Access to Molecular Diversity in Glycosaminoglycans: Combinatorial Synthesis of Eight Chondroitin Sulfate Disaccharides

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Glycosaminoglycans (GAGs), linear sulfated oligosaccharides, are involved in numerous biological events ranging from tissue structure to protein activity regulation. The combinatorial nature of their oligosaccharidic framework and sulfatation pattern (sulfoforms) prompted us to develop a combinatorial approach toward the synthesis of GAG fragments. Using a liquid-phase split and pool protocol, the eight basic chondroitin sulfate (CS) disaccharides have been prepared from a key CS disaccharide scaffold bearing orthogonal protecting groups. This approach saves 25 steps compared to a multi-parallel synthesis. We chose to prepare restricted libraries, but with a high structural confidence. Each step was followed by HPLC, ^{1}H- and ^{13}C-NMR, and ESI-MS analyses to ascertain the number and structures of the library members. The combinatorial protocol involves sulfatation/group manipulation sequences which rely on the fact that, although previously reported to be labile groups, sulfate esters withstand many classical reactions used in molecular glycochemistry. Thus, we used sulfate groups as efficient hydroxyl protecting groups in a combinatorial glucosyl to glucuronyl oxidation sequence involving a Swern oxidation, followed by direct conversion of the aldehyde to the methyl ester. Split and pool methodology is thus shown to be a powerful tool in gaining access to molecular diversity in GAGs and in the preparation of sulfoforms of a given oligosaccharide.

Introduction

Combinatorial chemistry occupies a prominent position in the drug discovery process but, although carbohydrates are involved in numerous important biological recognition events,[1] only a few sugar-based libraries have been prepared.[2] This is despite the fact that oligosaccharides have a potential for information content several orders of magnitude higher than that of any other biological oligomer.[3] Indeed, the carbohydrate code is still far from being fully understood. The preparation of oligosaccharide libraries and their biological screening should provide an efficient means of elucidating a wide variety of mechanisms of oligosaccharide-mediated or oligosaccharide-triggered biological events. This can be expected to be particularly true for glycosaminoglycans (GAGs), a family of linear sulfated oligosaccharides,[4] where subtle differences in sulfatation patterns result in significantly different biological properties.[5] We show herein that the introduction of combinatorial steps in the synthesis of chondroitin sulfate (CS) disaccharides allows the rapid generation of small libraries with high structural confidence. This is the first time that combinatorial chemistry has been used to generate all the natural sulfoforms[5] of a GAG disaccharide.[6] These compounds are not accessible by enzymatic or chemical degradation of the polymer and have to be chemically synthesized: chondroitinase digestion leads to unsaturated uronic acid residues, while chemical cleavage results in the formation of a 2,5-dehydromannosyl residue at the reducing end.[7] To date, no synthesis of 2′-*O*-sulfated CS fragments has ever been described, although some 2′-OH compounds have been prepared as methyl glycosides[8] or as GalNAc-β(1−4)-GlcUA disaccharides.[9]

Our CS disaccharide libraries were designed to map the CS structures involved in various biological processes: CS is an inhibitor of knee osteoarthritis progression.[10] It is a ligand of human complement protein C1q[11] and of L-selectin in clustered form.[12] CS also binds IL4,[13] has neurite outgrow activity,[14] and is implied in melanoma cell adhesion.[15] Along the chains of GAGs, variations in the sulfatation pattern and epimerization at C_5 of uronic acid give rise to great structural diversity. In fact, the CS structure allows eight basic sulfatation patterns, the combinatorial nature of which is easily accessible from disaccharide **1**.

The key intermediate **1** possesses orthogonal protecting groups, which may be independently manipulated. This allowed us to prepare the libraries **2**{1−4} and **3**{1−4}, containing the 8 sulfoforms of the basic CS disaccharide, in 13 steps from **1** using a liquid-phase split and pool protocol. This approach saves 25 steps compared to a multi-parallel synthesis, while structural characterization and deconvolution is greatly facilitated by the small size of the libraries.

Results and Discussion

Preparation of the Key Disaccharide 1 (Scheme 1)

From the known orthoester **4**,[16] the glycosyl donor **7** was prepared in five steps: compound **4** was deacetylated and then silylated through conversion into a stannyl ether derivative to give **5** in 70% yield over 3 steps.[17] This pro-

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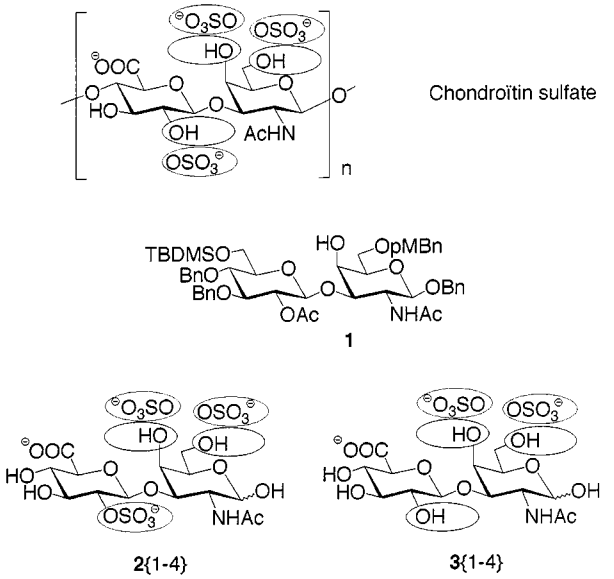
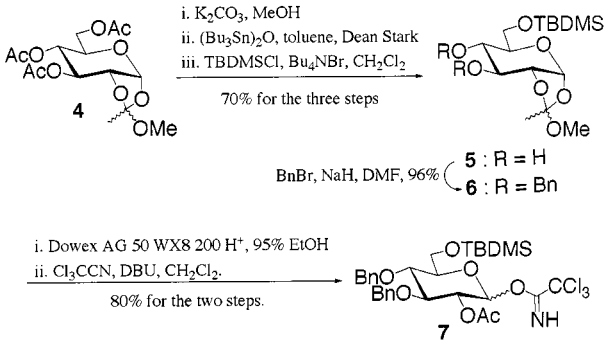


Figure 1. The eight CS sulfatation patterns are easily obtained from key disaccharide **1**

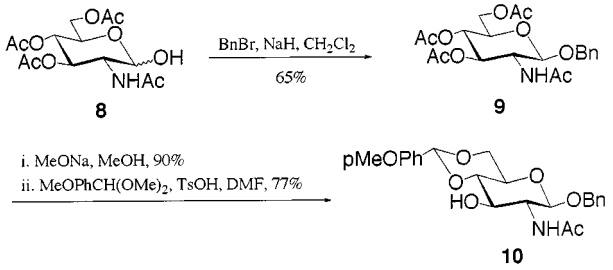
cedure avoided the formation of a tetracyclic $^1C_4$ 1,2,4-orthoester, which was obtained when TBDMSCl and pyridine were used for the silylation. Compound **5** was then benzylated to give **6** in 96% yield. This 1,2-orthoester was regioselectively opened in 95% EtOH, using Dowex 50 (H^+ form) as catalyst.[17] The resulting hemiacetal was further converted into the trichloroacetimidate **7** (80% yield over the 2 steps).



Scheme 1. Synthesis of glycosyl donor **7**

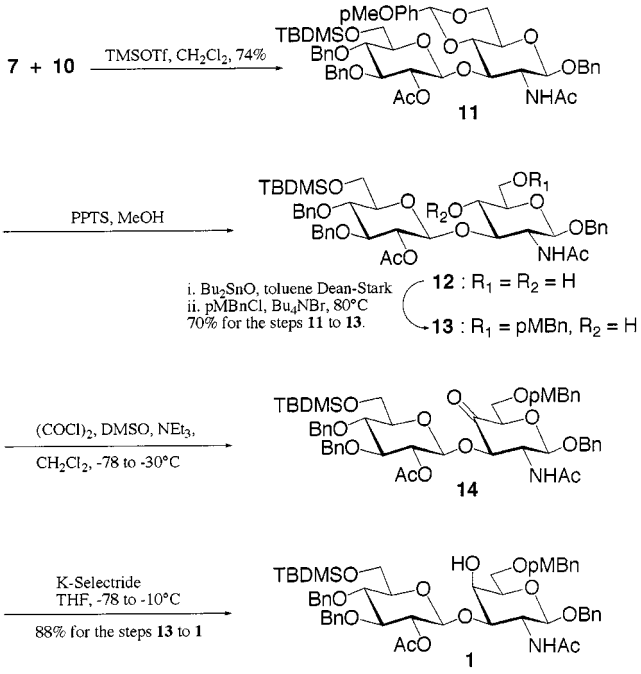
We exploited our recent finding on the control of the *O*-anomeric alkylation diastereoselectivity[18] to prepare the β-benzyl glycoside **9** (Scheme 2). The alkoxide generated from the hemiacetal **8** and sodium hydride in CH_2Cl_2 reacted with benzyl bromide to give exclusively the β glycoside **9** in 65% yield, which was obtained by direct crystallization from the reaction mixture. This compound was further processed to give the acceptor **10** as described previously.[19]

Coupling of **7** with **10** in CH_2Cl_2 using TMSOTf as catalyst gave an orthoester, which rearranged in situ to give the disaccharide **11**, isolated in 74% yield. Methanolysis of the methoxybenzylidene acetal gave the diol **12**, stannylene-promoted alkylation of which allowed us to prepare the disaccharide **13** in 70% yield. This two-step procedure gave much



Scheme 2. Synthesis of glycosyl acceptor **10**

more reproducible yields than the acetal reductive opening using Garreg's protocol.[19][20] The nucleophilic displacement of glucosaminyl C_4 triflates has been shown to provide an efficient access to their galacto counterparts,[21a,21b] but in the present case better yields were obtained by a Swern oxidation followed by K Selectride reduction, which allowed us to prepare disaccharide **1** with complete diastereoselectivity in 88% overall yield (Scheme 3).[22] It should be noted that when Li Selectride was used instead of K Selectride, 2′-*O*-deacetylation occurred due to the greater Lewis acidity of Li^+.



