchange with tetrabutylammonium bromide before releasing sulfoforms from the resin, based on the belief that the hydrophobic Bu_4N counterion (i) improved the stability of sulfate esters during cleavage, and (ii) aided in the swelling of resins in organic solvents.¹⁶ However, we have subsequently determined that sulfonation and cleavage does not require Bu_4N counterions to enhance process chemistry. This was confirmed by subjecting resin-immobilized GlcN S_3S_6S **1h** (containing a mixture of PyH^+ and Et_3NH^+ counterions) to HFIP cleavage without prior treatment with $\text{Bu}_4\text{N-Br}$, followed by passage through a Na ion-exchange column. Good yields of the Na salts were achieved after reverse-phase HPLC purification, and no degradation byproducts were observed. We thus do not need to perform Bu_4N ion exchange in our optimized solid-phase synthesis protocol.

Our optimized solid-phase synthesis generated sulfoforms with minimal byproduct formation in nearly all cases. To take one example, the resin-immobilized GlcN **18a** was subjected to 7 operations involving deprotection, sulfonation, and HFIP cleavage to generate GlcNAc-3 S_3S_6S (**1e**) with Et_3NH^+ counterions. The clean ^1H NMR of the as-isolated product supports the high quality of each conversion (Figure 2), validating this method of generating sulfoforms from a single, orthogonally protected precursor.

The modular deprotection/sulfonation steps can efficiently generate sulfoforms on trityl-PS resins with up to three sulfate esters per molecule, but generating derivatives with a larger number of sulfate esters is more challenging. The high charge density of such compounds creates a highly heterogeneous environment within the resin and can raise the barrier to ionic exchange. To test the limits of the solid-phase approach with trityl-PS resins, we attempted to generate a hexasulfate ester from a resin-immobilized GlcN disaccharide derivative (GlcN $S_3S_3S_6S(\alpha 1 \rightarrow 4)\text{GlcN}S_3S_6S$), but were unable to achieve complete sulfonation (unpublished results). This limitation might be addressed by using less hydrophobic substrates such as PEG-grafted PS resins, which have been used to assemble protected HS oligosaccharides.¹⁷ To our knowledge, on-resin deprotection and sulfonation steps for such derivatives have not yet been reported, although we note a case in which a sulfate ester was installed on a synthetic tetrasaccharide immobilized on a polymeric PEG support.¹⁸

In closing, we have demonstrated the generation of GlcN sulfoforms with 2'-aminoethyl linkers using solid-phase synthesis methods and orthogonally protected scaffolds. Each operation can be performed in high yields without the need for ion exchange, and the amine-terminated sulfoforms can be cleaved from trityl-PS resins under mild conditions.

Experimental details

All starting materials and reagents were obtained from commercial sources and used as received unless otherwise noted. All solvent were freshly distilled prior to use. All glucosamine sulfoforms were purified by HPLC using a Hydro-RP C18 reverse-phase column, with UV detection at 214 nm. IR spectra were acquired from NaCl plate, using a Thermo-Nicolet Nexus 670 FT-IR spectrometer. ^1H NMR spectra were recorded at 300, 400, or 500 MHz; ^{13}C NMR spectra were recorded at 75, 100, or 125 MHz. Chemical shifts were referenced to the solvent used (δ 7.27 and 77.00 for CDCl_3 , δ 3.31 and 49.15 for CD_3OD , and δ 4.80 in D_2O). Mass spectra were acquired using either a Hewlett-Packard 5989B or a Finnigan 40000 mass spectrometer. Optical rotations were measured by polarimetry at rt. Silica gel chromatography was performed with ICN SiliTech 32-63D.

Thiotolyl 4,6-*O*-benzylidene-2-deoxy-2-phthalimido- β -D-glucopyranoside (5)

Glucosamine hydrochloride (50 g, 232 mmol) was mechanically agitated with 1M NaOMe in MeOH (232 mL) for 2 h at rt, followed by addition of finely powdered phthalic anhydride (19 g, 128 mmol) and Et_3N (35.5 mL, 255 mmol). The mixture was stirred for 45 min, then treated with a second portion of phthalic anhydride (19 g, 128 mmol) and stirred for 24 h at rt. The mixture was cooled to -20°C for 4 h, filtered, washed with cold MeOH and dried under reduced pressure to yield a lighter yellow solid. The solid was redispersed in pyridine (500 mL) followed by slow addition of Ac_2O (330 mL) at 0°C and continuous agitation at rt for 48 h. The crude was concentrated under reduced pressure and purified by recrystallization in 95% EtOH to afford 1,3,4,6-tetra-*O*-acetyl-2-phthalimido-2-deoxy- β -D-glucopyranoside as an amorphous white solid (76 g, 69% over 3 steps).¹⁹ ^1H NMR (300 MHz, CDCl_3): δ 7.84 (dd, 2H, $J=3, 6$ Hz), 7.73 (dd, 2H, $J=3, 5.7$ Hz), 6.49 (d, 1H, $J=8.7$ Hz), 5.86 (dd, 1H, $J=9.3, 10.5$ Hz), 5.19 (t, 1H, $J=9.3$ Hz), 4.44 (dd, 1H, $J=8.7, 10.5$ Hz), 4.34 (dd, 1H, $J=3.9, 12.3$ Hz), 4.11 (dd, 1H, $J=2.4, 12.3$ Hz), 4.00 (ddd, 1H, $J=2.4, 4.8, 10.8$ Hz), 2.08 (s, 3H), 1.97 (s, 3H), 1.84 (s, 3H); ^{13}C NMR (75 MHz, CDCl_3): δ 170.70, 170.08, 169.55, 168.71, 167.44, 134.57, 131.26, 123.87, 89.82, 72.67, 70.56, 68.32, 61.58, 53.55, 20.82, 20.68, 20.48.

A solution of above tetraacetate (20 g, 41.9 mmol) and *p*-thiocresol (6.8 g, 54.5 mmol) in CH_2Cl_2 (40 mL) was cooled to 0°C and treated with $\text{BF}_3\cdot\text{Et}_2\text{O}$ (12 mL). The mixture was stirred at rt for 24 h, quenched with saturated NaHCO_3 solution (100 mL), extracted with CH_2Cl_2 (3×200 mL), washed with brine (50 mL), then dried over Na_2SO_4 and concentrated. The crude product was purified by recrystallization in 95% EtOH to afford thiotolyl 3,4,6-*O*-acetyl-2-deoxy-2-phthalimido- β -D-glucopyranoside as an amorphous white solid (19.7 g, 87%).¹⁹ ^1H NMR (300 MHz, CDCl_3): δ 7.86 (dd, 2H, $J=2.7, 5.1$ Hz), 7.75 (dd, 2H, $J=3, 5.4$ Hz), 7.29 (d, 2H, $J=7.2$ Hz), 7.06 (d, 2H, $J=7.5$ Hz), 5.77 (t, 1H, $J=9.9$ Hz), 5.64 (d, 1H, $J=10.5$ Hz), 5.11 (t, 1H, $J=9.6$ Hz), 4.24–4.30 (m, 2H), 4.19 (dd, 1H, $J=2.4, 12.3$ Hz), 3.87 (ddd, 1H, $J=3, 5.4, 10.8$ Hz), 2.31 (s, 3H), 2.09 (s, 3H), 2.01 (s, 3H), 1.82 (s, 3H); ^{13}C NMR (75 MHz, CDCl_3): δ 170.76, 170.22, 169.58, 167.95, 167.08, 138.89, 134.57, 134.43, 134.04, 131.71, 131.29, 129.77, 127.05, 123.82, 83.22, 75.95, 71.77, 68.79, 62.31, 53.69, 21.29, 20.90, 20.73, 20.54; IR (NaCl): 1749, 1719, 1384, 1227, 1037 cm^{-1} ; $[\alpha]_{\text{D}}^{20} = +40.3$ (c 1.01, CH_2Cl_2); HRESI-MS: m/z calcd for $\text{C}_{27}\text{H}_{27}\text{NNaO}_9\text{S}$ $[\text{M}+\text{Na}]^+$: 564.1304; found: 564.1301.

The triacetate above (15.8 g, 29.1 mmol) was dissolved in 2:3 CH₂Cl₂:MeOH (80 mL) and cooled to 0 °C, then treated with 1 M NaOMe solution in MeOH (10.5 mL, 10.5 mmol). The mixture was stirred at 0 °C for 3 h, neutralized with activated Dowex 50X-W-H⁺ ion-exchange resin, filtered, concentrated, and dried under reduced pressure. A solution of the crude triol in THF (97 mL) was treated with benzaldehyde dimethyl acetal (13 mL, 87.2 mmol) and TsOH·H₂O (554 mg, 2.91 mmol). The mixture was heated to reflux for 10 h, quenched with saturated NaHCO₃ solution (30 mL), extracted with CH₂Cl₂ (3 × 150 mL), dried over Na₂SO₄ and concentrated under reduced pressure. Purification by recrystallization in 95% EtOH yielded 4,6-*O*-benzylidene acetal **5** as an amorphous white solid (12.5 g, 85% over 2 steps). ¹H NMR (300 MHz, CDCl₃): δ 7.82 (dd, 2H, *J* = 5.4, 9.9 Hz), 7.64–7.72 (m, 2H), 7.41–7.51 (m, 2H), 7.22–7.35 (m, 5H), 7.06 (d, 2H, *J* = 8.4 Hz), 5.58 (d, 1H, *J* = 10.5 Hz), 5.52 (s, 1H), 4.55 (dt, 1H, *J* = 3.6, 9.9 Hz), 4.33 (dd, 1H, *J* = 4.2, 10.2 Hz), 4.27 (t, 1H, *J* = 10.5 Hz), 3.77 (t, 1H, *J* = 9.9 Hz), 3.58 (dt, 1H, *J* = 4.5, 8.7 Hz), 3.51 (t, 1H, *J* = 9.3 Hz), 3.30 (d, 1H, *J* = 3 Hz), 2.30 (s, 3H); ¹³C NMR (75 MHz, CDCl₃): δ 168.31, 167.61, 138.39, 136.96, 134.23, 133.22, 131.54, 129.74, 129.35, 128.37, 127.95, 126.37, 123.85, 123.37, 101.87, 84.49, 81.79, 70.28, 69.61, 68.54, 55.71, 21.15; IR (NaCl): 3474, 1776, 1713, 1386, 1092 cm⁻¹; [α]_D²⁰ = +31.2 (*c* 1.10, CH₂Cl₂); HRESI-MS: *m/z* calcd for C₂₈H₂₅NNaO₆S [M+Na]⁺: 526.1300; found: 526.1292.

Thiotolyl 3-*O*-acetyl-2-azido-4-*O*-benzyl-6-*O*-(*tert*-butyldiphenylsilyl)-2-deoxy-β-D-glucopyranoside (**6**)

Preparation of TfN₃: A solution of NaN₃ (73 g, 1125 mmol) in water (30 mL) and CH₂Cl₂ (30 mL) at 0 °C was treated with Tf₂O (38 mL, 225 mmol). The mixture was stirred for 2 h at 0 °C, extracted with CH₂Cl₂ (2 × 35 mL), washed with saturated aqueous Na₂CO₃ solution (75 mL), then brine (30 mL) and used immediately.

A solution of **5** (12.5 g, 24.9 mmol) and ethylene diamine (33 mL, 500 mmol) in *n*-butanol was stirred at 100 °C for 10 h in a pressure tube. The mixture was concentrated, azeotroped with toluene and dried under reduced pressure. This was redispersed in 66% aqueous MeOH (231 mL) and treated at 0 °C with K₂CO₃ (5.2 g, 37.5 mmol), CuSO₄·5 H₂O (312 mg, 1.25 mmol) and freshly prepared TfN₃ (70 mL, 3.2 M solution in CH₂Cl₂). An additional 30 mL of MeOH was added to homogenize the mixture, which was slowly warmed up to rt over 3 h and continually stirred for another 10 h at rt, concentrated and azeotroped with toluene, then dried under reduced pressure. The crude azide was dissolved in pyridine (150 mL) followed by addition of Ac₂O (75 mL) at 0 °C. The mixture was warmed up to rt over 2 h and continually stirred for another 10 h, concentrated, and dried under reduced pressure. Purification by silica gel chromatography (6% EtOAc in hexanes) yielded thiotolyl 3-*O*-acetyl-2-azido-4,6-*O*-benzylidene-2-deoxy-β-D-glucopyranoside as an amorphous white solid (9.3 g, 85% over 3 steps). ¹H NMR (300 MHz, CDCl₃): δ 7.48 (d, 1H, *J* = 7.5 Hz), 7.37–7.45 (m, 2H), 7.33–7.36 (m, 2H), 7.19 (d, 2H, *J* = 7.5 Hz), 5.47 (s, 1H), 5.24 (t, 1H, *J* = 10.2 Hz), 4.55 (d, 1H, *J* = 10.2 Hz), 3.38 (dd, 1H, *J* = 3.9, 10.5 Hz), 3.77 (t, 1H, *J* = 10.5 Hz), 3.48–3.58 (m, 2H), 3.39 (t, 1H, *J* = 9.9 Hz), 2.39 (s, 3H), 2.12 (s, 3H); ¹³C NMR (75 MHz, CDCl₃): δ 169.72, 139.37, 136.82, 134.49, 130.11, 129.26, 128.37, 126.71, 126.23, 101.56, 87.10, 78.37, 73.12, 70.76, 68.51, 63.57, 21.38, 20.93; IR (NaCl): 2110, 1754, 1368, 1216, 1099 cm⁻¹; [α]_D²⁰ = -121.0 (*c* 2.00, CH₂Cl₂); HRESI-MS: *m/z* calcd for C₂₂H₃₃N₃NaO₅S [M+Na]⁺: 464.1256; found: 464.1246.

The intermediate above (5 g, 11.3 mmol) was dissolved in a 1 M solution of BH₃ in THF (113 mL), then treated with a 1 M solution of Bu₂BOTf in THF (11.9 mL) at 0 °C in the presence of 2,6-lutidine (2.63 mL, 22.6 mmol).¹¹ The mixture was stirred for 10 h at 0 °C, then cooled to -78 °C and quenched with Et₃N (3.14 mL, 22.6 mmol), followed by the slow addition of cold MeOH (60 mL). The mixture was slowly warmed to rt, concentrated, then

purified by silica gel chromatography (20% EtOAc in hexanes) to yield the intermediate C6 alcohol (4.04 g, 10.68 mmol). This was dissolved in DMF (14 mL) and treated with imidazole (2.2 g, 32.04 mmol) and TBDPS-Cl (5.56 mL, 21.36 mmol). The mixture was stirred for 12 h at rt, quenched with saturated NaHCO₃ solution (40 mL), extracted with CH₂Cl₂ (2 × 100 mL), washed with brine (40 mL), dried over Na₂SO₄ then concentrated under reduced pressure. Purification by silica gel chromatography (6.25% EtOAc in hexanes) yielded 6-*O*-TBDPS ether **6** as an amorphous white solid (5.04 g, 62% over 2 steps). ¹H NMR (300 MHz, CDCl₃): δ 7.82 (dd, 2H, *J* = 1.8, 7.5 Hz), 7.73 (dd, 2H, *J* = 1.2, 7.5 Hz), 7.54 (d, 2H, *J* = 8.4 Hz), 7.25–7.45 (m, 9H), 7.15–7.18 (m, 2H), 7.07 (d, 2H, *J* = 8.1 Hz), 5.18 (t, 1H, *J* = 9.3 Hz), 4.61 (dd, 2H, *J* = 11.1, 19.8 Hz), 4.47 (d, 1H, *J* = 10.2 Hz), 4.02 (dd, 1H, *J* = 1.2, 11.7 Hz), 3.94 (dd, 1H, *J* = 3, 11.7 Hz), 3.79 (t, 1H, *J* = 9.3 Hz), 3.42 (d, 1H, *J* = 9.3 Hz), 3.35 (t, 1H, *J* = 9.9 Hz), 2.34 (s, 3H), 2.02 (s, 3H), 1.14 (s, 9H); ¹³C NMR (75 MHz, CDCl₃): δ 169.94, 138.81, 137.77, 135.97, 135.72, 134.26, 133.36, 132.83, 129.97, 128.62, 127.97, 127.89, 127.36, 86.14, 80.08, 76.32, 75.48, 74.91, 63.21, 62.37, 27.05, 21.35, 21.01, 19.547; IR (NaCl): 2030, 2857, 2109, 1753, 1218, 1112, 1045 cm⁻¹; [α]_D²⁰ = -60.1 (*c* 1.21, CH₂Cl₂); HRESI-MS: *m/z* calcd for C₃₈H₄₃N₃NaO₅SSi [M+Na]⁺: 704.2590; found: 704.2595.