Scheme 3. Synthesis of key disaccharide **1**

Combinatorial Synthesis of the Eight CS Disaccharides

O-Sulfate esters have previously been reported to be labile groups and have thus been introduced in the final steps of syntheses of sulfated oligosaccharides. On the contrary, we have found that they withstand many classical reactions used in molecular glycochemistry and indeed that they may be considered as base and low-temperature acid-stable protective groups. With this in mind, it was thus possible to

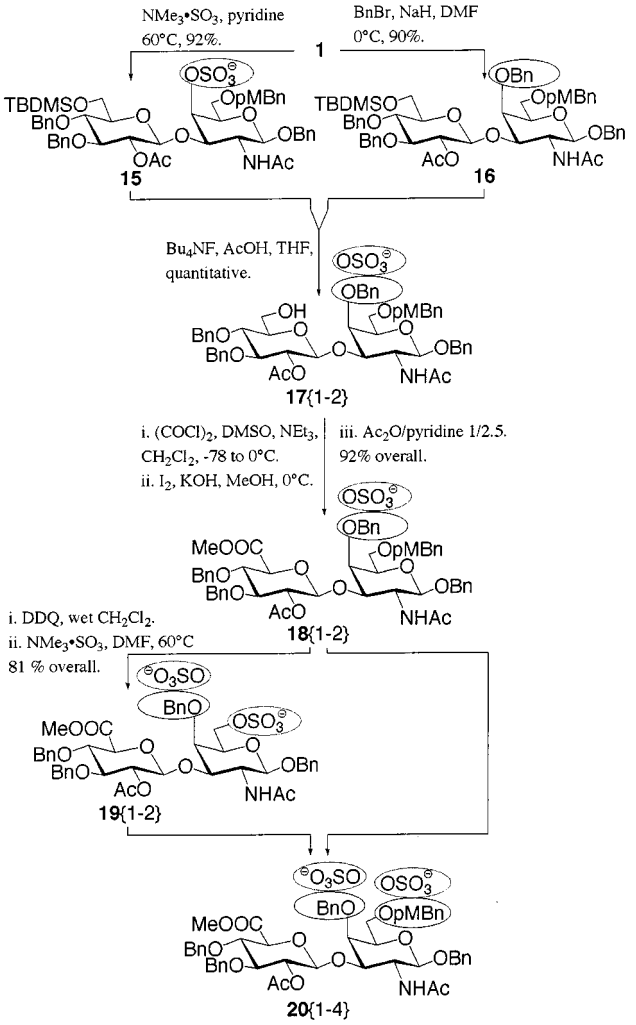
consider combinatorial steps involving *O*-sulfate esters. Thus, parallel sulfatation or benzylation of the disaccharide **1** gave compounds **15** and **16** in yields of 92 and 90%, respectively.

Throughout the combinatorial part of this work, C18 reversed-phase HPLC analyses were used to monitor the progression of each reaction and to ensure complete conversion of the starting materials (Table 1). Protected libraries were purified as tetrabutylammonium salts by gel permeation on LH-20 using MeOH/CH_2Cl_2, 1:1, as eluent. Use of the Bu_4N^+ countercation allowed single-step co-elution of the compound libraries and facile ^{1}H-NMR quantification of the sulfate groups.

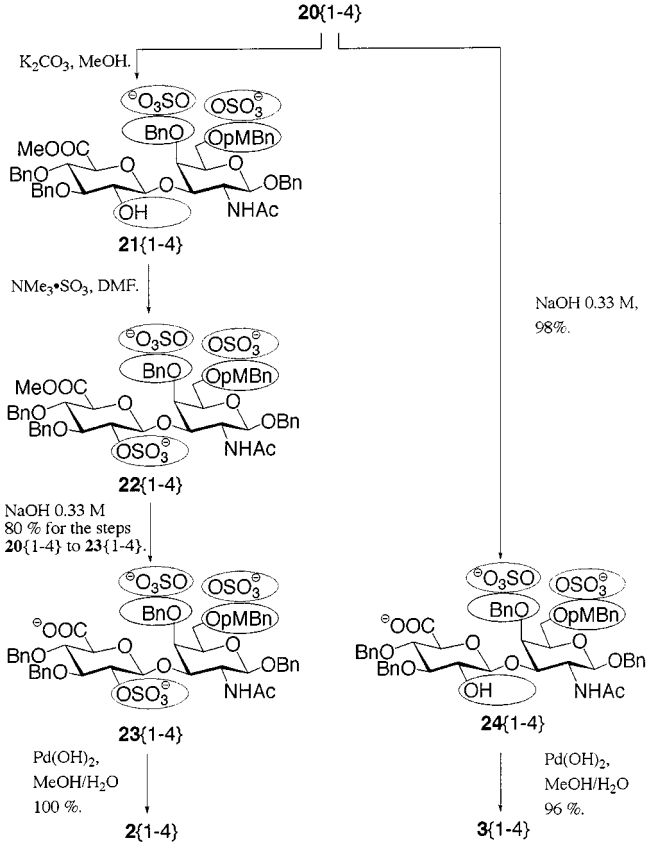
Compounds **15** and **16** were mixed in equimolar quantities and treated with Bu_4NF in THF to give **17**{1−2} in quantitative yield. In addition to HPLC traces, which indicated complete conversion of **15** and **16**, NMR data showed the disappearance of TBDMS group signals: d^1H = 0.900, 0.030 and $d^{13}C$ = 25.5, 18.0, and −5.5.

Several methods are available for C-6 primary alcohol oxidation in saccharides[23a−e] but no universal protocol has been proposed, even though this step is crucial in the chemistry of GAGs. Attempts to directly oxidize the library **17**{1−2} using TEMPO-mediated NaClO[23d] oxidation failed. However, we found that a two-step procedure, involving Swern oxidation followed by conversion of the aldehyde into a methyl ester by I_2/KOH oxidation,[24] allowed a clean conversion of both the sulfated and benzylated components of library **17**{1−2}. Using this procedure, **17**{1−2} was converted into the methyl esters library **18**{1−2} in 92% yield after reacetylation.[25] The HPLC trace of the library **18**{1−2} showed the presence of only two products (Table 1), while the ^{1}H- and ^{13}C-NMR spectra showed the appearance of the ester methoxy signals (d^1H = 3.706/3.674, $d^{13}C$ = 52.6/52.2) and the presence of 6 peaks in the ester/amide carbonyl region of the ^{13}C spectrum (δ = 171.8, 171.4, 171.1, 169.9, 169.8, and 168.6). We also tested the $NaClO_2$/2-methylbut-2-ene method[23b] for the oxidation of the intermediate aldehyde, but numerous products were obtained showing that this procedure is not compatible with the combinatorial oxidation of library **17**{1−2}.

A split was performed at this stage. Removal of the *p*MBn group using DDQ in wet CH_2Cl_2, followed by sulfatation, led to library **19**{1−2} in 81% yield over the two steps. NMR spectra confirmed loss of the *p*MBn group (d^1H = 6.860 and 3.780, $d^{13}C$ = 159.0/158.9, 113.5/158.9, and 54.9/54.8). The ^{1}H spectra additionally showed that the integration of the Bu_4N^+ signals had increased (Table 1), reflecting the presence of the additional 6-*O*-sulfate ester.



Scheme 4. Combinatorial synthesis of library **20**{1−4}



Scheme 5. Combinatorial synthesis of the 8 CS disaccharides

Libraries **18**{1−2} and **19**{1−2} were then mixed to give the four-component library **20**{1−4} (Scheme 4).

Library **20**{1−4} was then divided in two (Scheme 5). Deacetylation, using anhydrous K_2CO_3 in methanol, gave library **21**{1−4}, the structure of which was confirmed by the acetyl signal integration in the ^{1}H-NMR spectra (Table 1). Sulfatation of the 2′-hydroxyl group was performed using $NMe_3{\cdot}SO_3$ complex in DMF giving library **22**{1−4}. Once again, the integration of the Bu_4N^+ signals in the ^{1}H spectrum of **22**{1−4} (Table 1) showed the presence of the additional 2′-*O*-sulfate ester. Moreover, the ^{13}C-NMR spectra confirmed the loss of the 2′-*O*-acetyl group in the deacetylation step: no signals were found in the region δ = 20−21, while the NHAc signal persisted at δ = 23.5. Saponification of the methyl ester gave **23**{1−4} in 80% yield, while saponification of **20**{1−4} gave library **24**{1−4} in quantitative yield. In both cases, the carboxylate methoxy resonance in the region δ = 53.2−52.2 in the ^{13}C spectra of libraries **18**{1−4}, **19**{1−4}, and **22**{1−4} was no longer seen. Further hydrogenolysis quantitatively afforded the CS sulfoform libraries **2**{1−4} and **3**{1−4}.

Table 1. HPLC and ^{1}H-NMR data for libraries **17**{1−2} to **24**{1−4}

Library	Retention time[a] (min)	^{1}H-NMR relative integrals[b]	Aromatics	Bu_4N^+	Acetates
15 + **16**	11.85, 21.90				
17{1−2}	8.40, 16.25	calcd.	21.5	4.0	6.0
		found	21.5	4.0	5.8
18{1−2}	9.20, 17.60	calcd.	21.5	4.0	6.0
		found	21.5	4.0	6.3
19{1−2}	8.05, 11.15	calcd.	17.5	12.0	6.0
		found	17.5	14.9	6.9
21{1−4}	8.90, 12.00	calcd.	19.5	8.0	3.0
	12.50, 19.05	found	19.5	9.5	3.9
22{1−4}	6.85, 8.40	calcd.	19.5	16.0	3.0
	8.90, 12.00	found	19.5	17.7	3.2
23{1−4}	18.30, 20.05	calcd.	19.5	24.0	3.0
	21.10, 24.45	found	19.5	22.0	3.4
24{1−4}	7.05, 8.60	calcd.	19.5	16.0	3.0
	9.10, 12.20	found	19.5	17.1	3.6

[a] For HPLC elution conditions and detection see the Experimental Section General Remarks. − [b] Reference was set on the aromatic signals.

Characterization of the Libraries

The libraries presented here have a high degree of structural confidence: the number of members was assessed by HPLC, while equimolarity and structures were controlled by ^{1}H- and ^{13}C-NMR.

Table 2. Representative selected ^{13}C-NMR data showing the number and equimolarity of library members

Library	d^{13}C[a]	Assignment	Peak ratio
17{1−2}	20.1, 20.0	OAc	51:49
18{1−2}	54.93, 54.89	*p*MBn	52:48
19{1−2}	21.1, 21.2	**OAc**	47:53
23{1−4}	54.7, 54.5, 53.1, 52.9	C_2	20:25:57:57
24{1−4}	53.2, 53.2, 53.0, 52.9	C_2	28:27:22:23
2{1−4}	49.7, 49.6, 49.4, 49.3	C_2 α	21:24:28:28
	53.6, 53.4, 52.6, 52.4	C_2 β	22:26:26:26
3{1−4}	49.7, 49.6, 49.1, 49.0	C_2 α	21:24:28:25
	53.0, 52.9, 52.5, 52.4	C_2 β	27:20:31:22

[a] For NMR solvents, see Experimental Section. − [b] The α/β ratio is ca. 60:40 for all library compounds.

ESI-MS analyses were also performed, which showed the presence of the expected molecular ions for the two-component libraries **17**{1−2} to **19**{1−2} (Table 3). However, ESI-MS data could not be obtained directly for the four-component libraries, each multi-charged member giving rise

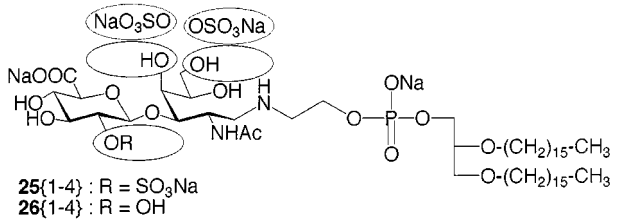


Figure 2. DHPE neoglycolipid libraries derived from **2**{1−4} and **3**{1−4}

Table 3. ESI-MS characterization of library members

Library	R_f	Ion	Calcd. *m/z*	Found *m/z*
17{1−2}	−	$C_{52}H_{59}NO_{13}Na$ [M + Na]	928.4	928.5
	−	$C_{45}H_{52}NO_{16}SNa_2$ [M + Na]	940.3	940.4
18{1−2}	−	$C_{53}H_{59}NO_{14}Na$ [M + Na]	956.4	956.5
	−	$C_{46}H_{52}NO_{17}SNa_2$ [M + Na]	968.3	968.4
19{1−2}	−	$C_{45}H_{50}NO_{16}S$ [M − Na]	892.3	892.3
	−	$C_{38}H_{43}NO_{19}S_2$ [M − 2 Na]$^{2-}$	440.6	440.5
25{1−4}	0.16	$C_{51}H_{99}N_2O_{20}PS$ [M − 3 Na + H]	561.3	561.4
	0.14	$C_{51}H_{99}N_2O_{23}PS_2$ [M − 4 Na + 2 H]	601.3	601.3
	0.12	$C_{51}H_{99}N_2O_{23}PS_2$ [M − 4 Na + 2 H]	601.3	601.4
	0.10	$C_{51}H_{98}N_2O_{26}PS_3$ [M − 5 Na + 2 H]	427.2	427.3
26{1−4}	0.21	$C_{51}H_{99}N_2O_{17}P$ [M − 2 Na]	521.3	521.4
	0.17	$C_{51}H_{99}N_2O_{20}PS$ [M − 3 Na + H]	561.3	561.4
	0.15	$C_{51}H_{99}N_2O_{20}PS$ [M − 3 Na + H]	561.3	561.4
	0.12	$C_{51}H_{99}N_2O_{23}PS_2$ [M − 4 Na + 2 H]	601.3	601.4

[a] HPTLC eluent: $CHCl_3$/MeOH/H_2O, 120:80:17.

to a complex ionization pattern together with SO_3 and H_2SO_4 elimination. The free oligosaccharides were thus derivatized as neoglycolipids **25**{1−4} and **26**{1−4} by reductive amination with dihexadecyl phosphatidylethanolamine (DHPE).[26] The four members were separated by HPTLC and analyzed by ESI-MS, giving the expected ions.

Conclusion

Split and pool methodology has been shown to be a powerful tool for attaining molecular diversity in GAGs and for the preparation of all sulfoforms of a given oligosaccharide. The eight basic chondroitin sulfate disaccharides have been prepared using split and pool technology, saving 25 steps over a multi-parallel synthesis, and have been structurally characterized. Sulfate esters have been shown to be stable under various reaction conditions and have thus been used as protecting groups in a glucosyl to glucuronyl oxidation step. We have also shown that a C_4 oxidation/reduction protocol is an efficient alternative to triflate displacement or galactal azidonitration for the preparation of galactosaminyl-containing oligosaccharides.

We are currently extending this combinatorial methodology to the preparation of broader libraries in the dermatan sulfate, heparin/heparan sulfate, and hyaluronan series.

Experimental Section

General Remarks: All moisture-sensitive reactions were performed under an argon atmosphere using oven-dried glassware. Solvents were evaporated in vacuo. All solvents were dried with standard drying agents[27] and freshly distilled prior to use. − Flash column chromatography was performed on A.C.C. silica gel 60 (6−35 μm). Size-exclusion chromatography was performed on Sephadex LH-20 (700 mL) using MeOH/CH_2Cl_2, 1:1, as eluent. Reactions were monitored by TLC on glass-backed silica gel 60 F_{254} plates with detection by UV at 254 nm or by charring with 5% ethanolic H_2SO_4. − Each combinatorial step was followed by HPLC performed on a Nucleosil 5 μm C18 200 × 4.6 mm column. The products were detected using a diode-array detector. The elution was performed at a flow rate of 2 mL/min with a 20 min linear AcOH/NEt_3 10 mM pH 7.0 buffer/CH_3CN gradient followed by 10 min CH_3CN: 70:30 to 0:100 for **15** + **16**, **17**{1−2} and **18**{1−2}; 80:20 to 0:100 for **19**{1−2}; 90:10 to 0:100 for **21**{1−4}, **22**{1−4} and **24**{1−4}. Buffer/MeOH, 80:20 to 0:100, followed by 10 min MeOH at 1 mL/min was used for **23**{1−4}. − Melting points were determined on a Büchi capillary apparatus and are uncorrected. − Optical rotations were measured on a Jasco DIP 370 digital polarimeter. − NMR spectra were recorded at room temperature with Bruker AC 250 or AM 400 spectrometers; ^{13}C-NMR spectra were recorded at 62.9 MHz; Me_4Si, solvent signals, or acetone in D_2O were used for δ calibration (CD_3OD: δ^1H = 3.310 and $\delta^{13}C$ = 49.0; $CDCl_3$: $\delta^{13}C$ = 77.0; acetone: δ^1H = 2.225 and $\delta^{13}C$ = 30.45). Except where otherwise stated, sulfated products were conditioned in the Bu_4N^+ form prior to NMR analysis. For the ^{1}H- and ^{13}C-NMR library spectra, signals attributed to the same atom in different molecules are presented in the following manner: $\delta_1/\delta_2/...$, (peak ratio). Phase-sensitive COSY were performed for **1**, **15**, and **16** by recording 256 or 512 FIDs with 1024 complex data points. Prior to Fourier transform, the data were zero-filled in the F1 dimension and multiplied by a π/3 shifted sinebell function in both dimensions. − Mass spectra were recorded in both positive and negative modes on a Finnigan MAT 95 S spectrometer using electrospray ionization. − Elemental analyses were performed at the C.N.R.S. (Gif-sur-Yvette, France).

Orthoester 5: Dry K_2CO_3 (400 mg, 3 mmol, 0.1 equiv.) was added to a stirred solution of **4** (10.9 g, 30 mmol) in methanol (100 mL). After 30 min at 22°C, the reaction was quenched with Dowex 50X8 200 (H^+ form) until pH 7 was reached. The mixture was then filtered, concentrated, and co-evaporated with toluene (2 × 100 mL). The residue was dissolved in toluene (200 mL) and $(Bu_3Sn)_2O$ (18 mL, 36 mmol, 1.2 equiv.) was added. The mixture was refluxed for 3 h with continuous removal of water by means of a Dean−Stark apparatus, then concentrated to a volume of 50 mL. After cooling to 0°C, anhydrous CH_2Cl_2 (20 mL), Bu_4NBr (11.6 g, 36 mmol, 1.2 equiv.), and TBDMSCl (6.3 g, 42 mmol, 1.4 equiv.) were added and the resulting mixture was stirred for 30 min at 22°C. The reaction mixture was then diluted with Et_2O (500 mL) and washed with ice-cold $NaHCO_3$ solution (5%, 300 mL) and water (2 × 300 mL). The organic layer was dried ($MgSO_4$), filtered, and concentrated. Flash chromatography (petroleum ether/AcOEt + 1% NEt_3, 9:1 to 1:1) of the residue afforded **5** as a mixture of *exo*/*endo* isomers (7.3 g, 70%, *endo*:*exo* 90:10). Crystallization (petroleum ether/Et_2O, 95:5) gave pure $\mathbf{5}_{exo}$ (6.3 g) as white crystals; m.p. 93−94°C. − ^{1}H NMR of $\mathbf{5}_{exo}$ (250 MHz, $CDCl_3$): δ = 5.770 (d, 1 H, *J* = 5.0 Hz, H_1), 4.315 (td, 1 H, *J* = 5.0, 0.5 Hz, H_2), 4.010−3.700 (m, 5 H, H_3, H_4, H_5, H_6 and $H_{6'}$), 3.300 (s, 3 H, OMe), 3.010 (d, 1 H, *J* = 5.0 Hz, OH), 2.710 (d, 1 H, *J* = 6.0 Hz, OH), 1.700 (s, 3 H, CH_3), 0.900 (s, 9 H, *t*Bu), 0.100 (s, 6 H, Me_2Si). − ^{13}C NMR: δ = 121.3, 97.7, 76.9, 72.9, 72.5, 70.2, 64.2, 50.4, 25.8, 21.7, 18.2, −5.5. − IR (KBr): $\tilde{\nu}$ = 3486 (br.), 3228 (br.), 3000−2750 cm^{-1}. − $C_{15}H_{30}O_7Si$: calcd. C 51.40, H 8.63; found C 51.55, H 8.51.

Orthoester 6: Benzyl bromide (2.9 mL, 24 mmol, 3.2 equiv.) was slowly added to a cooled solution (0°C) of **5** (2.54 g, 7.2 mmol) and NaH (60% in oil, 1.0 g, 25 mmol, 3.5 equiv.) in DMF (25 mL) under stirring. After 1 h at 0°C, MeOH (1 mL) was added, the mixture was diluted with Et_2O (200 mL), and washed with ice-cold water (3 × 100 mL). The organic layer was dried ($MgSO_4$), filtered, and then concentrated. Flash chromatography (petroleum ether/AcOEt + 1% NEt_3, 10:0 to 8:2) of the residue afforded the benzylated product **6** (3.7 g, 96%). − ^{1}H NMR (250 MHz, $CDCl_3$): δ = 7.450−7.200 (m, 10 H, arom.), 5.770 (d, 1 H, *J* = 5.0 Hz, H_1), 4.723 (d, 1 H, *J* = 11.5 Hz, CH_2Ph), 4.680 (d, 1 H, *J* = 11.0 Hz, CH_2Ph), 4.606 (d, 1 H, *J* = 11.5 Hz, CH_2Ph), 4.533 (d, 1 H, *J* = 10.5 Hz, CH_2Ph), 4.392 (dd, 1 H, *J* = 5.0, 3.5 Hz, H_2), 3.900−3.800 (m, 3 H), 3.725 (dd, 1 H, *J* = 9.0, 5.0 Hz), 3.645 (dt, 1 H, *J* = 9.5, 2.5 Hz), 3.290 (s, 3 H, OMe), 1.650 (s, 3 H, CH_3), 0.880 (s, 9 H, *t*Bu), 0.060 (s, 6 H, Me_2Si). − ^{13}C NMR: δ = 138.2, 137.7, 128.4−127.8, 121.2, 98.0, 79.6, 76.7, 74.5, 73.3, 72.0, 62.6, 50.4, 25.9, 21.7, 18.3, −5.2, −5.3. − IR (KBr): $\tilde{\nu}$ = 3000−2750 cm^{-1}. − $C_{15}H_{30}O_7Si$: calcd. C 65.63, H 7.98; found C 65.55, H 7.86.