2'-(9*H*-Fluoren-9-yl)methoxycarbonylaminoethyl 3-*O*-acetyl-2-azido-4-*O*-benzyl-6-*O*-(*tert*-butyldiphenylsilyl)-2-deoxy-α-*D*-glucopyranoside (7a**)**

A solution of ethanolamine (130 μL, 2.13 mmol) in CH₂Cl₂ (6 mL) was treated at 0 °C with Fmoc-Cl (500 mg, 1.93 mmol) in the presence of NaHCO₃ (974 mg, 11.6 mmol). The mixture was warmed up to rt over 2 h and continuously stirred for another 8 h, extracted with CH₂Cl₂ (3 × 100 mL), washed with water (30 mL), brine (30 mL), and dried over Na₂SO₄, then concentrated to afford Fmoc-protected ethanolamine in 96% yield as an amorphous white solid

A mixture of thioglycoside **6** (500 mg, 0.73 mmol) and 2'-hydroxyethyl 2-(9*H*-fluoren-9-yl)methylcarbamate (270 mg, 0.95 mmol) was azeotroped with toluene (3 × 4 mL), dried under reduced pressure for 1 h, then dissolved in 1:2 (CH₂Cl₂)₂:Et₂O (6 mL) and stirred with activated 4A molecular sieves for 1 h at rt under Ar. The mixture was cooled to -20 °C and treated with *N*-iodosuccinimide (180 mg, 0.8 mmol) and TfOH (10 μL, 0.11 mmol). The mixture was stirred continuously for another 5 h at -20 °C, quenched with Et₃N (35 μL, 0.22 mmol), warmed to rt, filtered through Celite, extracted with CH₂Cl₂ (3 × 70 mL), washed with brine (40 mL), dried over Na₂SO₄, then concentrated under reduced pressure to yield the corresponding Fmoc-protected 2'-aminoethyl glycoside as a 4.2:1 mixture of anomers. Purification by silica gel chromatography (11% EtOAc in hexanes) yielded α-GlcN derivative **7a** (486 mg, 80%) and β-GlcN derivative **7b** (116 mg, 19%) as colorless oils.

Major isomer **7a**: ¹H NMR (400 MHz, CDCl₃): δ 7.77 (d, 2H, *J* = 7.5 Hz), 7.72 (t, 4H, *J* = 6.7 Hz), 7.61 (dd, 2H, *J* = 4.6, 7.1 Hz), 7.37–7.49 (m, 8H), 7.27–7.35 (m, 5H), 7.20 (dd, 2H, *J* = 2.5, 7.6 Hz), 5.63 (m, 1H), 5.39 (t, 1H, *J* = 5.4 Hz), 5.01 (d, 1H, *J* = 3.3 Hz), 4.67 (s, 2H), 4.37 (d, 2H, *J* = 7.3 Hz), 4.22 (t, 1H, *J* = 7.1 Hz), 3.90–3.98 (m, 2H), 3.77–3.86 (m, 3H), 3.58 (t, 2H, *J* = 8.4 Hz), 3.35 (m, 1H), 3.17 (dd, 1H, *J* = 3.4, 10.6 Hz), 2.09 (s, 3H), 1.12 (s, 9H); ¹³C NMR (100 MHz, CDCl₃): δ 170.00, 156.35, 143.95, 143.82, 141.22, 137.63, 135.74, 135.53, 133.27, 132.85, 129.75, 128.44, 127.84, 127.71, 127.62, 127.00, 125.16, 119.86, 98.39, 74.89, 72.10, 71.83, 67.65, 66.87, 62.37, 61.50, 47.10, 40.60, 26.82, 20.90, 19.29; IR (NaCl): 2929, 2108, 1726, 1517, 1226, 1114, 1041 cm⁻¹; [α]_D²⁰ = +80.1 (*c* 0.89, CH₂Cl₂); HRESI-MS: *m/z* calcd for C₄₈H₅₂N₄NaO₈Si [M+Na]⁺: 863.3452; found: 863.3462.

Minor isomer **7b**: ^1H NMR (400 MHz, CDCl_3): δ 7.65–7.80 (m, 6H), 7.57 (dd, 2H, $J = 7.5$, 11.5 Hz), 7.26–7.46 (m, 13H), 7.20 (dd, 2H, $J = 2.1$, 7.5 Hz), 5.27 (t, 1H, $J = 5.7$ Hz), 5.07 (t, 1H, $J = 9.9$ Hz), 4.60–4.70 (m, 2H), 4.40 (dd, 2H, $J = 4.1$, 7.0 Hz), 4.32 (d, 2H, $J = 8.0$ Hz), 4.18 (t, 1H, $J = 6.8$ Hz), 3.89 (m, 2H), 3.81 (t, 1H, $J = 9.5$ Hz), 3.68 (m, 1H), 3.40–3.55 (m, 3H), 3.32 (d, 1H, $J = 9.5$ Hz), 2.05 (s, 3H), 1.09 (s, 9H); ^{13}C NMR (100 MHz, CDCl_3): δ 170.01, 156.60, 144.03, 141.42, 137.79, 135.98, 135.65, 133.49, 132.89, 129.96, 128.66, 128.10, 127.95, 127.93, 127.85, 127.78, 127.17, 125.25, 125.17, 120.15, 102.30, 75.88, 75.04, 74.00, 69.67, 66.71, 64.44, 62.32, 47.39, 41.17, 26.99, 21.09, 19.47; found: 863.3461; IR (NaCl): 2932, 2110, 1752, 1726, 1225, 1050 cm^{-1} ; $[\alpha]_D^{20} = -5.3$ (c 1.57, CH_2Cl_2); HRESI-MS: m/z calcd for $\text{C}_{48}\text{H}_{52}\text{N}_4\text{NaO}_8\text{Si}$ $[\text{M}+\text{Na}]^+$: 863.3452.

2'-Aminoethyl 3-O-acetyl-2-azido-4-O-benzyl-6-O-(*tert*-butyldiphenylsilyl)-2-deoxy- α -D-glucopyranoside (**8a**)

Fmoc-protected **7a** (840 mg, 1 mmol) was dissolved in 1:4 piperidine:DMF (5 mL) and stirred at rt for 30 min. The mixture was concentrated and purified by silica gel chromatography (EtOAc) to afford 2'-aminoethyl α -GlcN derivative **8a** as a colorless oil (612 mg, 99%). ^1H NMR (400 MHz, CDCl_3): δ 7.72 (dt, 4H, $J = 1.1$, 8.3 Hz), 7.36–7.46 (m, 6H), 7.25–7.36 (m, 3H), 7.20 (dd, 2H, $J = 2.1$, 7.7 Hz), 5.61 (m, 1H), 5.03 (d, 1H, $J = 3.6$ Hz), 4.66 (s, 2H), 3.90–4.03 (m, 2H), 3.83 (d, 2H, $J = 5.6$ Hz), 3.77 (m, 1H), 3.50 (m, 1H), 3.15 (dd, 1H, $J = 3.5$, 10.8 Hz), 2.80–2.95 (m, 2H), 2.06 (s, 3H), 1.11 (s, 9H); ^{13}C NMR (100 MHz, CDCl_3): δ 167.93, 137.71, 135.76, 135.53, 133.35, 132.92, 129.71, 128.42, 127.79, 127.70, 127.63, 127.59, 98.26, 76.21, 74.80, 72.16, 71.58, 70.65, 62.40, 61.55, 41.56, 26.82, 20.89, 19.30; IR (NaCl): 2929, 2856, 2106, 1748, 1225, 1111, 1042 cm^{-1} ; $[\alpha]_D^{20} = +96.5$ (c 1.33, CH_2Cl_2); HRESI-MS: m/z calcd for $\text{C}_{33}\text{H}_{43}\text{N}_4\text{O}_6\text{Si}$ $[\text{M}+\text{H}]^+$: 619.2952; found: 619.2955.

2'-Aminoethyl 3-O-acetyl-2-azido-4-O-benzyl-6-O-(*tert*-butyldiphenylsilyl)-2-deoxy- β -D-glucopyranoside (**8b**)

Fmoc-protected **7b** (266 mg, 0.32 mmol) was dissolved in 1:4 piperidine:DMF (5 mL) and stirred at rt for 30 min. The mixture was concentrated and purified by silica gel chromatography (EtOAc) to afford 2'-aminoethyl β -GlcN derivative **8b** as a colorless oil (194 mg, 99%). ^1H NMR (400 MHz, CDCl_3): δ 7.75 (dd, 2H, $J = 1.6$, 8.0 Hz), 7.70 (dd, 2H, $J = 1.0$, 7.5 Hz), 7.44 (t, 2H, $J = 7.2$ Hz), 7.38 (t, 4H, $J = 7.1$ Hz), 7.25–7.35 (m, 3H), 7.20 (dd, 2H, $J = 2.1$, 7.6 Hz), 5.08 (t, 1H, $J = 9.8$ Hz), 4.66 (q, 2H, $J = 11.1$ Hz), 4.42 (d, 1H, $J = 8.0$ Hz), 3.90–4.01 (m, 3H), 3.83 (t, 1H, $J = 9.5$ Hz), 3.62 (m, 1H), 3.46 (dd, 1H, $J = 8.0$, 10.3 Hz), 3.39 (td, 1H, $J = 2.5$, 9.6 Hz), 2.90–3.06 (m, 2H), 2.04 (s, 3H), 1.43 (br, 2H), 1.11 (s, 9H); ^{13}C NMR (100 MHz, CDCl_3): δ 169.83, 137.60, 135.81, 135.46, 133.36, 132.79, 129.71, 128.44, 127.85, 127.72, 127.70, 127.54, 101.99, 75.75, 75.66, 74.79, 73.94, 72.46, 64.36, 62.24, 41.85, 26.78, 20.88, 19.29; IR (KBr): 2930, 2857, 2110, 1752, 1226, 1112, 1047 cm^{-1} ; $[\alpha]_D^{20} = -13.8$ (c 0.72, CH_2Cl_2); HRESI-MS: m/z calcd for $\text{C}_{33}\text{H}_{43}\text{N}_4\text{O}_6\text{Si}$ $[\text{M}+\text{H}]^+$: 619.2952; found: 619.2949.

Thiotolyl 3-O-acetyl-4-O-benzyl-6-O-(*tert*-butyldiphenylsilyl)-2-deoxy-2-(trichloroethylcarbonylamino)- β -D-glucopyranoside (**9**)

3-O-acetate **6** (600 mg, 0.88 mmol) was dissolved in anhydrous MeOH (20 mL) and treated at rt with 1 M NaOMe solution in MeOH (264 μL , 0.26 mmol). The mixture was stirred at rt for 3 h, neutralized with activated Dowex 50X-W- H^+ ion-exchange resin, filtered, concentrated, and dried under reduced pressure. A solution of the crude alcohol in CH_2Cl_2 (10 mL) was treated at rt with Bu_3P (241 μL , 0.97 mmol), followed by addition of H_2O (10 mL) after 3 h. The mixture was stirred at rt for 1 day, concentrated, azeotroped with toluene (3×10 mL), and dried under reduced pressure. The crude amine was redispersed in pyridine

(10 mL) and treated with Troc-Cl (127 μ L, 0.92 mmol) at rt. The mixture was stirred at rt for 10 h and concentrated. The crude product was redispersed in pyridine (20 mL) and treated with Ac₂O (10 mL) at rt. The mixture was stirred at rt for 10 h, concentrated and purified by silica gel chromatography (20% EtOAc in hexanes) to afford Troc-protected derivative **9** as an amorphous white solid (581 g, 94%). ¹H NMR (400 MHz, CDCl₃): δ 7.83 (dd, 2H, *J* = 1.2, 7.9 Hz), 7.75 (dd, 2H, *J* = 1.0, 7.9 Hz), 7.51–7.37 (m, 8H), 7.16–7.23 (m, 2H), 7.07 (d, 4H, *J* = 8.1 Hz), 5.70 (d, 1H, *J* = 9.9 Hz), 5.28 (t, 1H, *J* = 9.8 Hz), 4.89 (d, 1H, *J* = 12.1 Hz), 4.78 (d, 1H, *J* = 12.0 Hz), 4.64 (d, 1H, *J* = 12.7 Hz), 4.62 (s, 2H), 3.77–3.95 (m, 4H), 3.40 (d, 1H, *J* = 9.6 Hz), 3.34 (s, 3H), 2.01 (s, 3H), 1.15 (s, 9H); ¹³C NMR (100 MHz, CDCl₃): δ 171.06, 154.33, 137.99, 137.59, 135.93, 135.56, 133.43, 133.22, 132.68, 129.70, 129.63, 128.94, 128.44, 127.88, 127.77, 127.68, 95.65, 87.14, 79.56, 76.39, 75.50, 74.88, 74.45, 62.17, 55.15, 26.88, 21.16, 20.94, 19.27; IR (NaCl): 2930, 2858, 1749, 1728, 1242, 1112, 1085, 1035 cm⁻¹; [α]_D²⁰ = -24.8 (*c* 0.81, CH₂Cl₂); HRESI-MS: *m/z* calcd for C₄₁H₄₆Cl₃NNaO₇SSi [M+Na]⁺: 852.1728; found: 852.1723.