Imidates 7_α and 7_β: Dowex 50X8 200 (H^+ form, 740 mg) was added to a stirred solution of compound **6** (3.7 g, 6.9 mmol) in EtOH (95%, 70 mL). After 3 h at 22°C, the mixture was filtered and concentrated. After repeated co-evaporation with toluene, anhydrous CH_2Cl_2 (17 mL) was added and the resulting solution was cooled to 0°C. Trichloroacetonitrile (2.1 mL, 21 mmol, 3 equiv.) and DBU (210 μL, 1.4 mmol, 0.2 equiv.) were then added. After 2 h at 22°C, the reaction mixture was subjected to flash column chromatography on silica. Elution (petroleum ether/AcOEt + 1% NEt_3, 10:0 to 9:1) gave a mixture of $\mathbf{7}_a$ and $\mathbf{7}_b$ (3.8 g, 65:45, 80%). In this

chromatographic step, a partial separation of the α and β isomers was achieved, allowing their separate NMR characterization. – ^{1}H NMR of **7**$_a$ (250 MHz, $CDCl_3$): δ = 8.520 (s, 1 H, NH), 7.420–7.250 (m, 10 H, Ph), 6.500 (d, 1 H, *J* = 3.5 Hz, H_1), 4.990 (dd, 1 H, *J* = 9.5, 3.5 Hz, H_2), 4.880 (d, 1 H, *J* = 10.5 Hz, CH_2Ph), 4.870 (d, 1 H, *J* = 11.5 Hz, CH_2Ph), 4.755 (d, 1 H, *J* = 11.5 Hz, CH_2Ph), 4.730 (d, 1 H, *J* = 10.5 Hz, CH_2Ph), 4.100 (ddd, 1 H, *J* = 9.5, 7.5, 1.5 Hz, H_5), 4.000–3.770 (m, 4 H, H_3, H_4, H_6 and $H_{6'}$), 1.940 [s, 3 H, CH_3 (Ac)], 0.900 (s, 9 H, *t*Bu), 0.080 (s, 3 H, MeSi), 0.050 (s, 3 H, MeSi). – ^{13}C NMR: δ = 170.0 (C=O), 161.0 (C=NH), 138.2, 138.1, 128.5–127.7, 94.1 (C_1), 79.4, 76.8, 75.4, 74.5, 72.5, 61.4, 25.8, 20.6, 18.2, –5.1, –5.5. – ^{1}H NMR of **7**$_b$ (250 MHz, $CDCl_3$): δ = 8.580 (s, 1 H, NH), 7.480–7.200 (m, 10 H, Ph), 5.745 (d, 1 H, *J* = 8.0 Hz, H_1), 5.198 (dd, 1 H, *J* = 9.0, 8.0 Hz, H_2), 4.838 (d, 2 H, *J* = 11.0 Hz, 2 CH_2Ph), 4.737 (d, 1 H, *J* = 11.0 Hz, CH_2Ph), 4.690 (d, 1 H, *J* = 11.0 Hz, CH_2Ph), 3.940–3.800 (m, 3 H, H_4, H_6 and $H_{6'}$), 3.734 (t, 1 H, *J* = 9.0 Hz, H_3), 3.488 (dt, 1 H, *J* = 9.5, 2.5 Hz, H_5), 1.930 [s, 3 H, CH_3 (Ac)], 0.890 (s, 9 H, *t*Bu), 0.080 (s, 3 H, SiMe), 0.030 (s, 3 H, SiMe).

β-Benzyl Glycoside 9: A solution of glucosaminyl derivative **8**[21a] (10.41 g, 30 mmol) in anhydrous CH_2Cl_2 (30 mL) was added dropwise to a cooled (–20°C) mixture of benzyl bromide (36 mL, 300 mmol, 10 equiv.) and NaH (60% in oil, 1.8 g, 45 mmol, 1.5 equiv.). The resulting mixture was allowed to warm to 20°C over a period of 2 h, maintained at this temperature for a further 10 h, and then quenched with acetic acid (1 mL). The mixture was then diluted with CH_2Cl_2 (500 mL) and washed with ice-cold water (3 × 100 mL). The organic layer was filtered through a phase-separating filter, concentrated, and co-evaporated with toluene (100 mL). Crystallization of the residue (from AcOEt/petroleum ether) gave **9** (8.53 g, 65%), the physical and spectral properties of which were in agreement with those reported previously.[19]

Preparation of Disaccharide 11: Crystalline compound **10** (5.3 g, 11.5 mmol), which co-crystallized with MeOH and which is poorly soluble in most organic solvents, was first suspended in toluene (200 mL) and this suspension was refluxed for 1 h prior to distillation to dryness. Anhydrous CH_2Cl_2 (150 mL) was then added, the mixture was refluxed for 45 min., and then concentrated to a volume of 50 mL. After cooling to 0°C, TMSOTf (130 μL, 0.7 mmol, 0.06 equiv.) was added. After 5 min, a solution of **7a**/**7b** (11.5 g, 17.5 mmol, 1.5 equiv.) in CH_2Cl_2 (10 mL) was added dropwise over a period of 30 min. The solution became clear after 1 h and stirring was continued for a further 15 h at 20°C. The reaction was then quenched with NEt_3 (160 μL) and the mixture was directly subjected to flash column chromatography on silica. Elution (petroleum ether/AcOEt, 8:2 to 1:1) afforded **11** (7.8 g, 74%), which was crystallized from Et_2O/petroleum ether; m.p. 125–130°C. – ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.450–7.200 (m, 17 H, arom.), 6.880 (d, 2 H, *J* = 11.0 Hz, MeOPh), 5.915 (d, 1 H, *J* = 7.0 Hz, NH), 5.434 (s, 1 H, MeOPhC*H*), 5.333 (d, 1 H, *J* = 8.0 Hz, H_1), 4.858 (d, 1 H, *J* = 11.5 Hz, CH_2Ph), 4.828 (dd, 1 H, *J* = 8.5, 8.0 Hz, H'_2), 4.759 (d, 1 H, *J* = 11.0 Hz, CH_2Ph), 4.733 (d, 1 H, *J* = 10.5 Hz, CH_2Ph), 4.638 (t, 1 H, *J* = 9.0 Hz, H_3), 4.615 (d, 1 H, *J* = 10.5 Hz, CH_2Ph), 4.614 (d, 1 H, *J* = 8.0 Hz, H'_1), 4.598 (d, 1 H, *J* = 11.0 Hz, CH_2Ph), 4.570 (d, 1 H, *J* = 11.5 Hz, CH_2Ph), 4.314 (dd, 1 H, *J* = 11.0, 5.0 Hz, H_6), 3.594 (s, 3 H, OMe), 3.755 (br. d, 1 H, *J* = 11.0 Hz, $H_{6'}$), 3.663 (t, 1 H, *J* = 9.0 Hz, H_4), 3.638–3.500 (m, 5 H, H_5, H'_6, $H'_{6'}$, H'_4, H_4), 3.058 (ddd, 1 H, *J* = 9.0, 8.0, 7.0 Hz, H_2), 2.958 (dt, 1 H, *J* = 9.0, 2.5 Hz, H'_5), 1.880 (s, 3 H, Ac), 1.780 (s, 3 H, Ac), 0.875 (s, 9 H, *t*Bu), 0.020 (s, 6 H, $SiMe_2$). – ^{13}C NMR: δ = 170.4, 169.6, 160.1, 138.2, 138.0, 137.1, 129.6, 128.4–127.4, 113.7, 101.6, 98.7, 82.8, 80.7, 77.4, 75.6, 75.3, 75.0, 74.9, 73.7, 71.6, 68.8, 65.7, 62.1, 58.3, 55.2 (PhOMe), 25.9 (CH_3, *t*Bu), 23.6 (NHAc), 20.8 (OAc), 18.2, –4.9, –5.4. – IR (KBr): $\tilde{\nu}$ = 3426 (br.), 3281 (br.), 3000–2800, 1750, 1653 cm^{-1}. – $C_{51}H_{65}NO_{13}Si$: calcd. C 65.99, H 7.06, N 1.51; found C 65.65, H 7.09, N 1.39. – [α] = –30 (CH_2Cl_2, *c* = 1.09).

Preparation of Disaccharide 13: To a solution of compound **11** (7.7 g, 8.3 mmol) in anhydrous methanol (180 mL) was added pyridinium *p*-toluenesulfonate (520 mg, 2 mmol, 0.25 equiv.). After 1 h at 20°C, a white precipitate was deposited. The mixture was then diluted with CH_2Cl_2 (500 mL), and washed successively with ice-cold aq. HCl (0.1 M, 100 mL), water (100 mL), 5% aq. $NaHCO_3$ (100 mL), and finally with water (3 × 100 mL). The organic layer was then filtered through a phase-separating filter, partially concentrated, and passed through a short silica gel column. Elution (CH_2Cl_2/MeOH, 9:1) gave the expected diol **12**, which was dried in vacuo over P_2O_5 overnight. – ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.400–7.150 (m, 15 H, arom.), 6.118 (d, 1 H, *J* = 7.0 Hz, NH), 5.026 (d, 1 H, *J* = 8.5 Hz, H_1), 4.943 (dd, 1 H, *J* = 9.0, 8.0 Hz, H'_2), 4.831 (d, 1 H, *J* = 12.0 Hz, CH_2Ph), 4.805 (d, 1 H, *J* = 11.5 Hz, CH_2Ph), 4.798 (d, 1 H, *J* = 11.0 Hz, CH_2Ph), 4.645 (d, 1 H, *J* = 11.5 Hz, CH_2Ph), 4.572 (d, 1 H, *J* = 11.0 Hz, CH_2Ph), 4.558 (d, 1 H, *J* = 12.0 Hz, CH_2Ph), 4.440 (d, 1 H, *J* = 8.0 Hz, H'_1), 4.400 (d, 1 H, *J* = 1.5 Hz, OH), 4.254 (dd, 1 H, *J* = 10.0, 7.5 Hz, H_3), 3.950–3.862 (m, 2 H), 3.620–3.700 (m, 3 H), 3.654 (t, 1 H, *J* = 9.0 Hz), 3.623 (dd, 1 H, *J* = 11.5, 6.0 Hz), 3.566 (t, 1 H, *J* = 9.0 Hz), 3.520–3.370 (m, 3 H), 3.130 (ddd, 1 H, *J* = 10.0, 8.5, 7.0 Hz, H_2), 1.950 (s, 3 H, Ac), 1.880 (s, 3 H, Ac), 0.880 (s, 9 H, *t*Bu), 0.030 (s, 6 H, $SiMe_2$). – ^{13}C NMR: δ = 170.4, 169.4, 137.9, 137.6, 137.3, 128.5–127.8, 100.1, 98.7, 83.0, 82.8, 77.9, 75.3, 75.1, 75.0, 73.1, 71.5, 61.0, 63.0, 62.1, 57.3, 25.9 (CH_3, *t*Bu), 23.6 (NHAc), 20.9 (OAc), 18.3, –5.6.

Compound **12** was subsequently suspended in toluene (350 mL) and Bu_2SnO (2.5 g, 10 mmol, 1.2 equiv.) was added. The mixture was then refluxed for 6 h with continuous removal of water by means of a Dean–Stark apparatus. The remaining solution was concentrated to a volume of 50 mL and then cooled to 80°C, whereupon Bu_4NBr (3.2 g, 10 mmol, 1.2 equiv.) and *p*-methoxybenzylchloride (1.7 mL, 12.5 mmol, 1.5 equiv.) were added. After 6 h, the mixture was cooled to 20°C, diluted with Et_2O (700 mL) and CH_2Cl_2 (30 mL), and then washed with 5% aq. $NaHCO_3$ solution (300 mL) and water (3 × 200 mL). The organic layer was filtered through a phase-separating filter, dried ($MgSO_4$), filtered, and concentrated. Flash chromatography (toluene/AcOEt, 8:2 to 6:4) of the residue gave **13** (5.34 g, 70%). Further elution (toluene/AcOEt, 2:8) afforded the desilylated compound (410 mg, 6%), which could be quantitatively resilylated using TBDMSCl/pyridine. Compound **13** was crystallized from Et_2O/petroleum ether in 94% yield; m.p. 168–171°C. – ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.420–7.150 (m, 17 H, arom.), 6.856 (d, 2 H, *J* = 8.0 Hz, *p*MBn), 6.655 (d, 1 H, *J* = 7.0 Hz, NH), 5.050 (d, 1 H, *J* = 8.0 Hz, H_1), 4.933 (t, 1 H, *J* = 8.0 Hz, H'_2), 4.895 (d, 1 H, *J* = 12.0 Hz, CH_2Ph), 4.800 (d, 1 H, *J* = 11.5 Hz, CH_2Ph), 4.795 (d, 1 H, *J* = 11.0 Hz, CH_2Ph), 4.643 (d, 1 H, *J* = 11.5 Hz, CH_2Ph), 4.605 (d, 1 H, *J* = 11.0 Hz, CH_2Ph), 4.563 (d, 1 H, *J* = 12.0 Hz, CH_2Ph), 4.540 (d, 1 H, *J* = 12.0 Hz, CH_2Ph), 4.505 (d, 1 H, *J* = 12.0 Hz, CH_2Ph), 3.423 (d, 1 H, *J* = 8.0 Hz, H'_1), 4.270 (dd, 1 H, *J* = 10.0, 8.0 Hz, H_3), 4.205 (d, 1 H, *J* = 1.5 Hz, OH), 3.860 (dd, 1 H, *J* = 11.0, 1.5 Hz, H_6), 3.793 (s, 3 H, OMe), 3.783 (dd, 1 H, *J* = 11.0, 2.0 Hz, H'_6), 3.700–3.565 (m, 4 H), 3.520 (ddd, 1 H, *J* = 9.0, 5.0, 1.5 Hz, H_5), 3.470–3.365 (m, 2 H), 3.073 (ddd, 1 H, *J* = 10.0, 8.0, 7.0 Hz, H_2), 1.936 (s, 3 H, Ac), 1.899 (s, 3 H, Ac), 0.863 (s, 9 H, *t*Bu), 0.023 (s, 6 H, $SiMe_2$). – From 1D TOCSY[28]: δ = 3.628 (dd, *J* = 11.0, 5.0 Hz, $H_{6'}$), 3.415 (dd, *J* = 9.0, 8.0 Hz, H_4). – ^{13}C NMR: δ = 170.4, 169.3, 159.0, 137.9, 137.7, 137.4, 136.9, 129.1, 128.5–127.8,

113.7, 100.1, 98.5, 83.2, 82.8, 77.5, 75.8, 75.4, 75.3, 74.9, 73.1, 73.0, 71.2, 69.8, 69.5, 69.3, 62.0, 57.3 (C_2), 55.2 (PhOMe), 25.9 (CH_3, *t*Bu), 23.7 (NHAc), 20.9 (OAc), 18.3, −5.5, −5.6. − IR (KBr): $\tilde{\nu}$ = 3449 (br.), 3289 (br.), 3100−2800, 1745, 1657, 1558 cm^{-1}. − $C_{51}H_{67}NO_{13}Si$: calcd. C 65.85, H 7.26, N 1.51; found C 65.49, H 7.22, N 1.48. − [α] = −17 (CH_2Cl_2, *c* = 1.52).

Preparation of Disaccharide 1: At −60°C, DMSO (11 mL, 160 mmol, 25 equiv.) was added dropwise to a solution of oxalyl chloride (2.8 mL, 32 mmol, 5 equiv.) in CH_2Cl_2 (60 mL). After 15 min at −60°C, a solution of **13** (5.95 g) in CH_2Cl_2 (60 mL) was added. The mixture was stirred for 1.5 h at −60°C and then NEt_3 (22 mL, 160 mmol, 25 equiv.) was added dropwise over a period of 5 min. After 2 h at −60°C, the mixture was slowly allowed to warm −30°C over a period of 3 h and the reaction was quenched at this temperature by the addition of aq. KH_2PO_4 (20%, 100 mL). The mixture was then diluted with Et_2O (500 mL), washed with water (2 × 200 mL), filtered through a phase-separating filter, and concentrated. Flash chromatography (toluene/AcOEt, 1:1) of the residue gave the ketone **14**, which was dried in vacuo over P_2O_5. − ^{13}C NMR ($CDCl_3$, 50:50 mixture of two conformers): δ = 200.1, 170.8, 170.0, 169.2, 159.1, 138.0, 137.9, 137.8, 137.7, 137.6, 137.4, 137.0, 129.9, 129.8, 129.3, 128.5−127.8, 113.7, 100.1, 100.6, 98.7, 98.4, 92.2, 82.9, 82.8, 82.3, 78.0, 77.7, 77.2, 76.0, 75.6, 75.2, 75.1, 74.9, 74.8, 73.3, 73.1, 73.0, 72.7, 71.4, 71.2, 68.5, 68.1, 63.1, 62.0, 59.2, 57.0, 55.1, 25.9, 25.8, 23.6, 23.4 (NHAc), 21.0/20.8 (OAc), 18.3, 18.2, −5.3, −5.6.

The ketone **14** was then dissolved in anhydrous THF (130 mL) and this solution was cooled to −78°C. A THF solution of K Selectride (1 M, 7.7 mL) was then added dropwise. After stirring at −78°C for 1 h, the mixture was allowed to warm to −10°C over a period of 3 h and the reaction was quenched with acetone (1 mL). CH_2Cl_2 (200 mL) was then added and the resulting solution was washed with aq. KH_2PO_4 (5%, 200 mL) and water (2 × 100 mL). The organic phase was then filtered through a phase-separating filter, concentrated, and co-evaporated with toluene (100 mL). Flash chromatography (petroleum ether/AcOEt, 6:4 to 4:6) of the residue gave **1** (5.3 g, 88%). − ^1H NMR (400 MHz, $CDCl_3$): δ = 7.400−7.200 (m, 17 H, arom.), 6.866 (d, 2 H, *J* = 8.0 Hz, *p*MBn), 5.815 (d, 1 H, *J* = 7.0 Hz, NH), 5.072 (d, 1 H, *J* = 8.5 Hz, H_1), 4.930 (dd, 1 H, *J* = 9.0, 8.0 Hz, H'_2), 4.885 (d, 1 H, *J* = 12.0 Hz, CH_2Ph), 4.805 (d, 2 H, *J* = 11.0 Hz, 2 CH_2Ph), 4.655 and 4.645 (d, 1 H, *J* = 11.0 Hz, CH_2Ph), 4.555 (dd, 1 H, *J* = 10.5, 3.0 Hz, H_3), 4.542 (d, 1 H, *J* = 12.0 Hz, CH_2Ph), 4.542 (d, 1 H, *J* = 11.5 Hz, CH_2Ph), 4.490 (d, 1 H, *J* = 8.0 Hz, H'_1), 4.488 (d, 1 H, *J* = 11.5 Hz, CH_2Ph), 4.045 (d, 1 H, *J* = 3.0 Hz, H_4), 3.785 (s, 3 H, OMe), 3.800−3.630 (m, 6 H, H_5, H_6, $H_{6'}$, H'_4, H'_6, $H'_{6'}$), 3.619 (t, 1 H, *J* = 9.0 Hz, H'_3), 3.325 (dt, 1 H, *J* = 9.5, 2.5 Hz, H'_5), 3.317 (ddd, 1 H, *J* = 10.5, 8.5, 7.0 Hz, H_2), 1.921 (s, 3 H, Ac), 1.868 (s, 3 H, Ac), 0.869 (s, 9 H, *t*Bu), 0.027 (s, 3 H, SiMe), 0.021 (s, 3 H, SiMe). − ^{13}C NMR: δ = 170.6, 169.4, 159.1, 138.0, 137.9, 137.5, 130.3, 129.2, 128.5−127.8, 113.7, 100.7, 98.3, 82.6, 77.9, 77.3, 75.9, 75.2, 75.0, 73.2, 73.1, 70.9, 69.3, 67.5, 61.8, 55.2 (C_2 or PhOMe), 54.5 (C_2 or PhOMe), 25.8 (CH_3, *t*Bu), 23.6 (NHAc), 20.8 (OAc), 18.2 (CSi, *t*Bu), −5.5 (SiMe), −5.6 (SiMe). − IR (KBr): $\tilde{\nu}$ = 3520 (br.), 3443 (br.), 3100−2800, 3286, 1745, 1656, 1563 cm^{-1}. − $C_{51}H_{67}NO_{13}Si$: calcd. C 65.85, H 7.26, N 1.51; found C 65.61, H 7.43, N 1.62. − [α] = −15 (CH_2Cl_2, *c* = 1.93).