2'-(9H-Fluoren-9-yl)methoxycarbonylaminoethyl 4-O-[3-O-acetyl-4-O-benzyl-2-deoxy-6-O-(*tert*-butyldiphenylsilyl)-2-(trichloroethylcarbonylamino)- β -D-glucopyranosyl]-2,3,6-tri-O-benzyl- β -D-glucopyranoside (10)

A mixture of glycosyl donor **9** (560 mg, 0.68 mmol) and glycosyl acceptor **15** (580 mg, 0.81 mmol) was azeotroped with toluene (3 $\times$ 10 mL), dried under reduced pressure for 1 h, then redissolved in 1:2 (CH₂Cl₂)₂:Et₂O (3 mL) with freshly activated 4A molecular sieves and stirred at rt for 1 h. NIS (198 mg, 0.88 mmol) was added and the mixture was cooled to -30 °C, followed by addition of TfOH (9 μ L, 0.1 mmol). The mixture was stirred at -30 °C for 6 h, quenched with Et₃N (32 μ L, 0.2 mmol), filtered through Celite, treated with aqueous Na₂S₂O₃ (30 mL), extracted with CH₂Cl₂ (3 $\times$ 100 mL), washed with brine (20 mL), then dried over Na₂SO₄ and concentrated. The crude product was purified by silica gel chromatography (20% EtOAc in hexanes) to afford 1,4- β -linked disaccharide **10** as an amorphous white solid (860 mg, 90%). ¹H NMR (400 MHz, CDCl₃): δ 7.78–7.90 (m, 4H), 7.73 (d, 2H, *J* = 6.0 Hz), 7.64 (d, 2H, *J* = 7.4 Hz), 7.30–7.47 (m, 24H), 7.15–7.27 (m, 6H), 5.57 (t, 1H, *J* = 6.3 Hz), 4.97 (t, 1H, *J* = 10.4 Hz), 4.68–4.90 (m, 7H), 4.68 (s, 2H), 4.40–4.57 (m, 5H), 4.35 (d, 1H, *J* = 8.0 Hz), 4.24 (t, 1H, *J* = 5.6 Hz), 4.00 (t, 1H, *J* = 8.9 Hz), 3.58–3.95 (m, 9H), 3.33–3.53 (m, 4H), 3.18 (d, 1H, *J* = 9.7 Hz), 2.00 (s, 3H), 1.14 (s, 9H); ¹³C NMR (100 MHz, CDCl₃): δ 170.55, 156.53, 154.26, 144.00, 143.92, 141.30, 139.00, 138.28, 137.79, 137.44, 135.90, 135.65, 133.20, 132.90, 129.75, 128.72, 128.45, 128.30, 128.03, 128.00, 127.80, 127.64, 127.38, 127.04, 125.08, 125.03, 120.00, 103.83, 100.31, 95.64, 81.86, 77.30, 76.38, 75.84, 75.78, 74.82, 74.87, 74.82, 74.58, 74.33, 74.10, 73.60, 69.87, 68.20, 66.49, 62.21, 57.15, 47.27, 41.51, 26.93, 20.85, 19.22; IR (NaCl): 2941, 2858, 1748, 1729, 1520, 1452, 1236, 1109, 1052 cm⁻¹; [α]_D²⁰ = -15.5 (*c* 0.84, CH₂Cl₂); ESI-MS: *m/z* calcd for C₇₈H₈₃Cl₃N₂NaO₁₅Si [M+Na]⁺: 1443.45; found: 1443.44.

2'-(9H-Fluoren-9-yl)methoxycarbonylaminoethyl 4-O-[3-O-acetyl-2-azido-4-O-benzyl-2-deoxy-6-O-(*tert*-butyldiphenylsilyl)- β -D-glucopyranosyl]-2,3,6-tri-O-benzyl- β -D-glucopyranoside (11)

Troc-protected **10** (282 mg, 0.2 mmol) was dissolved in 3:2 EtOH:H₂O (2 mL), treated with indium metal powder (46 mg, 0.4 mmol) and NH₄Cl (32 mg, 0.6 mmol), then stirred for 6 h at 98 °C in a high-pressure reaction vessel. The mixture was concentrated, redispersed in 2:1 MeOH:H₂O (15 mL) with K₂CO₃ (41 mg, 0.3 mmol) and CuSO₄·5H₂O (5 mg, 0.02 mmol), then treated at 0 °C with fresh prepared 0.03 M TfN₃ solution in CH₂Cl₂ (60 mL). The mixture was warmed to rt slowly over 2 h and stirred at rt for another 8 h. The mixture was quenched with solution of NaHCO₃ (50 mL), filtered through Celite, extracted with CH₂Cl₂ (3 $\times$ 50 mL), washed with brine (20 mL), then dried over Na₂SO₄ and concentrated. The crude product was purified by silica gel chromatography (20% EtOAc in hexanes) to afford

azide **11** as an amorphous white solid (230 mg, 91%). ^1H NMR (400 MHz, CDCl_3): δ 7.80 (dd, 4H, $J = 2.7, 7.4$ Hz), 7.72 (dd, 2H, $J = 1.1, 7.9$ Hz), 7.62 (d, 2H, $J = 7.5$ Hz), 7.46 (dd, 4H, $J = 7.7, 9.0$ Hz), 7.40 (t, 4H, $J = 8.1$ Hz), 7.27–7.38 (m, 15H), 7.25–7.25 (m, 7H), 5.58 (t, 1H, $J = 5.4$ Hz), 5.03 (t, 1H, $J = 9.3$ Hz), 4.89 (d, 2H, $J = 11.1$ Hz), 4.84 (d, 1H, $J = 12.5$ Hz), 4.76 (d, 1H, $J = 11.1$ Hz), 4.57–4.64 (m, 3H), 4.49 (d, 2H, $J = 8.0$ Hz), 4.46 (d, 1H, $J = 4.5$ Hz), 4.41 (dd, 2H, $J = 6.7, 11.2$ Hz), 4.23 (t, 1H, $J = 6.7$ Hz), 4.08 (t, 1H, $J = 9.3$ Hz), 3.60–3.92 (m, 8H), 3.38–3.55 (m, 4H), 3.32 (dd, 1H, $J = 8.3, 10.4$ Hz), 3.05 (d, 1H, $J = 9.6$ Hz), 2.08 (s, 3H), 1.12 (s, 9H); ^{13}C NMR (100 MHz, CDCl_3): δ 169.84, 156.51, 144.00, 143.90, 141.28, 138.38, 138.24, 137.71, 137.56, 135.87, 135.60, 133.13, 132.75, 129.75, 128.44, 128.32, 128.03, 127.98, 127.87, 127.81, 127.65, 127.63, 127.10, 127.01, 125.09, 125.01, 119.94, 103.82, 100.39, 81.86, 81.74, 77.26, 75.75, 74.85, 74.49, 74.30, 74.17, 73.43, 69.98, 68.53, 66.45, 65.27, 61.94, 47.26, 41.52, 26.92, 20.90, 19.20; IR (NaCl): 2930, 2858, 2109, 1752, 1722, 1357, 1222, 1111, 1053 cm^{-1} ; $[\alpha]_{\text{D}}^{20} = -4.9$ (c 0.71, CH_2Cl_2); MALDI-MS: m/z calcd for $\text{C}_{75}\text{H}_{80}\text{N}_4\text{NaO}_{13}\text{Si}$ $[\text{M}+\text{Na}]^+$: 1295.5389; found: 1295.4942.

2'-Aminoethyl 4-O-[3-O-acetyl-2-azido-4-O-benzyl-2-deoxy-6-O-(*tert*-butyldiphenyl-silyl)- β -D-glucopyranosyl]-2,3,6-O-benzyl- β -D-glucopyranoside (12**)**

Fmoc-protected **11** (184 mg, 0.14 mmol) was dissolved in 1:4 piperidine:DMF (5 mL) and stirred at rt for 30 min. The mixture was concentrated and purified by silica gel chromatography (5% MeOH in EtOAc) to afford 2'-aminoethyl β -glycoside **12** as a colorless oil (150 mg, 99%). ^1H NMR (400 MHz, CDCl_3): δ 7.80 (d, 2H, $J = 4.9$ Hz), 7.70 (d, 2H, $J = 7.2$ Hz), 7.20–7.52 (m, 17H), 7.17–7.25 (m, 5H), 5.02 (t, 1H, $J = 9.8$), 4.94 (d, 1H, $J = 11.0$ Hz), 4.85–4.90 (m, 2H), 4.79 (d, 1H, $J = 10.9$ Hz), 4.71 (d, 1H, $J = 12.2$ Hz), 4.64 (dd, 2H, $J = 11.3, 22.9$ Hz), 4.57 (d, 1H, $J = 12.3$ Hz), 4.50 (dd, 2H, $J = 8.3, 17.9$ Hz), 4.17 (t, 1H, $J = 8.7$ Hz), 3.98 (m, 1H), 3.85 (s, 2H), 3.60–3.85 (m, 5H), 3.55 (t, 2H, $J = 8.7$ Hz), 3.31 (t, 1H, $J = 9.4$ Hz), 3.07 (d, 1H, $J = 8.7$ Hz), 2.95 (br, 1H), 2.08 (s, 3H), 1.13 (s, 9H); ^{13}C NMR (100 MHz, CDCl_3): δ 169.84, 138.89, 138.33, 137.74, 135.87, 135.61, 133.13, 132.75, 129.75, 128.44, 128.29, 128.01, 127.95, 127.83, 127.62, 127.06, 103.64, 100.26, 81.89, 81.66, 77.33, 75.78, 75.74, 75.53, 74.86, 74.47, 74.17, 73.44, 72.41, 68.54, 65.17, 61.99, 26.92, 20.91, 19.19; IR (NaCl): 2930, 2856, 2109, 1752, 1223, 1109, 1055 cm^{-1} ; $[\alpha]_{\text{D}}^{20} = -5.1$ (c 0.55, CH_2Cl_2); ESI-MS: m/z calcd for $\text{C}_{60}\text{H}_{71}\text{N}_4\text{O}_{11}\text{Si}$ $[\text{M}+\text{H}]^+$: 1051.49; found: 1051.36.

2'-Azidoethyl 2,3,4,6-tetra-O-acetyl- β -D-glucopyranoside (13**).²⁰**

To a solution of β -D-glucose pentaacetate (10 g, 25.6 mmol), 2-bromoethanol (5.5 mL, 76.9 mmol) and DIPEA (223 μL , 1.3 mmol) in CH_2Cl_2 (60 mL) at 0 $^\circ\text{C}$ was added a 1 M $\text{BF}_3 \cdot \text{Et}_2\text{O}$ solution in CH_2Cl_2 (4.9 mL, 4.9 mmol) slowly. The mixture was slowly warmed to rt over 2 h, stirred continually at rt for another 10 h, quenched with saturated NaHCO_3 solution (100 mL), extracted with CH_2Cl_2 (3×200 mL), washed with brine (50 mL), then dried over Na_2SO_4 and concentrated. The crude product was purified by silica gel chromatography (25% EtOAc in hexanes) to afford an amorphous white solid (5.6 g). This was redispersed with NaN_3 (3.2 g, 49.5 mmol) in CH_2Cl_2 and heated to reflux for 12 h, extracted with CH_2Cl_2 (3×200 mL), washed with brine (50 mL), then dried over Na_2SO_4 and concentrated to afford 2'-azidoethyl β -glucoside **13** as an amorphous white solid (4.9 g, 46%). ^1H NMR (400 MHz, CDCl_3): δ 5.19 (t, 1H, $J = 9.5$ Hz), 5.08 (t, 1H, $J = 7.2$ Hz), 5.01 (dd, 1H, $J = 8.0, 9.6$ Hz), 4.58 (d, 1H, $J = 7.8$ Hz), 4.23 (dd, 1H, $J = 4.6, 12.3$ Hz), 4.13 (dd, 1H, $J = 2.4, 12.3$ Hz), 4.01 (ddd, 1H, $J = 1.0, 4.7, 10.9$ Hz), 3.65–3.72 (m, 2H), 3.47 (ddd, 1H, $J = 3.6, 8.4, 12.8$ Hz), 3.26 (ddd, 1H, $J = 3.6, 4.8, 12.8$ Hz), 2.07 (s, 3H), 2.03 (s, 3H), 2.00 (s, 3H), 1.98 (s, 3H); ^{13}C NMR (100 MHz, CDCl_3): δ 170.55, 170.16, 169.29, 100.54, 72.65, 71.79, 70.92, 68.48, 68.16, 61.69, 50.39, 20.63, 20.58, 20.49; IR (NaCl): 2945, 2106, 1756, 1369, 1226, 1039 cm^{-1} ; $[\alpha]_{\text{D}}^{20} = -31.2$ (c 1.14, CH_2Cl_2); ESI-MS: m/z calcd for $\text{C}_{16}\text{H}_{23}\text{N}_3\text{NaO}_{10}$ $[\text{M}+\text{Na}]^+$: 440.1281; found: 440.1290.

2'-Azidoethyl 2,3,6-tri-*O*-benzyl- β -D-glucopyranoside (14)

A solution of tetraacetate **13** (4.9 g, 11.8 mmol) was dissolved in anhydrous MeOH (40 mL) and treated at rt with 1 M NaOMe solution in MeOH (3.5 mL). The mixture was stirred at rt for 3 h, neutralized with activated Dowex 50X-W-H⁺ ion-exchange resin, filtered, concentrated, and dried under reduced pressure. A solution of the crude in THF (80 mL) was treated with benzaldehyde dimethyl acetal (5.3 mL, 35.4 mmol) and TsOH·H₂O (225 mg, 1.18 mmol). The mixture was heated to reflux for 10 h, quenched with saturated NaHCO₃ solution (30 mL), extracted with CH₂Cl₂ (3 × 150 mL), dried over Na₂SO₄ and concentrated under reduced pressure. The crude product was purified by silica gel chromatography (50% EtOAc in hexanes) to afford an amorphous white solid (3.7 g). This was redispersed with BnBr (5.1 mL, 42.3 mmol) in DMF and treated at 0 °C with NaH (1.3 g, 32.5 mmol). The mixture was slowly warmed to rt over 2 h and continuously stirred at rt for another 10 h, quenched with saturated NH₄Cl solution (100 mL), extracted with CH₂Cl₂ (3 × 200 mL), washed with brine (50 mL), then dried over Na₂SO₄ and concentrated. The crude product was purified by silica gel chromatography (14% EtOAc in hexanes) to afford the desired 2,3-di-*O*-benzyl glucoside as an amorphous white solid (4.5 g, 75%). ¹H NMR (400 MHz, CDCl₃): δ 7.52 (dd, 2H, *J* = 2.2, 7.9 Hz), 7.28–7.48 (m, 13H), 5.60 (s, 1H), 4.49 (dd, 2H, *J* = 1.7, 11.9 Hz), 4.82 (dd, 2H, *J* = 4.4, 11.4 Hz), 4.56 (d, 1H, *J* = 7.8 Hz), 4.38 (dd, 1H, *J* = 4.8, 10.4 Hz), 4.06 (ddd, 1H, *J* = 4, 6.4, 10.4 Hz), 3.62–3.86 (m, 2H), 3.38–3.55 (m, 2H); ¹³C NMR (100 MHz, CDCl₃): δ 138.37, 138.27, 137.19, 128.92, 128.31, 128.26, 128.20, 128.04, 127.97, 127.69, 127.60, 125.94, 103.99, 101.07, 82.03, 81.31, 80.75, 75.39, 75.07, 68.64, 68.49, 66.01, 50.91; IR (NaCl): 2883, 2104, 1094, 1072 cm⁻¹; [α]_D²⁰ = –33.5 (c 0.79, CH₂Cl₂); ESI-MS: *m/z* calcd for C₂₉H₃₀N₃NaO₆ [M+Na]⁺: 540.2111; found: 540.2102.