Preparation of the Sulfated Disaccharide 15: $NMe_3 \cdot SO_3$ (1.2 g, 8.6 mmol, 10 equiv.) was added to a solution of compound **1** (800 mg, 0.86 mmol) in anhydrous pyridine (7 mL, 86 mmol, 100 equiv.) in a screw-capped tube. After stirring for 24 h at 50°C, the reaction was quenched with dry methanol (800 μL, 20 mmol). After a further 1 h, the mixture was diluted with CH_2Cl_2 (50 mL) and washed with aq. $NaHCO_3$ solution (5%, 10 mL). The aqueous layer was extracted with CH_2Cl_2 (2 × 20 mL) and the combined organic layers were filtered through a phase-separating filter, concentrated, and co-evaporated with toluene (50 mL). Flash chromatography (CH_2Cl_2/MeOH, 97.5:2.5 to 95:5) of the residue afforded compound **15**, which was dissolved in 2 mL MeOH and passed through a Dowex 50X8 400 column (7 mL, Bu_4N^+ form). Elution (MeOH) gave **15** (1.0 g, 92%). − ^1H NMR (250 MHz, Na form, $CDCl_3$/CD_3OD, 8:2): δ = 7.400−7.100 (m, 17 H, arom.), 6.866 (d, 2 H, *J* = 10.0 Hz, *p*MBn), 4.887 (dd, 1 H, *J* = 9.0, 8.0 Hz, H'_2), 4.805 (d, 1 H, *J* = 12.0 Hz, CH_2Ph), 4.765 (d, 1 H, *J* = 2.5 Hz, H_4), 4.750, 4.735, 4.592 and 4.562 (d, 1 H, *J* = 11.0 Hz, CH_2Ph), 4.548 (d, 1 H, *J* = 12.0 Hz, CH_2Ph), 4.500 and 4.438 (d, 1 H, *J* = 11.0 Hz, CH_2Ph), 4.335 (d, 1 H, *J* = 8.0 Hz, H'_1), 4.316 (d, 1 H, *J* = 8.5 Hz, H_1), 3.995 (dd, 1 H, *J* = 11.0, 8.5 Hz, H_2), 3.835 (dd, 1 H, *J* = 5.5, 1.0 Hz, H_5), 3.790 (dd, 1 H, *J* = 11.0, 2.0 Hz, H'_6), 3.740 (s, 3 H, OMe), 3.643 (dd, 1 H, *J* = 11.0, 6.0 Hz, $H'_{6'}$), 3.580 (t, 1 H, *J* = 9.0 Hz, H'_3), 3.575 (dd, 1 H, *J* = 11.0, 2.5 Hz, H_3), 3.570 (dd, 1 H, *J* = 11.5, 5.5 Hz, $H_{6'}$), 3.485 (t, 1 H, *J* = 9.0 Hz, H'_4), 3.250 (ddd, 1 H, *J* = 9.0, 6.0, 2.0 Hz, H'_5), 1.976 (s, 3 H, Ac), 1.931 (s, 3 H, Ac), 0.867 (s, 9 H, *t*Bu), 0.055 (s, 3 H, SiMe), 0.016 (s, 3 H, SiMe). − ^{13}C NMR (Bu_4N form): δ = 170.9, 170.0, 158.7, 137.9, 137.7, 137.6, 130.5, 129.1, 128.2−127.1, 113.4, 101.0, 100.1, 83.0, 75.9, 74.6, 74.5, 74.2, 72.7, 70.7, 69.9, 62.2, 58.3 (NCH_2, Bu_4N^+), 54.9 (PhOMe), 51.6 (C_2), 25.5 (CH_3, *t*Bu), 23.5 (Bu_4N^+), 22.7 (NHAc), 20.6 (OAc), 19.3 (Bu_4N^+), 18.0 (CSi, *t*Bu), 13.2 (CH_3, Bu_4N^+), −5.6 (SiMe), −5.8 (SiMe). − IR (KBr): $\tilde{\nu}$ = 3465 (br.), 3285 (br.), 3100−2800, 1746, 1675, 1558, 1248 ($\nu_{C=O}$), 920 cm^{-1} (δ_{C-O-S}). − $C_{67}H_{102}N_2O_{16}SSi$: calcd. C 64.29, H 8.21, N 2.24; found C 63.57, H 8.01, N 2.16. − ESI-MS: calcd. for $C_{51}H_{66}NNa_2O_{16}SSi$ [M + Na] 1054.4; found 1054.2; calcd. for $C_{51}H_{67}NNaO_{13}Si$ [M + H − SO_3] 952.4; found 952.2. − [α] = −24 (CH_2Cl_2, *c* = 1.89).

Preparation of the Benzylated Disaccharide 16: A suspension of NaH (60% in oil, 38 mg, 0.95 mmol, 1.1 equiv.) in anhydrous DMF (1 mL) was added dropwise over a period of 1 h to a cooled solution (0°C) of compound **1** (800 mg, 0.86 mmol) and BnBr (1 mL, 8.5 mmol, 10 equiv.) in DMF (1 mL). After stirring for 30 min at 0°C, the mixture was diluted with Et_2O (50 mL), washed with ice-cold aq. KH_2PO_4 (5%, 20 mL) and water (2 × 20 mL). The organic phase was dried ($MgSO_4$), filtered, and concentrated. Flash chromatography (petroleum ether/AcOEt, 7:3 to 1:1) of the residue afforded compound **16** (790 mg, 90%). − ^1H NMR (250 MHz, $CDCl_3$): δ = 7.450−7.150 (m, 22 H, arom.), 6.856 (d, 2 H, *J* = 9.0 Hz, *p*MBn), 5.600 (d, 1 H, *J* = 7.0 Hz, NH), 4.965 (dd, 1 H, *J* = 9.0, 8.0 Hz, H'_2), 4.945 (d, 1 H, *J* = 8.0 Hz, H_1), 4.940 and 4.850 (d, 1 H, *J* = 11.5 Hz, CH_2Ph), 4.802 (d, 1 H, *J* = 11.0 Hz, CH_2Ph), 4.800 (d, 1 H, *J* = 10.5 Hz, CH_2Ph), 4.672 (d, 1 H, *J* = 10.5 Hz, CH_2Ph), 4.633 (d, 1 H, *J* = 11.0 Hz, CH_2Ph), 4.565 (dd, 1 H, *J* = 11.0, 2.5 Hz, H_3), 4.505 (d, 1 H, *J* = 8.0 Hz, H'_1), 4.500, 4.470, 4.462, and 4.395 (d, 1 H, *J* = 11.5 Hz, CH_2Ph), 3.995 (d, 1 H, *J* = 2.5 Hz, H_4), 3.813 (dd, 1 H, *J* = 9.0, 2.5 Hz, H'_6), 3.790 (s, 3 H, OMe), 3.755 (dd, 1 H, *J* = 9.0, 2.5 Hz, $H'_{6'}$), 3.730 (t, 1 H, *J* = 9.5 Hz, H'_4), 3.692 (d, 1 H, *J* = 12.5 Hz, H_6), 3.612 (t, 1 H, *J* = 9.0 Hz, H'_3), 3.610 (br. s, 1 H, H_5), 3.560 (dd, 1 H, *J* = 12.5, 1.5 Hz, $H_{6'}$), 3.490 (ddd, 1 H, *J* = 11.0, 8.0, 7.0 Hz, H_2), 3.310 (dt, 1 H, *J* = 9.5, 2.5 Hz, H'_5), 1.927 (s, 3 H, Ac), 1.891 (s, 3 H, Ac), 0.834 (s, 9 H, *t*Bu), 0.000 (s, 6 H, 2 SiMe). − ^{13}C NMR: δ = 170.6, 169.1, 159.2, 138.9, 138.1, 137.5, 130.1, 129.5, 128.4−127.8, 127.2, 113.7, 101.5, 98.6, 82.8, 77.2, 75.7, 75.2, 75.0, 74.9, 73.5, 73.1, 70.8, 68.5, 61.8, 55.2 (C_2 and PhOMe), 25.8 (CH_3, *t*Bu), 23.7 (NHAc), 20.9 (OAc), 18.2 (CSi, *t*Bu), −5.2 (SiMe), −5.5 (SiMe). − IR

(KBr): $\tilde{\nu}$ = 3460 (br.), 3285 (br.), 3100−2800, 1747, 1651, 1564 cm^{-1}. − $C_{58}H_{73}NO_{13}Si$: calcd. C 68.28, H 7.21, N 1.37; found C 67.62, H 7.31, N 1.37. − [α] = −29 (CH_2Cl_2, *c* = 1.43).

Preparation of Library 17{1−2}: THF solutions of Bu_4NF (1 M, 440 μL, 0.440 mmol, 1.5 equiv.) and AcOH (1 M, 220 μL, 0.220 mmol, 0.75 equiv.) were added to a mixture of compound **15** (185 mg, 0.15 mmol) and **16** (151 mg, 0.15 mmol) in anhydrous THF (2 mL) in a polypropylene flask. The reaction mixture was stirred for 3 h at 20°C and then directly purified by LH-20 gel permeation chromatography, which allowed co-elution of the library members. The fractions containing the products were concentrated to quantitatively afford the library **17**{1−2} (306 mg). HPLC retention times: 8.40 and 16.25 min. − ^{1}H NMR (250 MHz, $CDCl_3/CD_3OD$, 8:2): δ = 7.400−7.150 (m, 19.5 H, arom.), 6.863 (d, 2 H, *J* = 10.5 Hz, *p*MBn), 4.900−4.200 (m, 12 H), 3.900−3.300 (m, 12 H, with 2 singlets at 3.650/3.643, 1:1), 3.110−2.960 (m, 3.9 H, N^+-CH_2), 1.830/1.762/1.738/1.728 (4 s, 5.8 H, 4 Ac), 1.590−1.380 (m, 4 H, $N^+-CH_2CH_2$), 1.270 (sext., 4 H, *J* = 9.0 Hz, CH_2CH_3), 0.856 (t, 6 H, *J* = 9.0 Hz, CH_2CH_3). − ^{13}C NMR: δ = 170.9/170.7 (50:50, C=O), 170.0/169.2 (53:47, C=O), 158.9/157.7 (49:51, COMe, *p*MBn), 138.6, 137.9, 137.7, 137.6, 137.4, 130.4, 129.4, 129.2, 129.1, 128.2−127.0, 113.4/113.2 (49:51, Ph, *p*MBn), 101.1, 100.8, 100.5, 99.4, 82.4/82.3 (51:49), 78.0, 77.6, 77.1, 76.8, 75.4, 75.3, 74.9, 74.7, 74.4, 74.2, 73.6, 73.0, 72.9, 72.6, 72.5, 70.3, 69.8, 68.4, 61.2, 60.2, 58.0 (CH_2N, Bu_4N^+), 54.8 (PhOMe), 52.0/51.7 (52:48, C_2), 23.2 (Bu_4N^+), 22.6/22.5 (57:43, NHAc), 20.3/20.2 (49:51, OAc), 19.1 (Bu_4N^+), 13.1 (CH_3, Bu_4N^+). − ESI-MS: calcd. for $C_{52}H_{59}NNaO_{13}$ [M + Na] 928.4; found 928.5; calcd. for $C_{45}H_{52}NNa_2O_{16}S$ [M + Na] 940.3; found 940.4.