A solution of the protected intermediate above (4.4 g, 8.6 mmol) and Et₃SiH (5.5 mL, 34.2 mmol) in CH₂Cl₂ (86 mL) was cooled to –78 °C and treated with TfOH (3 mL, 34.2 mmol) in the presence of 4A molecular sieve. The mixture was stirred at –78 °C for 6 h, quenched with Et₃N (5.4 mL, 38.5 mmol) and MeOH (5 mL), warmed up to rt slowly over 1 h, filtered through Celite, extracted with CH₂Cl₂ (3 × 100 mL), washed with brine (20 mL), then dried over Na₂SO₄ and concentrated. The crude product was purified by silica gel chromatography (20% EtOAc in hexanes) to afford 6-*O*-benzyl ether **14** as an amorphous white solid (3.3 g, 75%). ¹H NMR (400 MHz, CDCl₃): δ 7.34 (m, 15H), 4.96 (t, 2H, *J* = 10.9 Hz), 4.74 (dd, 2H, *J* = 3.8, 11.0 Hz), 4.59 (dd, 2H, *J* = 11.6, 17.2 Hz), 4.46 (dd, 1H, *J* = 2.4, 5.6 Hz), 4.06 (ddd, 1H, *J* = 3.6, 5.6, 10.4 Hz), 3.78 (dd, 1H, *J* = 3.5, 10.4 Hz), 3.67–3.79 (m, 2H), 3.59 (d, 1H, *J* = 8.8 Hz), 3.40–3.55 (m, 5H), 2.51 (s, 1H); ¹³C NMR (100 MHz, CDCl₃): δ 138.47, 138.30, 137.80, 128.50, 128.37, 128.33, 128.06, 127.90, 127.81, 127.69, 127.65, 103.64, 83.85, 81.64, 75.21, 74.76, 74.10, 73.59, 71.21, 70.04, 68.12, 50.96; IR (NaCl): 3442, 2872, 2103, 1452, 1064 cm⁻¹; [α]_D²⁰ = –15.3 (c 0.90, CH₂Cl₂); ESI-MS: *m/z* calcd for C₂₉H₃₃N₃NaO₆ [M+Na]⁺: 542.2267; found: 542.2272.

2'-(9*H*-Fluoren-9-yl)methoxycarbonylaminoethyl 2,3,6-tri-*O*-benzyl- β -D-glucopyranoside (15)

A solution of 2'-azidoethyl glucoside **14** (2.4 g, 4.6 mmol) in CH₂Cl₂ (30 mL) was treated at rt with Bu₃P (1.3 mL, 5.1 mmol), followed by addition of H₂O (30 mL) after 3 h. The mixture was stirred at rt for 1 day, concentrated, azeotroped with toluene (3 × 10 mL), and dried under reduced pressure to afford a yellowish oil. This was redispersed with NaHCO₃ (2.3 g, 27.9 mmol) in CH₂Cl₂ (35 mL) and treated at 0 °C with Fmoc-Cl (1.2 g, 4.6 mmol) dissolved in CH₂Cl₂ (5 mL). The mixture was slowly warmed to rt over 2 h and stirred continually for another 10 h at rt, extracted with CH₂Cl₂ (3 × 100 mL), washed with brine (20 mL), then dried over Na₂SO₄ and concentrated. The crude product was purified by silica gel chromatography (20% EtOAc in hexanes) to afford Fmoc-protected **15** as an amorphous white solid (1.6 g, 54%). ¹H NMR (400 MHz, CDCl₃): δ 7.77 (d, 2H, *J* = 7.5 Hz), 7.61 (d,

2H, $J = 7.4$ Hz), 7.20–7.55 (m, 19H), 5.61 (t, 1H, $J = 5.0$ Hz), 4.96 (dd, 2H, $J = 11.5$, 20.1 Hz), 4.78 (d, 2H, $J = 11.4$ Hz), 4.52 (dd, 2H, $J = 12.1$, 26.7 Hz), 4.35–4.45 (m, 3H), 4.19 (t, 1H, $J = 6.7$ Hz), 3.79–3.90 (m, 2H), 3.75 (dd, 1H, $J = 3.2$, 10.2 Hz), 3.66 (dd, 1H, $J = 5.8$, 10.1 Hz), 3.59 (t, 1H, $J = 8.8$ Hz), 3.25–3.52 (m, 5H), 2.45 (br, 1H); ^{13}C NMR (100 MHz, CDCl_3): δ 156.52, 144.01, 143.87, 141.26, 138.46, 138.21, 137.67, 128.55, 128.42, 128.36, 127.98, 127.96, 127.89, 127.77, 127.69, 127.64, 126.99, 125.03, 119.93, 103.96, 83.92, 81.65, 75.22, 74.79, 73.97, 73.53, 71.23, 70.13, 69.96, 66.43, 47.23, 41.56; IR (NaCl): 3430, 3031, 2874, 1711, 1452, 1251, 1062 cm^{-1} ; $[\alpha]^{20}_{\text{D}} = -10.9$ (c 1.31, CH_2Cl_2); ESI-MS: m/z calcd for $\text{C}_{44}\text{H}_{45}\text{NNaO}_8$ $[\text{M}+\text{Na}]^+$: 738.3043; found: 738.3045.

2'-(9H-Fluoren-9-yl)methoxycarbonylaminoethyl 4-O-[3-O-acetyl-2-azido-4-O-benzyl-2-deoxy-6-O-(*tert*-butyldiphenylsilyl)- α -D-glucopyranosyl]-2,3,6-tri-O-benzyl- β -D-glucopyranoside (16)

A mixture of glycosyl acceptor **15** (503 mg, 0.7 mmol) and glycosyl donor **6** (400 mg, 0.59 mmol) was azeotroped with toluene (3×10 mL), dried under reduced pressure for 1 h, then redispersed in 1:2 (CH_2Cl_2): Et_2O (3 mL) with freshly activated 4A molecular sieves and stirred at rt for 1 h. NIS (145 mg, 0.65 mmol) was added and the mixture was cooled to -20 °C, followed by addition of TfOH (16 μL , 0.18 mmol). The mixture was stirred at -20 °C for 10 h, quenched with Et_3N (58 μL , 0.42 mmol), and filtered through Celite, then treated with saturated $\text{Na}_2\text{S}_2\text{O}_3$ (30 mL), extracted with CH_2Cl_2 (3×100 mL), washed with brine (20 mL), then dried over Na_2SO_4 and concentrated. The crude product was purified by silica gel chromatography (20% EtOAc in hexanes) to afford 1,4- α -linked disaccharide **16** as an amorphous white solid (447 mg, 60%). ^1H NMR (400 MHz, CDCl_3): δ 7.77 (dd, 2H, $J = 3.1$, 7.3 Hz), 7.62 (ddd, 4H, $J = 0.9$, 8.0, 12.3 Hz), 7.56 (t, 2H, $J = 7.1$ Hz), 7.25–7.50 (m, 24H), 7.21 (d, 2H, $J = 7.4$ Hz), 6.94–7.06 (m, 4H), 5.69 (d, 1H, $J = 3.7$ Hz), 5.65 (t, 1H, $J = 10.3$ Hz), 5.10 (d, 1H, $J = 10.9$ Hz), 4.90 (d, 1H, $J = 11.0$ Hz), 4.82 (d, 1H, $J = 10.8$ Hz), 4.69 (d, 1H, $J = 11.0$ Hz), 4.66 (s, 2H), 4.54 (m, 1H), 4.35 (dd, 1H, $J = 6.1$, 10.6 Hz), 4.25 (d, 1H, $J = 7.6$ Hz), 4.23 (d, 1H, $J = 15.2$ Hz), 4.15 (m, 1H), 3.74–3.90 (m, 4H), 3.69 (d, 2H, $J = 11.6$ Hz), 3.57 (d, 2H, $J = 10.5$ Hz), 3.21–3.57 (m, 7H), 3.06 (dd, 1H, $J = 3.7$, 10.8 Hz), 2.06 (s, 3H), 1.05 (s, 9H); ^{13}C NMR (100 MHz, CDCl_3): δ 170.03, 156.58, 144.07, 143.74, 141.39, 141.33, 138.47, 138.18, 138.02, 137.49, 135.82, 135.56, 133.49, 132.87, 129.68, 128.42, 128.15, 128.04, 127.89, 127.70, 127.62, 127.45, 127.31, 127.03, 126.94, 125.03, 124.79, 119.98, 104.02, 97.96, 84.62, 82.63, 75.74, 74.81, 74.64, 74.59, 73.57, 73.21, 73.08, 72.06, 70.83, 68.77, 65.79, 61.68, 61.41, 47.44, 41.76, 26.91, 20.92, 19.32; IR (NaCl): 2929, 2858, 2108, 1749, 1730, 1227, 1043 cm^{-1} ; $[\alpha]^{20}_{\text{D}} = +42.6$ (c 0.29, CH_2Cl_2); ESI-MS: m/z calcd for $\text{C}_{75}\text{H}_{80}\text{N}_4\text{NaO}_{13}\text{Si}$ $[\text{M}+\text{Na}]^+$: 1295.54; found: 1295.29.

2'-Aminoethyl 4-O-[3-O-acetyl-2-azido-4-O-benzyl-2-deoxy-6-O-(*tert*-butyl-diphenylsilyl)- α -D-glucopyranosyl]-2,3,6-tri-O-benzyl- β -D-glucopyranoside (17)

Fmoc-protected **16** (427 mg, 0.24 mmol) was dissolved in 1:4 piperidine:DMF (5 mL) and stirred at rt for 30 min. The mixture was concentrated and purified by silica gel chromatography (EtOAc) to afford 2'-aminoethyl β -glycoside **17** as a colorless oil (349 mg, 99%). ^1H NMR (400 MHz, CDCl_3): δ 7.65 (dd, 4H, $J = 6.9$, 15.0 Hz), 7.41–7.47 (m, 2H), 7.25–7.40 (m, 18H), 7.21 (dd, 2H, $J = 1.8$, 8.1 Hz), 7.13 (dd, 2H, $J = 1.8$, 7.5 Hz), 7.06 (dd, 2H, $J = 1.1$, 5.9 Hz), 5.73 (d, 1H, $J = 3.8$ Hz), 5.49 (t, 1H, $J = 9.5$ Hz), 5.12 (d, 1H, $J = 10.9$ Hz), 4.97 (d, 1H, $J = 11.0$ Hz), 4.83 (d, 1H, $J = 10.8$ Hz), 4.75 (d, 1H, $J = 11.0$ Hz), 4.68 (d, 1H, $J = 13.9$ Hz), 4.68 (d, 2H, $J = 2.6$ Hz), 4.46 (d, 1H, $J = 7.8$ Hz), 4.42 (d, 1H, $J = 5.7$ Hz), 4.41 (d, 1H, $J = 13.9$ Hz), 3.77–3.95 (m, 4H), 3.57–3.75 (m, 6H), 3.40–3.55 (m, 2H), 3.07 (dd, 1H, $J = 3.8$, 10.8 Hz), 2.82–2.97 (m, 2H), 2.10 (br, 1H), 2.05 (s, 3H), 1.08 (s, 9H); ^{13}C NMR (100 MHz, CDCl_3): δ 169.94, 138.46, 138.14, 137.96, 137.73, 135.79, 135.52, 133.49, 132.88, 129.62, 128.39, 128.35, 128.15, 127.86, 127.70, 127.64, 127.60, 127.54, 127.45, 127.39, 127.25, 103.52, 97.48, 84.68, 82.57, 75.75, 74.73, 74.66, 74.50, 73.99,

73.24, 72.93, 72.20, 72.02, 71.97, 68.95, 61.76, 61.39, 41.89, 26.87, 20.87, 19.29; IR (NaCl): 3030, 2930, 2857, 2107, 1751, 1360, 1225, 1090, 1039 cm^{-1} ; $[\alpha]_{\text{D}}^{20} = +53.9$ (*c* 1.21, CH_2Cl_2); ESI-MS: *m/z* calcd for $\text{C}_{60}\text{H}_{71}\text{N}_4\text{O}_{11}\text{Si}$ $[\text{M}+\text{H}]^+$: 1051.4889; found: 1051.4905.

2'-Aminoethyl 3-O-acetyl-2-azido-4-O-benzyl-6-O-(tert-butyldiphenylsilyl)-2-deoxy- α -D-glucopyranoside, bound to trityl-PS resin (18a)

Cl-Trityl-PS resin beads (1.29 g, 1.93 mmol) were suspended in dry pyridine (3 mL) for 5 min, followed by the addition of 2'-aminoethyl α -GlcN glycoside **8a** (597 mg, 0.96 mmol) and DMAP (47 mg, 0.39 mmol). The mixture was shaken for 2 days at 60 °C then cooled to rt. Anhydrous MeOH (0.5 mL) was added and the mixture was shaken at rt for 1 h. The resin was filtered, washed with 5% $i\text{Pr}_2\text{NEt}$ in 8:1 CH_2Cl_2 :MeOH (2×4 mL), then alternatively with DMF (2×4 mL) and CH_2Cl_2 (2×4 mL), then finally with additional CH_2Cl_2 (3×4 mL). The resin was dried under reduced pressure in the presence of KOH pellets to afford fully resin-bound α -GlcN derivative **18a**, with a loading ratio of 0.38 mmol/g. IR (KBr): 2925, 2107, 1749, 1644, 1491, 1447, 1223, 1074 cm^{-1} . To determine the loading ratio, 50 mg of **18a** was treated with 30% HFIP in CH_2Cl_2 (3 mL) at rt for 1 h. The combined washings were concentrated under reduced pressure for recovery of free α -GlcN derivative **8a**.

2'-Aminoethyl 3-O-acetyl-2-azido-4-O-benzyl-6-O-(tert-butyldiphenylsilyl)-2-deoxy- β -D-glucopyranoside, bound to trityl-PS resin (18b)

Cl-Trityl-PS resin beads (386 mg, 0.55 mmol) were suspended in dry pyridine (3 mL) for 5 min, followed by addition of 2'-aminoethyl β -GlcN glycoside **8b** (170 mg, 0.28 mmol) and DMAP (13 mg, 0.11 mmol). The mixture was shaken for 2 days at 60 °C, then cooled to rt. Anhydrous MeOH (0.5 mL) was added and the mixture was shaken at rt for 1 h. The resin was filtered, washed with 5% $i\text{Pr}_2\text{NEt}$ in 8:1 CH_2Cl_2 :MeOH (2×4 mL), then alternatively with DMF (2×4 mL) and CH_2Cl_2 (2×4 mL), then finally with additional CH_2Cl_2 (3×4 mL). The resin was dried under reduced pressure in the presence of KOH pellets to afford fully resin-bound β -GlcN derivative **18b**, with a loading ratio of 0.27 mmol/g. To determine the loading ratio, 50 mg of **18b** was treated with 30% HFIP in CH_2Cl_2 (3 mL) under standard cleavage conditions. The combined washings were then concentrated for recovery of free β -GlcN derivative **8b**.

2'-Aminoethyl 4-O-[3-O-acetyl-2-azido-4-O-benzyl-2-deoxy-6-O-(tert-butyldiphenyl-silyl)- β -D-glucopyranosyl]-2,3,6-tri-O-benzyl- β -D-glucopyranoside, bound to trityl-PS resin (19)

Cl-Trityl-PS resin beads (294 mg, 0.44 mmol) were suspended in dry pyridine (3 mL) for 5 min, followed by addition of GlcN($\beta 1 \rightarrow 4$)-Glc β derivative **12** (232 mg, 0.22 mmol) and DMAP (10.8 mg, 0.088 mmol). The mixture was shaken for 2 days at 60 °C, then cooled to rt. Anhydrous MeOH (0.3 mL) was added and the mixture was shaken at rt for 1 h. The resin was filtered, washed with 5% $i\text{Pr}_2\text{NEt}$ in 8:1 CH_2Cl_2 :MeOH (2×4 mL), then alternatively with DMF (2×4 mL) and CH_2Cl_2 (2×4 mL), then finally with additional CH_2Cl_2 (3×4 mL). The resin was dried under reduced pressure in the presence of KOH pellets to afford fully resin-bound GlcN($\beta 1 \rightarrow 4$)-Glc β derivative **19**, with a ratio of 0.17–0.18 mmol/g. To determine the loading ratio, 50 mg of **19** was treated with 30% HFIP in CH_2Cl_2 (3 mL) under standard cleavage conditions. The combined washings were concentrated under reduced pressure for recovery of free GlcN($\beta 1 \rightarrow 4$)-Glc β derivative **12**.