Preparation of Library 18{1−2}: DMSO (210 μL, 3 mmol, 10 equiv.) was added dropwise to a cooled (−78°C) solution of oxalyl chloride (52 μL, 0.6 mmol, 2 equiv.) in CH_2Cl_2 (2 mL). After 15 min. at −78°C, a solution of compounds **17**{1−2} (311 mg, 0.3 mmol) in CH_2Cl_2 (1.5 mL) was added. The mixture was stirred for a further 15 min. at −78°C and then NEt_3 (418 μL, 3 mmol, 10 equiv.) was added. The mixture was allowed to warm to 0°C over a period of 3 h and then the reaction was quenched with MeOH (500 μL). The mixture was then concentrated and co-evaporated with toluene (10 mL). A solution of the residue in MeOH (2 mL) was passed through a Dowex 50X8 400 column (4.8 mL, Bu_4N^+ form). Elution with MeOH and further purification on LH-20 gave a mixture, which was co-evaporated with toluene (10 mL) and dried over P_2O_5 in vacuo. At this stage, HPLC analysis showed the presence of multiple products, probably aldehyde hydrates and hemiketals. The mixture was dissolved in anhydrous methanol (4 mL) and the solution was cooled to 0°C. Methanolic KOH (0.8 M, 1.63 mL, 1.3 mmol, 4.3 equiv.) and methanolic I_2 (0.4 M, 1.63 mL, 0.65 mmol, 2.15 equiv.) were then added. After stirring for 15 min at 0°C, the reaction was quenched with methanolic AcOH (1 M, 100 μL) and saturated aq. $Na_2S_2O_3$ was added until the iodine color no longer persisted. Silica gel (70−210 μm, 10 mL) was then added and the mixture was concentrated. The resulting powder was deposited on a 10 mL silica gel pad and eluted with CH_2Cl_2/MeOH (4:1, 100 mL). HPLC at this stage showed the presence of the expected oxidized compounds along with deacetylated products. The mixture was concentrated, co-evaporated with toluene (20 mL), and reacetylated with Ac_2O (1.5 mL) in pyridine (2.5 mL). After stirring overnight at 20°C, HPLC showed the presence of only two products. The reaction mixture was concentrated, co-evaporated with toluene (3 × 30 mL), and passed through a Dowex 50X8 400 column (7 mL, Bu_4N^+ form). Elution (MeOH) and purification on LH-20 in the usual manner allowed concomitant elution of the library members. The fractions containing the library were concentrated in the presence of silica gel (70−210 μm, 10 mL). The resulting powder was deposited on a silica gel pad (10 mL) and eluted with CH_2Cl_2/MeOH (95:5, 100 mL, then 90:10, 50 mL) to give library **18**{1−2} (290 mg, 92%). HPLC retention times: 9.20 and 17.60 min. − ^{1}H NMR (250 MHz, $CDCl_3/CD_3OD$, 8:2): δ = 7.400−7.150 (m, 19.5 H, arom.), 6.860 (d, 2 H, *J* = 10.5 Hz, *p*MBn), 5.045 (t, 0.5 H, *J* = 8.5 Hz, H'_2 of the sulfated compound), 5.010 (t, 0.5 H, *J* = 8.5 Hz, H'_2 of the benzylated compound), 4.920−4.450 (m, 11 H), 4.375 (d, 0.5 H, *J* = 11.5 Hz, CH_2Ph of the benzylated compound), 4.273 (d, 0.5 H, *J* = 11.5 Hz, CH_2Ph of the benzylated compound), 4.250−4.100 (m, 4 H, contains MeOH signal), 4.050−3.800 (m, 4.5 H), 3.800−3.450 (m, 8.6 H, with 3 singlets: 3.780 PhOMe, 3.706/3.674 COOMe), 3.450−3.350 (m, 1 H), 3.230−2.080 (m, 4.4 H, N^+-CH_2), 1.985/1.968/1.901/1.890 (4 s, 6.3 H, 4 Ac), 1.700−1.500 (m, 4 H, $N^+-CH_2CH_2$), 1.396 (sext., 4 H, *J* = 7.0 Hz, CH_2CH_3), 0.990 (t, 6 H, *J* = 7.0 Hz, CH_2CH_3). − ^{13}C NMR: δ = 171.8/171.4/171.1/169.9/169.8/168.6 (6 C=O), 159.0/158.9 (52:48, COMe, *p*MBn), 138.2, 137.5, 137.4, 137.3, 137.2, 137.1, 130.0, 129.7, 129.4, 129.3, 128.6, 128.2−127.3, 113.5/113.4 (54:46, Ph, *p*MBn), 101.7, 101.3, 98.91, 81.6, 81.1, 79.2, 78.6, 78.3, 77.2, 75.1, 74.9, 74.8, 74.5, 74.2, 73.8, 73.4, 73.2, 72.9, 72.8, 72.5, 72.4, 70.3, 70.2, 69.5, 69.4, 68.6, 60.4, 58.3, 54.9/54.8 (52:48, PhOMe), 53.9 (NCH_2, Bu_4N^+), 53.4 (C_2), 52.6 (COOMe), 52.2 (C_2 and COOMe), 23.4 (Bu_4N^+), 22.7/22.6 (56:44, NHAc), 20.4/20.3 (45:55, OAc), 19.3 (Bu_4N^+), 13.1 (CH_3, Bu_4N^+). − ESI-MS: calcd. for $C_{53}H_{59}NNaO_{14}$ [M + Na] 956.4; found 956.5; calcd. for $C_{46}H_{52}NNa_2O_{17}S$ [M + Na] 968.3; found 968.4.

Preparation of Library 19{1−2}: DDQ (47 mg, 0.2 mmol, 1.5 equiv.) was added to a stirred mixture of **18**{1−2} (142 mg, 0.135 mmol) in CH_2Cl_2 (1.5 mL) and H_2O (300 μL) in a flask protected from light. After 1.5 h at 20°C, MeOH (1 mL) was added and the resulting homogeneous solution was purified on LH-20 to give the deprotected compounds (109 mg). DMF (1 mL) was then added and the resulting solution was transferred to a screw-capped tube. Then, $NMe_3 \cdot SO_3$ (100 mg, 0.72 mmol, 6 equiv.) was added. After stirring for 3 h at 60°C, MeOH (250 μL) was added, and the resulting mixture was applied to the top of an LH-20 column. Once again, the library members were eluted together. The collected fractions containing the library were concentrated with silica gel (70−210 μm, 10 mL). The resulting powder was deposited on a 10 mL silica gel pad and eluted with CH_2Cl_2/MeOH (9:1, 100 mL). The collected fractions were concentrated, diluted with MeOH, and passed through a Dowex 50X8 400 column (7 mL, Bu_4N^+ form). Elution (MeOH) gave **19**{1−2} (138 mg, 81% overall yield). HPLC retention times: 8.05 and 11.15 min. − ^{1}H NMR (250 MHz, CD_3OD): δ = 7.500−7.150 (m, 17.5 H, arom.), 5.040−4.850 (m, 4.5 H, contains MeOH signal), 4.850−4.500 (m, 4 H), 4.050−3.800 (m, 9.2 H), 4.500−4.280 (m, 2.2 H), 4.230−4.000 (m, 3.7 H), 4.000−3.900 (m, 1.7 H), 3.900−3.610 (m, 7.1 H, contains 2 singlets: 3.746/3.739, 52:48 COOMe), 3.280−3.130 (m, 14.9 H, N^+-CH_2), 1.988/1.937/1.930/1.912 (4 s, 6.9 H, 4 Ac), 1.720−1.550 (m, 14.9 H, $N^+-CH_2CH_2$), 1.404 (sext., 15 H, *J* = 7.0 Hz, CH_2CH_3), 1.015 (t, 21 H, *J* = 7.0 Hz, CH_2CH_3). − ^{13}C NMR: δ = 173.1/173.0/171.4/171.1/170.4/170.3 (6 C=O), 140.1, 139.6, 139.5, 139.4, 139.2, 139.1, 130.0, 129.4−128.5, 103.3/103.1/102.1/101.9 (31:22:24:24, C_1 and C'_1), 83.6, 83.1, 81.0, 80.9, 80.4, 77.9, 76.8, 76.4, 76.2, 76.1, 75.9, 75.8, 75.7, 75.5, 75.3, 74.9, 74.0, 71.6/71.4 (51:49), 70.0, 67.3, 59.4, 59.3 (NCH_2, Bu_4N^+), 53.2 (COOMe), 53.0 (2 C_2 and COOMe), 24.8 (Bu_4N^+), 23.3/23.2 (55:45, NHAc), 21.2/21.1 (50:50, OAc), 20.7 (Bu_4N^+), 14.0 (CH_3, Bu_4N^+). − ESI-MS: calcd. for $C_{45}H_{50}NO_{16}S$ [M − Na] 892.3; found 892.3; calcd. for $C_{38}H_{43}NO_{19}S_2$ [M − 2 Na]$^{2-}$ 440.6; found 440.5.

Library 20{1−4} was prepared by mixing **18**{1−2} (92 mg, 0.088 mmol) and **19**{1−2} (110 mg, 0.088 mmol).

Preparation of Library 23{1−4}: Anhydrous K_2CO_3 (11 mg, 0.078 mmol, 1 equiv.) was added to a solution of library **20**{1−4} (90 mg, 0.078 mmol) in anhydrous methanol (1.5 mL). The reaction mixture was stirred for 3 h at 20°C, neutralized with Dowex 50X8 200 (H^+ form), filtered, and passed through a Dowex 50X8 400 column (7 mL, Bu_4N^+ form). Elution (MeOH) and purification on an LH-20 column gave the 2′-*O*-deacetylated library **21**{1−4} (85 mg). HPLC retention times: 8.90, 12.00, 12.50, and 19.05 min; for ^{1}H-NMR integration analyses, see Table 1.

$NMe_3{\cdot}SO_3$ (80 mg, 0.57 mmol, 7.5 equiv.) was added to a solution of **21**{1−4} (85 mg) in anhydrous DMF (600 μL). The mixture was stirred for 24 h at 60°C and then the reaction was quenched with MeOH (200 μL). The resulting mixture was first purified on an LH-20 column and then subjected to cation-exchange on a Dowex 50X8 400 column (7 mL, Bu_4N^+ form). Elution (MeOH) gave the 2′-*O*-sulfated products **22**{1−4} (110 mg). HPLC retention times: 6.85, 8.40, 8.90, and 12.00 min; for ^{1}H-NMR integration analyses, see Table 1. − ^{13}C NMR ($CDCl_3$): δ = 174.0/173.8/173.7/172.0/171.8/171.3/171.2 (C=O), 160.7/160.6 (54:46, COMe, *p*MBn), 140.4, 140.3, 140.1−140.0 (4 peaks), 139.7, 139.5, 139.4, 139.3−139.2 (4 peaks), 131.9, 131.3, 130.7, 130.5, 130.4, 129.7−128.2, 114.7/114.6 (59:41, Ph, *p*MBn), 102.4/102.0 (broad peaks, C_1 and C'_1), 83.8, 83.7, 80.5, 80.0, 78.9, 78.7, 78.5, 78.4, 77.6, 77.4, 77.3, 76.9, 76.7, 76.6, 76.1, 75.9, 75.7, 75.6, 75.5, 75.3, 75.2, 74.8−74.6 (4 peaks), 74.2, 73.9, 73.8, 73.1, 73.0, 71.8, 71.5, 71.4, 70.1, 69.5, 66.9, 59.4 (CH_2N, Bu_4N^+), 55.7 (PhOMe), 54.3/54.2/53.0/52.8/52.7 (4 C_2 and COOMe), 24.6 (Bu_4N^+), 23.5 (NHAc), 20.6 (Bu_4N^+), 14.0 (CH_3, Bu_4N^+).

Library **22**{1−4} was dissolved in THF/H_2O (1:1, 4 mL) and aq. NaOH (2 M, 800 μL) was added. After stirring for 2 h at 20°C, the pH was lowered to 7 with Dowex 50X8 200 (H^+ form). The resulting mixture was then filtered, concentrated, and passed through a Dowex 50X8 400 column (7 mL, Bu_4N^+ form). Elution (MeOH) followed by LH 20 chromatography gave library **23**{1−4} (105 mg, 80% overall yield). HPLC retention times: 18.30, 20.05, 21.10, and 24.45 min. − ^{1}H NMR (250 MHz, CD_3OD): δ = 7.450−7.100 (m, 18.5 H, arom.), 6.920−6.830 (m, 1 H, *p*MBn), 5.210−5.230 (m, 0.4 H), 5.150−4.750 (m, 8.8 H, contains MeOH signal), 4.750−4.400 (m, 8.1 H), 4.400−3.420 (m, 12.5 H, contains 2 singlets: 3.768/3.740, PhOMe), 3.260−3.100 (m, 21.0 H, N^+-CH_2), 2.040/2.035/1.950/1.935 (4 s, 3.4 H, 4 Ac), 1.700−1.520 (m, 22.0 H, $N^+-CH_2CH_2$), 1.392 (sext., 22.0 H, *J* = 7.0 Hz, CH_2CH_3), 1.000 (t, 30.5 H, *J* = 7.0 Hz, CH_2CH_3). − ^{13}C NMR: δ = 174.3/174.2/173.9/173.8/173.7/173.5/172.6/172.5 (8 C=O), 160.8/160.7 (58:42, COMe, *p*MBn), 140.5, 140.4, 139.8−139.6 (5 peaks), 139.5, 139.4, 139.3, 139.2, 131.8, 131.4, 130.6, 130.5, 130.0, 129.6−128.2, 114.8/114.7 (54:46, Ph, *p*MBn), 103.0/102.6/101.9/101.8/101.7/101.0/100.4 (C_1 and C'_1), 83.8, 83.7, 81.5, 81.2, 80.7, 80.5, 80.3, 80.0, 79.3, 78.9, 77.6, 77.5, 77.4, 77.0, 76.8, 76.1, 75.8, 75.2, 75.1, 75.0, 74.9, 74.4, 74.0, 73.9, 73.5, 71.8, 71.4, 71.3, 69.9, 69.8, 67.4, 59.4 (CH_2N, Bu_4N^+), 55.7 (PhOMe), 54.7/54.5/53.1/52.9 (27:27:25:20, C_2), 24.7 (NCH_2, Bu_4N^+), 23.5 (NHAc), 20.7 (Bu_4N^+), 14.0 (CH_3, Bu_4N^+).

Preparation of Library 24{1−4}: Library **20**{1−4} was saponified as described above using aq. NaOH (2 M, 800 μL in THF/H_2O, 1:1, 4 mL), although in this case the reaction required 30 h stirring at 20°C to reach completion. After purification as above, library **24**{1−4} was obtained (118 mg, 98%). HPLC retention times: 7.05, 8.60, 9.10, and 12.20 min. − ^{1}H NMR (250 MHz, CD_3OD): δ = 7.500−7.150 (m, 18.5 H, arom.), 6.920−6.830 (m, 1 H, *p*MBn), 5.050−3.950 (m, 26.8 H, contains MeOH signal), 3.950−3.390 (m, 9.5 H, contains 1 singlet at 3.760, PhOMe), 3.300−3.140 (m, 17.1 H, N^+-CH_2), 1.958/1.912 (2 s, 3.6 H, 4 Ac), 1.740−1.550 (m, 17.1 H, $N^+-CH_2CH_2$), 1.410 (sext., 17.1 H, *J* = 7.5 Hz, CH_2CH_3), 1.015 (t, 23.8 H, *J* = 7.5 Hz, CH_2CH_3). − ^{13}C NMR: δ = 174.3/173.5/173.2/172.9/172.7/172.3 (23:27:11:13:14:13, 8 C=O), 160.7 (COMe, *p*MBn), 140.3, 140.24, 140.20, 140.1, 139.5, 139.1, 139.0, 131.7, 131.2, 130.6, 129.8−128.6, 114.7/114.6 (51:49, Ph, *p*MBn), 106.8/106.6/103.9/103.8/102.0/101.9 (13:13:13:12:27:22, 4 C_1 and 4 C'_1), 85.2, 85.0, 82.6, 82.2, 80.8, 80.6, 80.2, 80.1, 77.0, 76.9, 76.7, 76.6, 76.1, 75.8, 75.7, 75.1, 74.8, 74.6, 74.3, 74.2, 73.9, 73.8, 71.7, 71.6, 71.5, 71.4, 70.0, 69.5, 67.8, 59.3 (CH_2N, Bu_4N^+), 55.7 (PhOMe), 53.2/53.1/53.0/52.9 (28:27:22:23, C_2), 24.7 (Bu_4N^+), 23.2 (NHAc), 20.6 (Bu_4N^+), 14.1 (CH_3, Bu_4N^+).

Preparation of Library 2{1−4}: A suspension of $Pd(OH)_2$ (20% on carbon, 105 mg) and compounds **23**{1−4} (105 mg, 0.063 mmol) in MeOH/H_2O (1:1, 4 mL) was stirred for 24 h under H_2 (1 atm.), the pH being continuously adjusted to 7 by the addition of aq. NaOH (0.1 M). The mixture was then filtered through a Celite 545 pad (1 mL). Elution (MeOH/H_2O, 1:1, then water) gave a solution, which was partially concentrated and passed successively through columns of Dowex AG 50WX8 200 (2 mL, Na^+ form) and biobeads SX2 (2 mL), both of which were eluted with water. The resulting aqueous solution was lyophilized to quantitatively afford the library **2**{1−4} (40 mg). − ^{13}C NMR (D_2O): δ = 176.2/176.0/175.3/175.2/175.1/174.9/174.7 (C=O), 102.2/101.9/101.4/101.1/101.0/95.7/95.1/91.5/91.3/91.2/91.1/91.0 (C_1 and C'_1), 80.2, 80.1, 79.9, 77.3, 77.2, 77.0, 76.9, 76.6, 76.3, 76.2, 75.3, 75.0, 74.8, 74.6, 74.4, 72.8, 72.7, 72.6, 71.7, 71.6, 70.7, 70.5, 68.7, 68.5, 68.4/68.3/68.0 (sulfated C_6), 67.8, 67.7, 67.5, 67.4, 61.5−61.2 (5 peaks: non-sulfated C_6), 53.6/53.4/52.6/52.4 (22:26:26:26, C_2b), 49.7/49.6/49.4/49.3 (21:24:28:28, C_2a), 22.7/22.6/22.5/22.3 (NHAc). − For HPTLC and ESI-MS characterization after neoglycolipid conjugation, see Table 3.

Preparation of Library 3{1−4}: A suspension of $Pd(OH)_2$ (20% on carbon, 110 mg) and library **24**{1−4} (110 mg, 0.082 mmol) was stirred for 24 h under H_2 (1 atm.), the pH being continuously adjusted to 7 by the addition of aq. NaOH (0.1 M) as described above. In this case, the reaction needed 60 h stirring at 20°C to reach completion. After purification, library **3**{1−4} was obtained (41 mg, 96%). − ^{13}C NMR (D_2O): δ = 176.3/175.2/174.9 (C=O), 104.3/104.1/103.5/103.5/95.4/95.4/95.2/91.5/91.4 (C_1 and C'_1), 80.7, 80.4, 77.8, 77.6, 77.5, 77.3, 76.6, 76.4, 75.6, 75.4, 75.2, 74.7, 73.0, 72.7, 72.5, 72.0, 70.5, 70.4, 68.7, 68.5, 68.4/68.3/68.2/68.0 (sulfated C_6), 67.9, 67.8, 61.5/61.4/61.3 (non-sulfated C_6), 53.0/52.9/52.5/52.4 (27:20:31:22, C_2b), 49.7/49.6/49.1/49.0 (23:24:28:25, C_2a), 22.5/22.3 (NHAc). − For HPTLC and ESI-MS characterization after neoglycolipid conjugation, see Table 3.

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