2'-Aminoethyl 4-O-[3-O-acetyl-2-azido-4-O-benzyl-2-deoxy-6-O-(*tert*-butyldiphenyl-silyl)- α -D-glucopyranosyl]-2,3,6-tri-O-benzyl- β -D-glucopyranoside, bound to trityl-PS resin (20**)**

Cl-Trityl-PS resin beads (267 mg, 0.40 mmol) were suspended in dry pyridine (3 mL) for 5 min followed by addition of GlcN(α 1 $\rightarrow$ 4)-Glc β derivative **17** (140 mg, 0.13 mmol) and DMAP (6.5 mg, 0.053 mmol). The mixture was shaken for 2 days at 60 °C, then cooled to rt. Anhydrous MeOH (0.3 mL) was added and the mixture was shaken at rt for 1 h. The resin was filtered, washed with 5% *i*Pr₂NEt in 8:1 CH₂Cl₂:MeOH (2 $\times$ 4 mL), then alternatively with DMF (2 $\times$ 4 mL) and CH₂Cl₂ (2 $\times$ 4 mL), then finally with additional CH₂Cl₂ (3 $\times$ 4 mL). The resin was dried under reduced pressure in the presence of KOH pellets to afford resin-bound GlcN(α 1 $\rightarrow$ 4)-Glc β derivative **20**, with a ratio of 0.17–0.18 mmol/g. To determine the loading ratio, 50 mg of **20** was treated with 30% HFIP in CH₂Cl₂ (3 mL) under standard cleavage conditions. The combined washings were concentrated under reduced pressure for recovery of free GlcN(α 1 $\rightarrow$ 4)-Glc β derivative **17**.

2'-Aminoethyl 2-acetamido-4-O-benzyl-2-deoxy- α -D-glucopyranoside (1a**)**

Op. 1: Resin-bound α -GlcN derivative **18a** (44 mg, 0.0167 mmol sugar) was swollen in CH₂Cl₂ (3 mL) for 5 min, then treated with Bu₃P (25 μ L, 0.1 mmol). The mixture was shaken for 5 h at rt, filtered, then subjected to standard workup conditions to give the intermediate *N*-ylide. *Op. 2:* The resin was treated with 95:5 THF:H₂O (4 mL), shaken for 1 day at rt, washed with THF (2 $\times$ 3 mL), then subjected to standard workup conditions to give the resin-bound primary amine. *Op. 3:* The resin was swollen in pyridine (3 mL) for 5 min, treated with Ac₂O (1.5 mL) and shaken for 1 day at rt. The resin was filtered, washed with 4:1 DMF:pyridine (2 $\times$ 3 mL), then subjected to standard workup conditions to give the *N*-acetylated intermediate. *Op. 4:* The resin was swollen in THF (0.3 mL) for 5 min, treated with 1 M TBAF in THF (2.7 mL), and shaken for 1 day at rt. The resin was filtered, washed with THF (2 $\times$ 3 mL), then subjected to standard workup conditions to give the C6 alcohol. *Op. 5:* The resin was swollen in CH₂Cl₂ (2 mL) for 5 min, treated with 1 M NaOMe in MeOH (50 μ L) and shaken for 5 h at rt. The resin was filtered, washed with 1:1 MeOH:CH₂Cl₂ (2 $\times$ 3 mL), then subjected to standard workup conditions to give the fully deprotected resin-bound α -GlcN. *Op. 6:* The resin was treated with 30% HFIP in CH₂Cl₂ under standard cleavage conditions. Purification by reverse-phase HPLC yielded 2'-aminoethyl α -GlcN **1a** as an amorphous white solid (5.1 mg, 87% over 6 operations). ¹H NMR (400 MHz, CD₃OD): δ 7.23–7.44 (m, 5H), 4.95 (d, 1H, *J* = 10.8 Hz), 4.75 (d, 1H, *J* = 3.6 Hz), 4.65 (d, 1H, *J* = 11.0 Hz), 3.99 (dd, 1H, *J* = 3.5, 10.5 Hz), 3.84 (dd, 1H, *J* = 8.5, 10.4 Hz), 3.77 (dd, 1H, *J* = 2.0, 9.8 Hz), 3.71 (dd, 1H, *J* = 5.0, 19.2 Hz), 3.57–3.69 (m, 2H), 3.43 (t, 1H, *J* = 9.2 Hz), 3.33–3.42 (m, 2H), 2.76–2.87 (m, 2H), 1.99 (s, 3H); ¹³C NMR (100 MHz, CD₃OD): δ 173.69, 139.94, 129.28, 129.07, 128.68, 98.86, 80.02, 76.05, 73.53, 73.05, 70.27, 62.32, 55.57, 42.05, 22.57; IR (NaCl): 3292, 2920, 1656, 1576, 1315, 1068, 1029 cm⁻¹; [α]_D²⁰ = +58.1 (*c* 0.31, MeOH); ESI-MS: *m/z* calcd for C₁₇H₂₆N₂O₆Na [M+Na]⁺: 377.1689; found: 377.1697.

2'-Aminoethyl 2-acetamido-4-O-benzyl-2-deoxy-6-O-sulfonato- α -D-glucopyranoside, sodium salt (1b**)**

Op. 1: Resin-bound α -GlcN derivative **18a** (44 mg, 0.0167 mmol sugar) was swollen in CH₂Cl₂ (3 mL) for 5 min, then treated with Bu₃P (25 μ L, 0.1 mmol). The mixture was shaken for 5 h at rt, filtered, then subjected to standard workup conditions to give the intermediate *N*-ylide. *Op. 2:* The resin was treated with 95:5 THF:H₂O (4 mL), shaken for 1 day at rt, washed with THF (2 $\times$ 3 mL), then subjected to standard workup conditions to give the resin-bound primary amine. *Op. 3:* The resin was swollen in pyridine (3 mL) for 5 min, treated with Ac₂O (1.5 mL) and shaken for 1 day at rt. The resin was filtered, washed with 4:1 DMF:pyridine (2 $\times$ 3 mL), then subjected to standard workup conditions to give the *N*-

acetylated intermediate. *Op. 4:* The resin was swollen in THF (0.3 mL) for 5 min, treated with 1 M TBAF in THF adjusted to pH 7 with AcOH (2.7 mL), and shaken for 1 day at rt. The resin was filtered, washed with 5:1 THF:pyridine (2 × 3 mL), then subjected to standard workup conditions to give the C6 alcohol. *Op. 5:* The resin was swollen in dry DMF (3 mL) for 5 min, then treated with SO₃•Py (27 mg, 0.17 mmol) and shaken for 10 h at rt. The resin was filtered, washed with 1:2 MeOH:pyridine (2 × 3 mL), then subjected to standard workup conditions to give the resin-bound 6-*O*-sulfate. *Op. 6:* The resin was swollen in CH₂Cl₂ (2 mL) for 5 min, treated with 1 M NaOMe in MeOH (50 μL) and shaken for 5 h at rt. The resin was filtered, washed with 1:1 MeOH:CH₂Cl₂ (2 × 3 mL), then subjected to standard workup conditions to give the fully deprotected resin-bound 6-*O*-sulfate. *Op. 7:* The resin was treated with 30% HFIP in CH₂Cl₂ under standard cleavage conditions. *Op. 8:* The crude was passed through an ion-exchange column (Dowex Marathon MSC, Na form) and purified by reverse-phase HPLC to yield 2'-aminoethyl α-GlcN 6-*O*-sulfate **1b** (sodium salt) as an amorphous white solid (5.5 mg, 76% over 8 operations). ¹H NMR (400 MHz, CD₃OD): δ 7.41 (d, 2H, *J* = 7.1 Hz), 7.23–7.34 (m, 3H), 4.92 (d, 1H, *J* = 10.8 Hz), 4.78 (d, 1H, *J* = 3.7 Hz), 4.72 (d, 1H, *J* = 10.5 Hz), 4.34 (dd, 1H, *J* = 1.8, 11.0 Hz), 4.12 (dd, 1H, *J* = 6.2, 10.9 Hz), 4.03 (dd, 1H, *J* = 3.8, 10.8 Hz), 3.83–3.97 (m, 2H), 3.81 (dd, 1H, *J* = 9.0, 10.7 Hz), 3.52 (m, 1H), 3.41 (t, 1H, *J* = 9.4 Hz), 3.03 (t, 2H, *J* = 4.8 Hz), 2.01 (s, 3H); ¹³C NMR (100 MHz, CD₃OD): δ 173.63, 139.77, 129.47, 129.24, 128.67, 99.90, 79.87, 76.10, 73.59, 71.00, 68.88, 68.00, 55.40, 41.60, 22.63; IR (NaCl): 3449, 2925, 1659, 1543, 1223, 1222, 1068, 1013 cm⁻¹; [α]_D²⁰ = +64.7 (*c* 0.41, MeOH); ESI-MS: *m/z* calcd for C₁₇H₂₅N₂O₉S [M]⁻: 433.1281; found: 433.1279.

2'-Aminoethyl 2-acetamido-4-*O*-benzyl-2-deoxy-3-*O*-sulfonato-α-D-glucopyranoside, sodium salt (**1c**)

Op. 1: Resin-bound α-GlcN derivative **18a** (44 mg, 0.0167 mmol sugar) was swollen in CH₂Cl₂ (3 mL) for 5 min, then treated with Bu₃P (25 μL, 0.1 mmol). The mixture was shaken for 5 h at rt, filtered, then subjected to standard workup conditions to give the intermediate *N*-ylide. *Op. 2:* The resin was treated with 95:5 THF:H₂O (4 mL), shaken for 1 day at rt, washed with THF (2 × 3 mL), then subjected to standard workup conditions to give the resin-bound primary amine. *Op. 3:* The resin was swollen in pyridine (3 mL) for 5 min, treated with Ac₂O (1.5 mL) and shaken for 1 day at rt. The resin was filtered, washed with 4:1 DMF:pyridine (2 × 3 mL), then subjected to standard workup conditions to give the *N*-acetylated intermediate. *Op. 4:* The resin was swollen in CH₂Cl₂ (2 mL) for 5 min, treated with 1 M NaOMe in MeOH (50 μL) and shaken for 5 h at rt. The resin was filtered, washed with 1:1 MeOH:CH₂Cl₂ (2 × 3 mL), then subjected to standard workup conditions to give to give the C3 alcohol. *Op. 5:* The resin was swollen in dry DMF (3 mL) for 5 min, then treated with SO₃•Py (27 mg, 0.17 mmol) and shaken for 10 h at rt. The resin was filtered, washed with 1:2 MeOH:pyridine (2 × 3 mL), then subjected to standard workup conditions to give the resin-bound 3-*O*-sulfate. *Op. 6:* The resin was swollen in THF (0.3 mL) for 5 min, treated with 1 M TBAF in THF (2.7 mL), and shaken for 1 day at rt. The resin was filtered, washed with THF (2 × 3 mL), then subjected to standard workup conditions to give the fully deprotected resin-bound 3-*O*-sulfate. *Op. 7:* The resin was treated with 30% HFIP in CH₂Cl₂ under standard cleavage conditions. *Op. 8:* The crude was passed through an ion-exchange column (Dowex Marathon MSC, Na form) and purified by reverse-phase HPLC to yield 2'-aminoethyl α-GlcN 3-*O*-sulfate **1c** (sodium salt) as an amorphous white solid (4.6 mg, 64% over 8 operations). ¹H NMR (400 MHz, CD₃OD): δ 7.43 (d, 2H, *J* = 6.9 Hz), 7.22–7.31 (m, 3H), 5.17 (d, 1H, *J* = 10.3 Hz), 4.98 (d, 1H, *J* = 3.3 Hz), 4.72 (dd, 1H, *J* = 8.6, 11.0 Hz), 4.52 (d, 1H, *J* = 10.3 Hz), 3.97 (dd, 1H, *J* = 3.3, 11.0 Hz), 3.73–3.86 (m, 2H), 3.61–3.70 (m, 2H), 3.55 (t, 1H, *J* = 8.9 Hz), 3.49 (m, 1H), 2.99 (t, 2H, *J* = 4.7 Hz), 1.98 (s, 3H); ¹³C NMR (100 MHz, CD₃OD): δ 173.72, 139.73, 129.99, 129.15, 128.69, 98.63, 79.10, 77.84, 76.09, 73.61, 67.69, 62.17, 55.09, 41.27, 22.90; IR (NaCl): 3359, 2925, 1664,

1651, 1225, 1122, 1052 cm^{-1} ; $[\alpha]_{\text{D}}^{20} = +59.3$ (c 0.24, MeOH); ESI-MS: m/z calcd for $\text{C}_{17}\text{H}_{25}\text{N}_2\text{O}_9\text{S}$ $[\text{M}]^-$: 433.1281; found: 433.1284.

2'-Aminoethyl 2-amino-4-O-benzyl-2-deoxy-2-N-sulfonato- α -D-glucopyranoside, sodium salt (1d)

Op. 1: Resin-bound α -GlcN derivative **18a** (120 mg, 0.0456 mmol sugar) was swollen in CH_2Cl_2 (3 mL) for 5 min, then treated with Bu_3P (68 μL , 0.274 mmol). The mixture was shaken for 5 h at rt, filtered, then subjected to standard workup conditions to give the intermediate *N*-ylide. *Op. 2:* The resin was treated with 95:5 THF:H₂O (3 mL), shaken for 1 day at rt, washed with THF (2×3 mL), then subjected to standard workup conditions to give the resin-bound primary amine. *Op. 3:* The resin was swollen in dry pyridine (3 mL) for 5 min, then treated with Et_3N (0.6 mL), $\text{SO}_3 \cdot \text{Py}$ (73 mg, 0.46 mmol) and shaken for 1 day at rt. The resin was filtered, washed with 1:2 MeOH:pyridine (2×3 mL), then subjected to standard workup conditions to give the resin-bound *N*-sulfate. *Op. 4:* The resin was swollen in THF (0.3 mL) for 5 min, treated with 1 M TBAF in THF (2.7 mL), and shaken for 1 day at rt. The resin was filtered, washed with THF (2×3 mL), then subjected to standard workup conditions to give the C6 alcohol. *Op. 5:* The resin was swollen in CH_2Cl_2 (3 mL) for 5 min, treated with 1 M NaOMe in MeOH (140 μL) and shaken for 5 h at rt. The resin was filtered, washed with 1:1 MeOH: CH_2Cl_2 (2×3 mL), then subjected to standard workup conditions to give the fully deprotected resin-bound *N*-sulfate. *Op. 6:* The resin was treated with 30% HFIP in CH_2Cl_2 under standard cleavage conditions. *Op. 7:* The crude was passed through an ion-exchange column (Dowex Marathon MSC, Na form) and purified by reversed-phase HPLC to yield 2'-aminoethyl α -GlcN 2-*N*-sulfate **1d** (sodium salt) as an amorphous white solid (13 mg, 69% over 7 operations). ^1H NMR (400 MHz, CD_3OD): δ 7.23–7.40 (m, 5H), 5.19 (d, 1H, $J = 3.8$ Hz), 4.97 (d, 1H, $J = 10.9$ Hz), 4.63 (d, 1H, $J = 10.9$ Hz), 3.89 (ddd, 1H, $J = 3.5, 5.5, 11.6$ Hz), 3.77 (dd, 1H, $J = 1.3, 9.6$ Hz), 3.74 (dd, 1H, $J = 5.0, 7.0$ Hz), 3.62 (m, 3H), 3.42 (t, 1H, $J = 9.3$ Hz), 3.17 (ddd, 1H, $J = 3.0, 5.5, 13.5$ Hz), 3.06 (ddd, 1H, $J = 3.1, 7.7, 13.2$ Hz); ^{13}C NMR (100 MHz, CD_3OD): δ 129.25, 129.15, 128.63, 98.92, 79.76, 75.82, 74.14, 72.77, 68.10, 62.48, 59.96, 41.24; IR (NaCl): 3390, 2920, 1207, 1309 cm^{-1} ; $[\alpha]_{\text{D}}^{20} = +89.3$ (c 0.41, MeOH); ESI-MS: m/z calcd for $\text{C}_{15}\text{H}_{23}\text{N}_2\text{O}_8\text{S}$ $[\text{M}-\text{H}]^-$: 391.1175; found: 391.1180.

2'-Aminoethyl 2-acetamido-4-O-benzyl-2-deoxy-3,6-di-O-sulfonato- α -D-glucopyranoside, disodium salt (1e)

Op. 1: Resin-bound α -GlcN derivative **18a** (120 mg, 0.0456 mmol sugar) was swollen in CH_2Cl_2 (3 mL) for 5 min, then treated with Bu_3P (67 μL , 0.27 mmol). The mixture was shaken for 5 h at rt, filtered, then subjected to standard workup conditions to give the intermediate *N*-ylide. *Op. 2:* The resin was treated with 95:5 THF:H₂O (4 mL), shaken for 1 day at rt, washed with THF (2×3 mL), then subjected to standard workup conditions to give the resin-bound primary amine. *Op. 3:* The resin was swollen in pyridine (3 mL) for 5 min, treated with Ac_2O (1.5 mL) and shaken for 1 day at rt. The resin was filtered, washed with 4:1 DMF:pyridine (2×3 mL), then subjected to standard workup conditions to give the *N*-acetylated intermediate. *Op. 4:* The resin was swollen in THF (0.3 mL) for 5 min, treated with 1 M TBAF in THF (2.7 mL), and shaken for 1 day at rt. The resin was filtered, washed with THF (2×3 mL), then subjected to standard workup conditions to give the C6 alcohol. *Op. 5:* The resin was swollen in CH_2Cl_2 (2 mL) for 5 min, treated with 1 M NaOMe in MeOH (137 μL) and shaken for 5 h at rt. The resin was filtered, washed with 1:1 MeOH: CH_2Cl_2 (2×3 mL), then subjected to standard workup conditions to give the corresponding 3,6-diol. *Op. 6:* The resin was swollen in dry pyridine (3 mL) for 5 min, then treated with Et_3N (0.6 mL), $\text{SO}_3 \cdot \text{Py}$ (362 mg, 2.28 mmol) and shaken for 2 day at 55 $^\circ\text{C}$. The resin was filtered, washed with 1:2 MeOH:pyridine (2×3 mL), then subjected to standard workup conditions to give the resin-bound 3,6-di-*O*-sulfate. *Op. 7:* The resin was

treated with 30% HFIP in CH_2Cl_2 under standard cleavage conditions. *Op. 8:* The crude was passed through an ion-exchange column (Dowex Marathon MSC, Na form) and purified by reverse-phase HPLC to yield 2'-aminoethyl α -GlcN 3,6-di-*O*-sulfate **1e** (disodium salt) as an amorphous white solid (17.3 mg, 68% over 8 operations). ^1H NMR (400 MHz, CD_3OD): δ 7.50 (dd, 2H, $J = 1.4, 8.3$ Hz), 7.22–7.33 (m, 3H), 5.13 (d, 1H, $J = 10.1$ Hz), 5.01 (d, 1H, $J = 3.3$ Hz), 4.71 (dd, 1H, $J = 8.6, 10.8$ Hz), 4.60 (d, 1H, $J = 10.1$ Hz), 4.34 (dd, 1H, $J = 2.0, 11.1$ Hz), 4.08 (dd, 1H, $J = 6.1, 10.8$ Hz), 3.89–4.03 (m, 3H), 3.57–3.62 (m, 1H), 3.54 (t, 1H, $J = 9.1$ Hz), 3.17 (t, 2H, $J = 5.0$ Hz), 1.98 (s, 3H); ^{13}C NMR (100 MHz, CD_3OD): δ 173.64, 139.47, 130.34, 129.13, 128.69, 98.59, 78.82, 77.81, 75.95, 71.48, 68.21, 65.27, 55.01, 40.62, 22.91; IR (NaCl): 2925, 1659, 1225, 1052, 1024 cm^{-1} ; $[\alpha]_{\text{D}}^{20} = +87.8$ (c 0.13, MeOH); ESI-MS: m/z calcd for $\text{C}_{17}\text{H}_{25}\text{N}_2\text{O}_{12}\text{S}_2$ $[\text{M}+\text{H}]^+$: 513.0849; found: 513.0853.

2'-Aminoethyl 2-amino-4-*O*-benzyl-2-deoxy-2,6-di-*N,O*-sulfonato- α -D-glucopyranoside, disodium salt (1f**)**

Op. 1: Resin-bound α -GlcN derivative **18a** (120 mg, 0.0456 mmol sugar) was swollen in CH_2Cl_2 (3 mL) for 5 min, then treated with 1 M TBAF in THF (2.7 mL), and shaken for 1 day at rt. The resin was filtered, washed with THF (2×3 mL), then subjected to standard workup conditions to give the C6 alcohol. *Op. 2:* The resin was swollen in CH_2Cl_2 (3 mL) for 5 min, then treated with Bu_3P (67 μL , 0.27 mmol). The mixture was shaken for 5 h at rt, filtered, then subjected to standard workup conditions to give the intermediate *N*-ylide. *Op. 3:* The resin was treated with 95:5 THF:H₂O (4 mL), shaken for 1 day at rt, washed with THF (2×3 mL), then subjected to standard workup conditions to give the resin-bound 2,6-amino alcohol. *Op. 4:* The resin was swollen in dry DMF (3 mL) for 5 min, then treated with $\text{SO}_3 \cdot \text{Py}$ (73 mg, 0.46 mmol) and shaken for 10 h at rt. The resin was filtered, washed with 1:2 MeOH:pyridine (2×3 mL), then subjected to standard workup conditions to give the resin-bound 6-*O*-sulfate. *Op. 5:* The resin was swollen in dry pyridine (3 mL) for 5 min, then treated with Et_3N (0.6 mL), $\text{SO}_3 \cdot \text{Py}$ (73 mg, 0.46 mmol) and shaken for 1 day at rt. The resin was filtered, washed with 1:2 MeOH:pyridine (2×3 mL), then subjected to standard workup conditions to give the resin-bound 2,6-di-*N,O*-sulfate. *Op. 6:* The resin was swollen in CH_2Cl_2 (3 mL) for 5 min, treated with 1 M NaOMe in MeOH (137 μL) and shaken for 5 h at rt. The resin was filtered, washed with 1:1 MeOH: CH_2Cl_2 (2×3 mL), then subjected to standard workup conditions to give the fully deprotected resin-bound 2,6-di-*N,O*-sulfate. *Op. 7:* The resin was treated with 30% HFIP in CH_2Cl_2 under standard cleavage conditions. *Op. 8:* The crude was passed through an ion-exchange column (Dowex Marathon MSC, Na form) and purified by reverse-phase HPLC to yield 2'-aminoethyl α -GlcN 2,6-di-*N,O*-sulfate **1f** (disodium salt) as an amorphous white solid (10.3 mg, 44% over 8 operations). ^1H NMR (400 MHz, CD_3OD): δ 7.40 (d, 2H, $J = 7.2$ Hz), 7.20–7.32 (m, 3H), 5.15 (d, 1H, $J = 3.8$ Hz), 4.90 (d, 1H, $J = 10.6$ Hz), 4.71 (d, 1H, $J = 10.6$ Hz), 4.34 (dd, 1H, $J = 2.0, 10.8$ Hz), 4.07 (dd, 1H, $J = 6.4, 10.8$ Hz), 3.85–4.00 (m, 3H), 3.71 (dd, 1H, $J = 8.9, 10.2$ Hz), 3.61 (ddd, 1H, $J = 3.2, 7.6, 11.2$ Hz), 3.40 (m, 1H), 3.01–3.17 (m, 2H); ESI-MS: m/z calcd for $\text{C}_{15}\text{H}_{22}\text{N}_2\text{Na}_2\text{O}_{11}\text{S}_2$ $[\text{M}+\text{H}+2 \text{Na}]^+$: 539.0358; found: 539.0354.

2'-Aminoethyl 2-amino-4-*O*-benzyl-2-deoxy-2,3-di-*N,O*-sulfonato- α -D-glucopyranoside, disodium salt (1g**)**

Op. 1: Resin-bound α -GlcN derivative **18a** (120 mg, 0.0456 mmol sugar) was swollen in CH_2Cl_2 (3 mL) for 5 min, treated with 1 M NaOMe in MeOH (137 μL) and shaken for 5 h at rt. The resin was filtered, washed with 1:1 MeOH: CH_2Cl_2 (2×3 mL), then subjected to standard workup conditions to give the corresponding C3 alcohol. *Op. 2:* The resin was swollen in CH_2Cl_2 (3 mL) for 5 min, then treated with Bu_3P (67 μL , 0.27 mmol). The mixture was shaken for 5 h at rt, filtered, then subjected to standard workup conditions to give the intermediate *N*-ylide. *Op. 3:* The resin was treated with 95:5 THF:H₂O (4 mL), shaken for 1 day at rt, washed with THF (2×3 mL), then subjected to standard workup

conditions to give the resin-bound 2,3-amino alcohol. *Op. 4:* The resin was swollen in dry pyridine (3 mL) for 5 min, then treated with Et₃N (0.6 mL), SO₃•Py (362 mg, 2.28 mmol) and shaken for 2 day at 55 °C. The resin was filtered, washed with 1:2 MeOH:pyridine (2 × 3 mL), then subjected to standard workup conditions to give the resin-bound 2,3-di-*N,O*-sulfate. *Op. 5:* The resin was swollen in DMF (2 mL) for 5 min, treated with 1 M TBAF in THF (2 mL), and shaken for 1 day at rt. The resin was filtered, washed with THF (2 × 3 mL), then subjected to standard workup conditions to give the fully deprotected resin-bound 2,3-di-*N,O*-sulfate. *Op. 6:* The resin was treated with 30% HFIP in CH₂Cl₂ under standard cleavage conditions. *Op. 7:* The crude was passed through an ion-exchange column (Dowex Marathon MSC, Na form) and purified by reverse-phase HPLC to yield 2'-aminoethyl α-GlcN 2,3-di-*N,O*-sulfate **1g** (disodium salt) as an amorphous white solid (15.9 mg, 68% over 7 operations). ¹H NMR (400 MHz, CD₃OD): δ 7.43 (d, 2H, *J* = 6.8 Hz), 7.23–7.35 (m, 3H), 5.26 (d, 1H, *J* = 3.4 Hz), 5.15 (d, 1H, *J* = 10.4 Hz), 4.64 (dd, 1H, *J* = 8.6, 10.7 Hz), 4.53 (d, 1H, *J* = 10.5 Hz), 3.89 (m, 1H), 3.73 (d, 1H, *J* = 9.7 Hz), 3.52–3.68 (m, 4H), 3.46 (dd, 1H, *J* = 3.4, 10.7 Hz), 2.98–3.10 (m, 2H); ¹³C NMR (100 MHz, CD₃OD): δ 138.27, 128.46, 127.63, 127.14, 97.45, 78.17, 76.52, 74.56, 71.73, 65.22, 60.74, 57.50, 39.21; IR (NaCl): 3389, 2919, 1207, 1039 cm⁻¹; [α]_D²⁰ = +65.9 (*c* 0.71, MeOH); ESI-MS: *m/z* calcd for C₁₅H₂₃N₂O₁₁S₂ [M+H]⁺: 471.0743; found: 471.0741.

2'-Aminoethyl 2-amino-4-*O*-benzyl-2-deoxy-2,3,6-tri-*N,O*-sulfonato-α-*D*-glucopyranoside, trisodium salt (**1h**)

Op. 1: Resin-bound α-GlcN derivative **18a** (120 mg, 0.0456 mmol sugar) was swollen in CH₂Cl₂ (3 mL) for 5 min, then treated with 1 M TBAF in THF (2.7 mL), and shaken for 1 day at rt. The resin was filtered, washed with THF (2 × 3 mL), then subjected to standard workup conditions to give the C6 alcohol. *Op. 2:* The resin was swollen in CH₂Cl₂ (3 mL) for 5 min, treated with 1 M NaOMe in MeOH (137 μL) and shaken for 5 h at rt. The resin was filtered, washed with 1:1 MeOH:CH₂Cl₂ (2 × 3 mL), then subjected to standard workup conditions to give the 3,6-diol. *Op. 3:* The resin was swollen in CH₂Cl₂ (3 mL) for 5 min, then treated with Bu₃P (67 μL, 0.27 mmol). The mixture was shaken for 5 h at rt, filtered, then subjected to standard workup conditions to give the intermediate *N*-ylide. *Op. 4:* The resin was treated with 95:5 THF:H₂O (4 mL), shaken for 1 day at rt, washed with THF (2 × 3 mL), then subjected to standard workup conditions to give the resin-bound fully deprotected α-GlcN. *Op. 5:* The resin was swollen in dry pyridine (3 mL) for 5 min, then treated with Et₃N (0.6 mL), SO₃•Py (362 mg, 2.28 mmol) and shaken for 2 day at 55 °C. The resin was filtered, washed with 1:2 MeOH:pyridine (2 × 3 mL), then subjected to standard workup conditions to give the resin-bound 2-*N*,3-*O*,6-*O*-trisulfate. *Op. 6:* The resin was treated with 30% HFIP in CH₂Cl₂ under standard cleavage conditions. *Op. 7:* The crude was passed through an ion-exchange column (Dowex Marathon MSC, Na form) and purified by reverse-phase HPLC to yield 2'-aminoethyl α-GlcN 2,3,6-trisulfate **1h** (trisodium salt) as an amorphous white solid (18.1 mg, 64% over 7 operations). ¹H NMR (400 MHz, CD₃OD): δ 7.52 (dd, 2H, *J* = 1.4, 8.3 Hz), 7.17–7.36 (m, 3H), 5.24 (d, 1H, *J* = 3.1 Hz), 5.13 (d, 1H, *J* = 9.9 Hz), 4.64 (t, 1H, *J* = 8.9 Hz), 4.63 (d, 1H, *J* = 10.0 Hz), 4.26 (dd, 1H, *J* = 2.0, 10.8 Hz), 4.16 (dd, 1H, *J* = 5.1, 10.4 Hz), 3.86–4.09 (m, 2H), 3.61–3.75 (m, 2H), 3.48 (dd, 1H, *J* = 3.2, 10.5 Hz), 3.14 (ddd, 1H, *J* = 3.1, 6.4, 13.4 Hz), 3.02 (ddd, 1H, *J* = 3.5, 7.3, 13.2 Hz); ¹³C NMR (100 MHz, CD₃OD): δ 139.60, 130.42, 129.05, 128.59, 98.93, 79.56, 77.84, 76.00, 71.10, 67.85, 66.49, 58.97, 40.65; IR (NaCl): 2925, 1225, 1047 cm⁻¹; [α]_D²⁰ = +50.3 (*c* 0.25, MeOH); ESI-MS: *m/z* calcd for C₁₅H₂₁N₂O₁₄S₃Na₂ [M+2 Na]⁺: 594.9950; found: 594.9959.

2'-Aminoethyl 2-acetamido-4-O-benzyl-2-deoxy-6-O-sulfonato- β -D-glucopyranoside, sodium salt (2b)

Op. 1: Resin-bound β -GlcN derivative **18b** (180 mg, 0.0481 mmol sugar) was swollen in CH_2Cl_2 (3 mL) for 5 min, then treated with Bu_3P (72 μL , 0.29 mmol). The mixture was shaken for 5 h at rt, filtered, then subjected to standard workup conditions to give the intermediate *N*-ylide. *Op. 2:* The resin was treated with 95:5 THF:H₂O (4 mL), shaken for 1 day at rt, washed with THF (2 $\times$ 3 mL), then subjected to standard workup conditions to give the resin-bound primary amine. *Op. 3:* The resin was swollen in pyridine (3 mL) for 5 min, treated with Ac_2O (1.5 mL) and shaken for 1 day at rt. The resin was filtered, washed with 4:1 DMF:pyridine (2 $\times$ 3 mL), then subjected to standard workup conditions to give the *N*-acetylated intermediate. *Op. 4:* The resin was swollen in THF (0.3 mL) for 5 min, treated with 1 M TBAF in THF adjusted to pH 7 with AcOH (2.7 mL), and shaken for 1 day at rt. The resin was filtered, washed with 5:1 THF:pyridine (2 $\times$ 3 mL), then subjected to standard workup conditions to give the C6 alcohol. *Op. 5:* The resin was swollen in dry DMF (3 mL) for 5 min, then treated with $\text{SO}_3\cdot\text{Py}$ (115 mg, 0.72 mmol) and shaken for 10 h at rt. The resin was filtered, washed with 1:2 MeOH:pyridine (2 $\times$ 3 mL), then subjected to standard workup conditions to give the resin-bound 6-*O*-sulfate. *Op. 6:* The resin was swollen in CH_2Cl_2 (2 mL) for 5 min, treated with 1 M NaOMe in MeOH (144 μL) and shaken for 5 h at rt. The resin was filtered, washed with 1:1 MeOH: CH_2Cl_2 (2 $\times$ 3 mL), then subjected to standard workup conditions to give the fully deprotected resin-bound 6-*O*-sulfate. *Op. 7:* The resin was treated with 30% HFIP in CH_2Cl_2 under standard cleavage conditions. *Op. 8:* The crude was passed through an ion-exchange column (Dowex Marathon MSC, Na form) and purified by reverse-phase HPLC to yield 2'-aminoethyl β -GlcN 6-*O*-sulfate **2b** (sodium salt) as an amorphous white solid (15.8 mg, 72% over 8 operations). ^1H NMR (500 MHz, CD_3OD): δ 7.36–7.46 (m, 2H), 7.27–7.36 (m, 2H), 7.24 (m, 1H), 4.91 (d, 1H, J = 10.7 Hz), 4.69 (d, 1H, J = 10.7 Hz), 4.40 (d, 1H, J = 8.4 Hz), 4.30 (dd, 1H, J = 2.0, 11.1 Hz), 4.15 (dd, 1H, J = 5.5, 11.0 Hz), 3.86–3.96 (m, 2H), 3.75 (dd, 1H, J = 8.4, 10.3 Hz), 3.62 (dd, 1H, J = 8.7, 10.3 Hz), 3.56 (m, 1H), 3.41 (t, 1H, J = 8.7 Hz), 3.08 (m, 1H), 2.97 (m, 1H), 1.98 (s, 3H); ^{13}C NMR (125 MHz, CD_3OD): δ 172.60, 138.17, 127.88, 127.77, 127.22, 101.15, 77.89, 74.61, 74.42, 73.36, 66.38, 66.27, 55.74, 39.70, 21.46; $[\alpha]_{\text{D}}^{20}$ = -6.93 (c 1.05, MeOH); ESI-MS: m/z calcd for $\text{C}_{17}\text{H}_{25}\text{N}_2\text{O}_9\text{S} [\text{M}]^-$: 433.1281; found: 433.1279.

2'-Aminoethyl 2-amino-4-O-benzyl-2-deoxy-2,6-di-*N,O*-sulfonato- β -D-glucopyranoside, disodium salt (2f)

Op. 1: Resin-bound β -GlcN derivative **18b** (180 mg, 0.0481 mmol sugar) was swollen in CH_2Cl_2 (3 mL) for 5 min, then treated with 1 M TBAF in THF (2.7 mL), and shaken for 1 day at rt. The resin was filtered, washed with THF (2 $\times$ 3 mL), then subjected to standard workup conditions to give the C6 alcohol. *Op. 2:* The resin was swollen in CH_2Cl_2 (3 mL) for 5 min, then treated with Bu_3P (72 μL , 0.29 mmol). The mixture was shaken for 5 h at rt, filtered, then subjected to standard workup conditions to give the intermediate *N*-ylide. *Op. 3:* The resin was treated with 95:5 THF:H₂O (4 mL), shaken for 1 day at rt, washed with THF (2 $\times$ 3 mL), then subjected to standard workup conditions to give the resin-bound 2,6-amino alcohol. *Op. 4:* The resin was swollen in dry DMF (3 mL) for 5 min, then treated with $\text{SO}_3\cdot\text{Py}$ (115 mg, 0.72 mmol) and shaken for 10 h at rt. The resin was filtered, washed with 1:2 MeOH:pyridine (2 $\times$ 3 mL), then subjected to standard workup conditions to give the resin-bound 6-*O*-sulfate. *Op. 5:* The resin was swollen in dry pyridine (3 mL) for 5 min, then treated with Et_3N (0.6 mL), $\text{SO}_3\cdot\text{Py}$ (115 mg, 0.72 mmol) and shaken for 1 day at rt. The resin was filtered, washed with 1:2 MeOH:pyridine (2 $\times$ 3 mL), then subjected to standard workup conditions to give the resin-bound 2,6-di-*N,O*-sulfate. *Op. 6:* The resin was swollen in CH_2Cl_2 (3 mL) for 5 min, treated with 1 M NaOMe in MeOH (144 μL) and shaken for 5 h at rt. The resin was filtered, washed with 1:1 MeOH: CH_2Cl_2 (2 $\times$ 3 mL), then subjected to standard workup conditions to give the fully deprotected resin-bound 2,6-di-*N,O*-sulfate.

Op. 7: The resin was treated with 30% HFIP in CH₂Cl₂ under standard cleavage conditions. *Op. 8:* The crude was passed through an ion-exchange column (Dowex Marathon MSC, Na form) and purified by reverse-phase HPLC to yield 2'-aminoethyl β-GlcN 2,6-di-*N,O*-sulfate **2f** (disodium salt) as an amorphous white solid (10.4 mg, 42% over 8 operations). ¹H NMR (400 MHz, CD₃OD): δ 7.51 (dd, 2H, *J* = 1.4, 8.3 Hz), 7.20–7.33 (m, 3H), 5.12 (d, 1H, *J* = 10.2 Hz), 4.61 (d, 1H, *J* = 9.8 Hz), 4.41 (d, 1H, *J* = 7.9 Hz), 4.25 (d, 1H, *J* = 10.4 Hz), 4.18 (m, 1H), 4.10 (td, 1H, *J* = 4.1, 11.2 Hz), 3.70 (m, 1H), 3.61 (d, 2H, *J* = 6.5 Hz), 3.39–3.48 (m, 2H), 3.12 (m, 2H); ¹³C NMR (125 MHz, CD₃OD): δ 138.03, 128.95, 127.54, 127.10, 103.05, 79.54, 75.96, 74.35, 73.18, 66.21, 65.30, 59.31, 39.12; [α]_D²⁰ = +8.57 (*c* 0.93, MeOH); ESI-MS: *m/z* calcd for C₁₅H₂₂N₂NaO₁₁S₂ [M+Na]⁺: 493.0563; found: 493.0565.

2'-Aminoethyl 4-O-[2-acetamido-4-O-benzyl-2-deoxy-6-O-sulfonato-β-D-glucopyranosyl]-2,3,6-tri-O-benzyl-β-D-glucopyranoside, sodium salt (3b)

Op. 1: Resin-bound GlcN(β1→4)Glc derivative **19** (110 mg, 0.0187 mmol sugar) was swollen in CH₂Cl₂ (3 mL) for 5 min, then treated with Bu₃P (28 μL, 0.11 mmol). The mixture was shaken for 5 h at rt, filtered, then subjected to standard workup conditions to give the intermediate *N*-ylide. *Op. 2:* The resin was treated with 95:5 THF:H₂O (4 mL), shaken for 1 day at rt, washed with THF (2 × 3 mL), then subjected to standard workup conditions to give the resin-bound primary amine. *Op. 3:* The resin was swollen in pyridine (3 mL) for 5 min, treated with Ac₂O (1.5 mL) and shaken for 1 day at rt. The resin was filtered, washed with 4:1 DMF:pyridine (2 × 3 mL), then subjected to standard workup conditions to give the *N*-acetylated intermediate. *Op. 4:* The resin was swollen in THF (0.3 mL) for 5 min, treated with 1 M TBAF in THF adjusted to pH 7 with AcOH (2.7 mL), and shaken for 1 day at rt. The resin was filtered, washed with 5:1 THF:pyridine (2 × 3 mL), then subjected to standard workup conditions to give the C6 alcohol. *Op. 5:* The resin was swollen in dry DMF (3 mL) for 5 min, then treated with SO₃•Py (45 mg, 0.28 mmol) and shaken for 10 h at rt. The resin was filtered, washed with 1:2 MeOH:pyridine (2 × 3 mL), then subjected to standard workup conditions to give the resin-bound 6-*O*-sulfate. *Op. 6:* The resin was swollen in CH₂Cl₂ (2 mL) for 5 min, treated with 1 M NaOMe in MeOH (56 μL) and shaken for 5 h at rt. The resin was filtered, washed with 1:1 MeOH:CH₂Cl₂ (2 × 3 mL), then subjected to standard workup conditions to give the fully deprotected resin-bound 6-*O*-sulfate. *Op. 7:* The resin was treated with 30% HFIP in CH₂Cl₂ under standard cleavage conditions. *Op. 8:* The crude was passed through an ion-exchange column (Dowex Marathon MSC, Na form) and purified by reverse-phase HPLC to yield 2'-aminoethyl β-linked GlcN(β1→4)Glc 6-*O*-sulfate **3b** (sodium salt) as an amorphous white solid (11.5 mg, 67% over 8 operations). ¹H NMR (500 MHz, CD₃OD): δ 7.15–7.48 (m, 20H), 5.00 (d, 1H, *J* = 11.4 Hz), 4.84 (d, 1H, *J* = 10.6 Hz), 4.78 (d, 1H, *J* = 11.5 Hz), 4.66–4.75 (m, 3H), 4.54–4.65 (m, 3H), 4.50 (d, 1H, *J* = 7.5 Hz), 4.22 (dd, 1H, *J* = 2.0, 11.6 Hz), 4.04 (dd, 1H, *J* = 5.3, 10.8 Hz), 3.80–3.99 (m, 4H), 3.67–3.76 (m, 3H), 3.57–3.65 (m, 2H), 3.34–3.48 (m, 2H), 2.95–3.12 (m, 2H), 1.89 (s, 3H); ¹³C NMR (125 MHz, CD₃OD): δ 172.13, 138.85, 138.43, 138.28, 137.99, 128.09, 128.00, 127.81, 127.74, 127.71, 127.40, 127.34, 127.14, 127.04, 126.79, 102.85, 99.33, 81.41, 81.22, 77.96, 75.34, 74.42, 74.28, 74.00, 73.84, 73.48, 72.80, 68.84, 66.42, 66.23, 57.21, 39.87, 21.64; [α]_D²⁰ = +19.5 (*c* 0.49, MeOH); ESI-MS: *m/z* calcd for C₄₄H₅₄N₂NaO₁₄S [M+H+Na]⁺: 889.3194; found: 889.3197.

2'-Aminoethyl 4-O-[2-amino-4-O-benzyl-2-deoxy-2,6-di-*N,O*-sulfonato-β-D-glucopyranosyl]-2,3,6-tri-O-benzyl-β-D-glucopyranoside, disodium salt (3f)

Op. 1: Resin-bound GlcN(β1→4)Glc derivative **19** (110 mg, 0.0187 mmol sugar) was swollen in CH₂Cl₂ (3 mL) for 5 min, then treated with 1 M TBAF in THF (2.7 mL), and shaken for 1 day at rt. The resin was filtered, washed with THF (2 × 3 mL), then subjected to standard workup conditions to give the C6 alcohol. *Op. 2:* The resin was swollen in CH₂Cl₂ (3 mL) for 5 min, then treated with Bu₃P (28 μL, 0.11 mmol). The mixture was

shaken for 5 h at rt, filtered, then subjected to standard workup conditions to give the intermediate *N*-ylide. *Op. 3*: The resin was treated with 95:5 THF:H₂O (4 mL), shaken for 1 day at rt, washed with THF (2 × 3 mL), then subjected to standard workup conditions to give the resin-bound 2,6-amino alcohol. *Op. 4*: The resin was swollen in dry DMF (3 mL) for 5 min, then treated with SO₃•Py (41 mg, 0.26 mmol) and shaken for 10 h at rt. The resin was filtered, washed with 1:2 MeOH:pyridine (2 × 3 mL), then subjected to standard workup conditions to give the resin-bound 6-*O*-sulfate. *Op. 5*: The resin was swollen in dry pyridine (3 mL) for 5 min, then treated with Et₃N (0.6 mL), SO₃•Py (41 mg, 0.26 mmol) and shaken for 1 day at rt. The resin was filtered, washed with 1:2 MeOH:pyridine (2 × 3 mL), then subjected to standard workup conditions to give the resin-bound 2,6-di-*N,O*-sulfate. *Op. 6*: The resin was swollen in CH₂Cl₂ (3 mL) for 5 min, treated with 1 M NaOMe in MeOH (56 μL) and shaken for 5 h at rt. The resin was filtered, washed with 1:1 MeOH:CH₂Cl₂ (2 × 3 mL), then subjected to standard workup conditions to give the fully deprotected resin-bound 2,6-di-*N,O*-sulfate. *Op. 7*: The resin was treated with 30% HFIP in CH₂Cl₂ under standard cleavage conditions. *Op. 8*: The crude was passed through an ion-exchange column (Dowex Marathon MSC, Na form) and purified by reverse-phase HPLC to yield 2'-aminoethyl β-linked GlcN(β1→4)Glc 2,6-di-*N,O*-sulfate **3f** (disodium salt) as an amorphous white solid (6.4 mg, 41% over 8 operations). ¹H NMR (500 MHz, CD₃OD): δ 7.49 (d, 2H, *J* = 7.1 Hz), 7.32–7.40 (m, 6H), 7.16–7.31 (m, 12H), 5.03 (d, 1H, *J* = 9.9 Hz), 4.94 (d, 1H, *J* = 11.4 Hz), 4.75 (dd, 2H, *J* = 5.3, 11.3 Hz), 4.51–4.64 (m, 5H), 4.46 (d, 1H, *J* = 8.1 Hz), 4.35 (dd, 1H, *J* = 8.7, 9.8 Hz), 4.22 (dd, 1H, *J* = 2.0, 11.0 Hz), 4.01–4.09 (m, 2H), 3.71–3.98 (m, 6H), 3.50 (t, 1H, *J* = 8.7 Hz), 3.43 (t, 1H, *J* = 8.1 Hz), 3.35 (m, 1H), 2.98–3.15 (m, 2H), 2.84 (dd, 1H, *J* = 8.1, 9.9 Hz); ¹³C NMR (125 MHz, CD₃OD): δ 138.49, 138.40, 138.00, 137.70, 128.90, 128.11, 127.85, 127.73, 127.57, 127.55, 127.51, 127.37, 127.10, 127.04, 126.98, 109.23, 102.72, 99.56, 82.22, 81.41, 80.76, 75.49, 74.31, 74.11, 73.88, 73.85, 73.77, 73.40, 72.65, 68.54, 66.06, 65.68, 56.97, 39.69; [α]_D²⁰ = +88.3 (c 0.12, MeOH); ESI-MS: *m/z* calcd for C₄₂H₅₀N₂Na₃O₁₆S₂ [M+3 Na]⁺: 971.2296; found: 971.2301.

2'-Aminoethyl 4-*O*-[2-acetamido-4-*O*-benzyl-2-deoxy-6-*O*-sulfonato-α-D-glucopyranosyl]-2,3,6-tri-*O*-benzyl-β-D-glucopyranoside, sodium salt (4b**)**

Op. 1: Resin-bound GlcN(α1→4)Glc disaccharide derivative **20** (110 mg, 0.0187 mmol sugar) was swollen in CH₂Cl₂ (3 mL) for 5 min, then treated with Bu₃P (28 μL, 0.11 mmol). The mixture was shaken for 5 h at rt, filtered, then subjected to standard workup conditions to give the intermediate *N*-ylide. *Op. 2*: The resin was treated with 95:5 THF:H₂O (4 mL), shaken for 1 day at rt, washed with THF (2 × 3 mL), then subjected to standard workup conditions to give the resin-bound primary amine. *Op. 3*: The resin was swollen in pyridine (3 mL) for 5 min, treated with Ac₂O (1.5 mL) and shaken for 1 day at rt. The resin was filtered, washed with 4:1 DMF:pyridine (2 × 3 mL), then subjected to standard workup conditions to give the *N*-acetylated intermediate. *Op. 4*: The resin was swollen in THF (0.3 mL) for 5 min, treated with 1 M TBAF in THF adjusted to pH 7 with AcOH (2.7 mL), and shaken for 1 day at rt. The resin was filtered, washed with 5:1 THF:pyridine (2 × 3 mL), then subjected to standard workup conditions to give the C6 alcohol. *Op. 5*: The resin was swollen in dry DMF (3 mL) for 5 min, then treated with SO₃•Py (45 mg, 0.28 mmol) and shaken for 10 h at rt. The resin was filtered, washed with 1:2 MeOH:pyridine (2 × 3 mL), then subjected to standard workup conditions to give the resin-bound 6-*O*-sulfate. *Op. 6*: The resin was swollen in CH₂Cl₂ (2 mL) for 5 min, treated with 1 M NaOMe in MeOH (56 μL) and shaken for 5 h at rt. The resin was filtered, washed with 1:1 MeOH:CH₂Cl₂ (2 × 3 mL), then subjected to standard workup conditions to give the fully deprotected resin-bound 6-*O*-sulfate. *Op. 7*: The resin was treated with 30% HFIP in CH₂Cl₂ under standard cleavage conditions. *Op. 8*: The crude was passed through an ion-exchange column (Dowex Marathon MSC, Na form) and purified by reverse-phase HPLC to yield 2'-aminoethyl β-linked GlcN(α1→4)Glc disaccharide 6-*O*-sulfate **4b** (sodium salt) as an amorphous white solid

(11.4 mg, 69% over 8 operations). ^1H NMR (500 MHz, CD_3OD): δ 7.42–7.49 (m, 2H), 7.11–7.41 (m, 18H), 5.34 (d, 1H, $J = 3.7$ Hz), 4.52–4.73 (m, 6H), 4.46 (d, 1H, $J = 11.8$ Hz), 4.26 (dd, 1H, $J = 1.5, 10.7$ Hz), 4.11 (dd, 1H, $J = 5.5, 10.6$ Hz), 4.03 (dd, 1H, $J = 3.8, 10.7$ Hz), 3.86–3.97 (m, 2H), 3.70–3.84 (m, 5H), 3.66 (dd, 1H, $J = 8.9, 10.8$ Hz), 3.61 (m, 1H), 3.51 (t, 1H, $J = 7.9$ Hz), 3.40 (t, 1H, $J = 10.0$ Hz), 2.95–3.18 (m, 2H), 1.73 (s, 3H); ^{13}C NMR (125 MHz, CD_3OD): δ 171.90, 138.30, 137.48, 137.41, 128.09, 128.03, 127.97, 127.86, 127.76, 127.67, 127.41, 127.34, 127.20, 102.89, 97.19, 83.69, 81.90, 78.37, 74.71, 74.03, 73.87, 73.64, 73.13, 72.84, 72.20, 70.55, 68.90, 66.61, 66.33, 53.71, 39.88, 21.03; $[\alpha]_{\text{D}}^{20} = +31.5$ (c 0.26, MeOH); ESI-MS: m/z calcd for $\text{C}_{44}\text{H}_{54}\text{N}_2\text{NaO}_{14}\text{S}$ $[\text{M}+\text{H}+\text{Na}]^+$: 889.3194; found: 889.3190.

2'-Aminoethyl 4-O-[2-amino-4-O-benzyl-2-deoxy-2,6-di-*N,O*-sulfonato- α -D-glucopyranosyl]-2,3,6-tri-O-benzyl- β -D-glucopyranoside, disodium salt (4f)

Op. 1: Resin-bound GlcN($\alpha 1 \rightarrow 4$)Glc disaccharide derivative **20** (100 mg, 0.017 mmol sugar) was swollen in CH_2Cl_2 (3 mL) for 5 min, then treated with 1 M TBAF in THF (2.7 mL), and shaken for 1 day at rt. The resin was filtered, washed with THF (2×3 mL), then subjected to standard workup conditions to give the C6 alcohol. *Op. 2:* The resin was swollen in CH_2Cl_2 (3 mL) for 5 min, then treated with Bu_3P (26 μL , 0.1 mmol). The mixture was shaken for 5 h at rt, filtered, then subjected to standard workup conditions to give the intermediate *N*-ylide. *Op. 3:* The resin was treated with 95:5 THF:H₂O (4 mL), shaken for 1 day at rt, washed with THF (2×3 mL), then subjected to standard workup conditions to give the resin-bound 2,6-amino alcohol. *Op. 4:* The resin was swollen in dry DMF (3 mL) for 5 min, then treated with $\text{SO}_3 \cdot \text{Py}$ (41 mg, 0.26 mmol) and shaken for 10 h at rt. The resin was filtered, washed with 1:2 MeOH:pyridine (2×3 mL), then subjected to standard workup conditions to give the resin-bound 6-*O*-sulfate. *Op. 5:* The resin was swollen in dry pyridine (3 mL) for 5 min, then treated with Et_3N (0.6 mL), $\text{SO}_3 \cdot \text{Py}$ (41 mg, 0.26 mmol) and shaken for 1 day at rt. The resin was filtered, washed with 1:2 MeOH:pyridine (2×3 mL), then subjected to standard workup conditions to give the resin-bound 2,6-di-*N,O*-sulfate. *Op. 6:* The resin was swollen in CH_2Cl_2 (3 mL) for 5 min, treated with 1 M NaOMe in MeOH (51 μL) and shaken for 5 h at rt. The resin was filtered, washed with 1:1 MeOH: CH_2Cl_2 (2×3 mL), then subjected to standard workup conditions to give the fully deprotected resin-bound 2,6-di-*N,O*-sulfate. *Op. 7:* The resin was treated with 30% HFIP in CH_2Cl_2 under standard cleavage conditions. *Op. 8:* The crude was passed through an ion-exchange column (Dowex Marathon MSC, Na form) and purified by reverse-phase HPLC to yield 2'-aminoethyl β -linked GlcN($\alpha 1 \rightarrow 4$)Glc disaccharide 2,6-di-*N,O*-sulfate **4f** (disodium salt) as an amorphous white solid (6.7 mg, 42% over 8 operations). ^1H NMR (400 MHz, CD_3OD): δ 7.10–7.48 (m, 20H), 5.54 (d, 1H, $J = 3.6$ Hz), 4.93–5.03 (m, 3H), 4.53–4.76 (m, 5H), 4.44 (d, 1H, $J = 12.2$ Hz), 4.30 (dd, 1H, $J = 1.6, 10.8$ Hz), 3.60–4.05 (m, 9H), 3.52 (t, 1H, $J = 6.8$ Hz), 3.36–3.45 (m, 3H), 2.87–3.12 (m, 2H); ^{13}C NMR (125 MHz, CD_3OD): δ 138.51, 138.33, 137.69, 137.63, 128.39, 128.03, 127.97, 127.89, 127.80, 127.70, 127.44, 127.26, 127.10, 102.36, 97.52, 82.00, 81.43, 78.15, 74.15, 73.85, 73.54, 73.32, 73.19, 73.12, 72.80, 69.89, 68.80, 66.96, 66.03, 58.61, 39.84; $[\alpha]_{\text{D}}^{20} = +53.3$ (c 0.30, MeOH); ESI-MS: m/z calcd for $\text{C}_{42}\text{H}_{53}\text{N}_2\text{NaO}_{16}\text{S}_2$ $[\text{M}+2\text{H}+\text{Na}]^+$: 905.2837; found: 905.2828.

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Figure 1. GlcN sulfoforms with 2'-aminoethyl linkers (**1–4**), prepared by solid-phase synthesis. R = H, Ac, or SO_3^- ; for specific sulfoforms, see Table 2.

Figure 2. ¹H NMR spectrum (400 MHz, CD₃OD) of sulfoform **1e** (3,6-di-*O*-sulfate, bis-triethylammonium salt) after cleavage from solid-phase support, prior to Na ion exchange and HPLC purification (color figure available online).

Scheme 1.

Synthesis of orthogonally protected GlcN with 2'-aminoethyl linker

Reaction conditions: (a) (i) $\text{NH}_2(\text{CH}_2)_2\text{NH}_2$, BuOH, 100 °C; (ii) TfN_3 , K_2CO_3 , CuSO_4 , $\text{CH}_2\text{Cl}_2/\text{MeOH}/\text{H}_2\text{O}$, 0 °C to rt; (iii) $\text{Ac}_2\text{O}/\text{Py}$, 0 °C to rt (85% over three steps). (b) (i) BH_3 , Bu_2BOTf , THF, 0 °C; (ii) TBDPS-Cl , imidazole, DMF, rt (62% over two steps). (c) NIS/TfOH , AE-Fmoc, $\text{Cl}(\text{CH}_2)_2\text{Cl}/\text{Et}_2\text{O}$, -20 °C (80%). (d) 20% piperidine in DMF, rt (99%).

Abbreviations: AE-Fmoc = 2'-aminoethyl-2-(9H-fluorenyl)methoxycarbamate; Phth = phthalimidyl; TBDPS = *tert*-butyldiphenylsilyl; Tol = *p*-tolyl.

Scheme 2.

Synthesis of GlcN(β 1 $\rightarrow$ 4)Glc disaccharide with β -linked 2'-aminoethyl group

Reaction conditions: (a) (i) NaOMe, MeOH, rt; (ii) Bu₃P, CH₂Cl₂, rt; (iii) H₂O:CH₂Cl₂ 1:1, rt; (iv) Troc-Cl, pyridine, rt; (v) Ac₂O/Py, rt (94% over 5 steps). (b) **15** (see Scheme 3), NIS/TfOH, CH₂Cl₂, -30 °C (90%). (c) (i) In powder, NH₄Cl, EtOH/H₂O, 98 °C; (ii) TfN₃, CuSO₄, K₂CO₃, CH₂Cl₂/MeOH, 0 °C to rt (91% over 2 steps). (d) piperidine, DMF, rt (99%). Abbreviations: Troc = trichloroethoxycarbonyl.

Scheme 3.

Synthesis of GlcN(α1→4)Glc disaccharide with β-linked 2'-aminoethyl group

Reaction conditions: (a) (i) NaOMe, MeOH, rt; (ii) PhCH(OMe)₂, TsOH, THF, reflux; (iii) NaH, BnBr, DMF, 0 °C to rt (75% over 3 steps). (b) Et₃SiH, TfOH, 4A mol sieves, CH₂Cl₂, -78 °C (75%). (c) (i) Bu₃P, CH₂Cl₂, rt; (ii) H₂O:CH₂Cl₂ 1:1, rt; (iii) Fmoc-Cl, NaHCO₃, CH₂Cl₂, 0 °C to rt (54% over 3 steps). (d) Donor **6**, NIS, TfOH, Cl(CH₂)₂Cl/Et₂O, -20 °C (60%). (e) piperidine, DMF, rt (99%).

Table 1

Loading of 2'-aminoethyl-linked derivatives onto trityl-PS resin

GlcN derivative	product (loading ratio)
8a	18a (0.38 mmol/g)
8b	18b (0.27 mmol/g)
12	19 (0.18 mmol/g)
17	20 (0.18 mmol/g)

Reaction conditions: Cl-Trityl-PS resin, DMAP, pyridine, 60°C, 48 h.

Table 2

Sulfoforms generated by orthogonal deprotection and sulfonation on trityl-PS resins

Sulfate pattern ^a	Product, ^b yield, no. ops ^c
a	1a , 87%, 6 ops (a, b, c, d, g, k)
b	1b , 76%, 8 ops (a, b, c, f, g, h, k, l) 2b , 72%, 8 ops (a, b, c, f, g, h, k, l) 3b , 67%, 8 ops (a, b, c, f, g, h, k, l) 4b , 69%, 8 ops (a, b, c, f, g, h, k, l)
c	1c , 64%, 8 ops (a, b, c, g, h, d, k, l)
d	1d , 69%, 7 ops (a, b, i, d, g, k, l)
e	1e , 68%, 8 ops (a, b, c, d, g, j, k, l)
f	1f , 44%, 8 ops (d, a, b, h, i, g, k, l) 2f , 42%, 8 ops (d, a, b, h, i, g, k, l) 3f , 41%, 8 ops (d, a, b, h, i, g, k, l) 4f , 42%, 8 ops (d, a, b, h, i, g, k, l)
g	1g , 68%, 7 ops (g, a, b, j, e, k, l)

Sulfate pattern ^a	Product, ^b yield, no. ops ^c
<p>h</p>	1h , 64%, 7 ops (d, g, a, b, j, k, l)

^a **1**: GlcN- α ; **2** GlcN- β ; **3** GlcN(β 1 $\rightarrow$ 4)Glc- β ; **4** GlcN(α 1 $\rightarrow$ 4)Glc- β (see Figure 1)

^b All products were isolated as sodium salts.

^c Each step was conducted at rt for 24 h, unless otherwise noted. Reagents and conditions: (a) Bu₃P, CH₂Cl₂, 5 h; (b) 95% aq THF; (c) Ac₂O, pyridine; (d) TBAF (pH 10), THF; (e) TBAF (pH 10), THF/DMF; (f) TBAF (pH 7), THF; (g) NaOMe, MeOH/CH₂Cl₂; (h) SO₃-Py, DMF, 10 h; (i) SO₃-Py, Py/Et₃N; (j) SO₃-Py, Py/Et₃N, 55 °C, 40 h; (k) 30% HFIP, CH₂Cl₂, 1 h; (l) Na ion-exchange chromatography.